



Nanobiotech in Holistic Health:

Innovations for Integrated
Well-being

Editors

Zaib un Nisa
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PREFACE

The 21st century has ushered in an era of profound scientific advancement where the boundaries between disciplines blur to create transformative innovations. Among these, nanotechnology and biotechnology have emerged as powerful, synergistic tools shaping the future of medicine, agriculture, environmental sustainability, and overall human and animal well-being. *Nanobiotech in Holistic Health: Innovations for Integrated Well-being* is an ambitious and timely compilation that highlights the convergence of these two fields and their potential to foster integrated solutions for health and sustainability challenges. This book reflects the diversity and depth of nanobiotechnology by bringing together contributions that span the spectrum from basic research to applied science. It opens with compelling insights into how nanotechnology can revolutionize precision agriculture and enhance food security, while addressing the toxicological safety of nanoparticles. It then explores cutting-edge therapeutic applications such as the use of mesenchymal stem cells for nerve injuries, nanoparticle-based treatments for cancer, respiratory disorders, and antimicrobial resistance, and regenerative medicine innovations that promise to redefine healthcare. The chapters also highlight emerging roles of nanoparticles in genetic engineering, genome editing, and drug delivery systems, illustrating their ability to target diseases with unprecedented precision and efficiency. Equally notable are the contributions on veterinary and environmental health—ranging from controlling vector-borne diseases of animals, treating bovine mastitis, and enhancing poultry nutrition, to addressing plant pathogens and supporting wildlife conservation. The book even extends to futuristic topics such as lab-grown meat, CRISPR technologies in cancer therapy, biosensors for diagnostics, and circular economy approaches for biomass conversion. What makes this book unique is its holistic perspective. Rather than viewing health in silos—human, animal, or environmental—these chapters collectively embrace the One Health philosophy, recognizing that well-being is a product of the interconnected health of all living systems. The integration of nanotechnology and biotechnology represents not just an academic pursuit, but a practical and visionary pathway toward sustainable, resilient, and equitable health solutions for the planet. We extend our deepest appreciation to **Unique Scientific Publishers** for their unwavering support, foresight, and commitment to advancing interdisciplinary scholarship. Their efforts in fostering and disseminating knowledge have been instrumental in making this book a reality. Their dedication to academic excellence and global scientific collaboration is evident in the quality and scope of this publication. It is our hope that *Nanobiotech in Holistic Health: Innovations for Integrated Well-being* serves as both a comprehensive resource and a source of inspiration for scientists, clinicians, students, policymakers, and innovators alike. May it stimulate collaboration across fields, spark new research questions, and guide meaningful applications of nanobiotechnology in service of a healthier and more sustainable future for all.

Editors

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Role of Nanotechnology for Precision Agriculture and Food Security

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Abstract

Nanotechnology in precision agriculture provides answers for understanding agriculture's complex difficulties and ensuring food security. Nanotechnology is the use of small-scale materials to improve agricultural practices. Nanotechnology enables farmers to optimize resource utilization such as water and fertilizers resulting in enhanced agricultural productivity. Nano fertilizers provide nutrients to plants more rapidly than conventional fertilizers, resulting in enhanced plant development. Nanotechnology in agriculture is the source of nanopesticides. The nano insecticides compared to traditional pesticides fast action and minimum harm to environment. Nanosensors are a crucial component of precision irrigation system showcasing the significant contribution of nanotechnology in this field. The nanosensors helps farmers to monitor and control water consumption and prevent loss of natural resources. Nanotechnology aids in the precise delivery of water to agriculture. Challenges and ethical considerations must be considered. Nanomaterials may affect humans, animals, natural resources, and the environment. To use them safely, they must be checked. Additionally, everyone must grasp the benefits and risks of nanotechnology in agriculture. Nanotechnology can improve agriculture yields, food security, and environmental sustainability. Nanotechnology and problem-solving can help us create a more secure and efficient food system for everyone.

Keywords: Food security, Food safety, Bio fertilizers, Nanotechnology

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Introduction

To optimize profit, the farming community consistently prioritizes reducing the cost of agricultural inputs. Farmers use fungicides, herbicides, and fertilizers to maximize crop productivity to accomplish this goal (Zhang et al., 2021). The third agricultural revolution, or the well-known "green revolution" of the 1950s and 1960s, has considerably increased agricultural output worldwide and slowed the spread of hunger and malnutrition. Nonetheless, the global population has grown by more than 5 billion since the start of the green revolution. The demographic census has alarmingly projected that by 2050, there will be around 9.60 billion people on earth (Zhang et al., 2021).

Numerous scientific disciplines, including physics, chemistry, pharmaceutical science, material science, medicine, and agriculture, have used nanotechnology. Numerous opportunities in the area of agriculture were made possible by the encouraging outcomes in other domains (Amoatey et al., 2021). The EU Directorate-General for Internal Policies defines precision agriculture as a farming management concept that processes and responds to inter and intra-field crop variations to form a decision support system for whole farm management and maximize output from available resources. Nanotechnology in agriculture has enabled precision farming. Nanotechnology considers nanoparticles under 100 nm (Yadav et al., 2023).

Precision agriculture based on nanotechnology measures crop-based and environmental characteristics using computers, GPS, and remote sensing devices (Sivarethinamohan & Sujatha, 2021). The review looks at how precision agriculture, cloud computing, smartphone-based biosensors, and nanotechnology methods and devices can be used to tag, monitor, and track agricultural products. It also discusses the risks and legal, social, and economic ramifications of nanotechnology in agribusiness.

In addressing concerns of food security, environmental sustainability, and socioeconomic development, the chapter highlights the potential for nanotechnology to increase the productivity and efficiency of agricultural systems (Sahoo et al., 2023). As it plays a useful role we should also consider its drawbacks to the environment. The nano-technological solutions that seek to achieve sustainability in the food processing and agriculture sectors and also an eco-friendly way for sustainability (Khan et al., 2022).

Definition of Nanotechnology

Nanotechnology is a research and technology development at the atomic, molecular, and macromolecular level, helps with controlled manipulation as well study of structures and devices with dimension scales in the 1- to 100-nanometer range (Zehra et al., 2021).

3 Importance of Precision Agriculture

Precision agriculture (PA) is a multidisciplinary concept that uses information technology to increase agricultural output and quality. One of the most important and exciting areas of technology is wireless sensor networks (WSN). We collect, monitor, and analyze agricultural data using this technology. With the help of this interdisciplinary technology, agricultural productivity will rise without sacrificing quality thanks to features like crop strength assessment, insect and disease monitoring, and animal tracking (Kumar & Ilango, 2018). Precision agriculture integrates new technologies like Geographic Information Systems (GIS), Global Positioning Systems (GPS), and Remote Sensing (RS) to help farm producers manage within-field variability to increase the cost-benefit ratio. One of the main contribution of precision agriculture to achieve food security by enhanced and amplified food production (Calicioglu et al., 2019). Food security exists when everyone has physical, social, and economic access to enough safe, nutritious food to meet their dietary needs and live an active and healthy life. Applying this paradigm to agriculture may help us comprehend crop output restrictions and precision agriculture's solutions. This insight may help us develop effective food security solutions for future generations (Zehra et al., 2021).

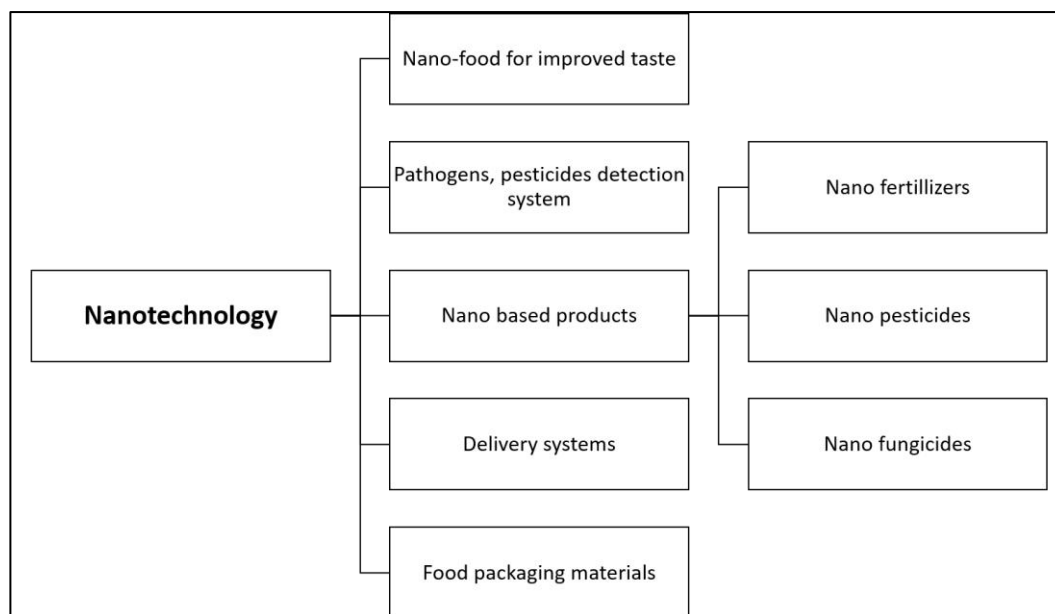


Fig. 1: Nanotechnology for the development of new tastes and textures, delivery of nutrients, pathogen detection or pesticide delivery systems, encapsulation of nutraceuticals and other agents, and food-packaging materials for safety

4 Current Challenges in Agriculture and Food Security

Climate change is affecting the world's weather and water conditions, causing shortages and droughts in some areas and disasters like cyclones and floods in others. The current rate of consumption will worsen the situation. By 2025, water shortages will affect two-thirds of the world's population, increasing the susceptibility of ecosystems (López-Vinent et al., 2020). Climate change will alter numerous agricultural productivity-critical environmental elements. An extensive multi-model assessment of global temperature increases indicated that agricultural droughts increase by 22% in duration and 51% in frequency under a +3°C scenario. Both indexes increased 6.5% and 9.4% from preindustrial values from 1981 to 2010. Runoff rises by 25% but lowers by -20% due to more severe weather events (Seppelt et al., 2022).

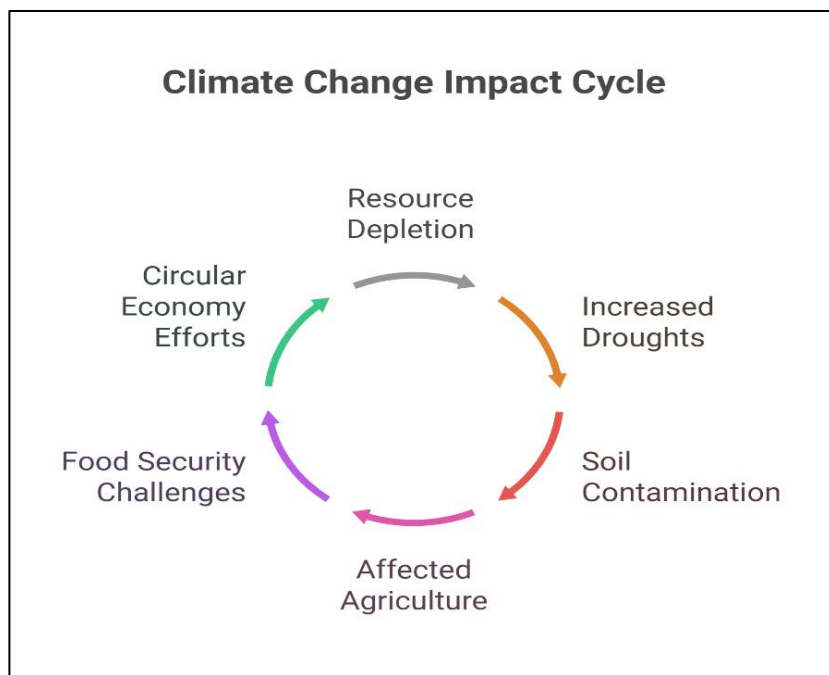
Agriculture uses more water than any other industry, yet excessive and careless use leads to significant water loss. The soil is the topmost layer of the ground that is capable of supporting life. One of the largest threats to the environment and human health is soil contamination (Amoatey et al., 2021). Due to water scarcity, treating wastewater may boost soil fertility in dry and semi-arid regions of the world. However, the wastewater effluent can contaminate the soil environment and subsequently, plant metabolism and groundwater quality can be negatively impacted, ultimately affecting human health (Pereira & Cunha Marques, 2020).

Bacterial populations, harvest season, photosynthesis, and harvest respiration will vary with global warming. It converts organic nutrients to inorganic ones and lowers fertilizer efficiency. It also increases soil evapotranspiration, depleting natural resources (Periakaruppan et al., 2023). The circular economy concept seeks to maximize resource allocation efficiency in a semi-closed system to generate more outputs from fewer inputs and maintain growth (Panwar et al., 2021). The issue of food security demands the ability to deal with escalating food shortages for a world population that is constantly expanding. With an estimated 1.7 billion more people on the planet by the year 2050, humanity is placing growing pressure on the finite resources needed to produce our food (Bleeker et al., 2023).

5 Role of Nanotechnology in Addressing Challenges

Nanotechnology can produce foods of exceptional quality in a much more enhanced and practical form, with increased nutritional bioavailability. The increased use of nanotechnology in crop production and food processing is the subject of several research studies (Qureshi et al., 2023). Nanotechnology is one of the most promising fields for increasing food availability and producing new goods with positive impacts on the environment, energy, food, medicine, electronics, and water. With novel and unique uses in agricultural and food research, it is a rapidly emerging and expanding area (Sadeghi et al., 2017). Reducing the amount of pesticides sprayed, minimizing nutrient losses during fertilization, and increasing output via pest and nutrient management are a few areas where nanomaterials in agriculture are emerging. The use of nanotechnology is also playing a role in water conservation (Ulusoy, 2023).

Fig. 2: Impact of climate



6 Fundamentals of Nanotechnology

Nanotechnology refers to the process of creating and manipulating structures, tools, and systems by monitoring their size and shape at the nanometer scale, which ranges from 1 to 100 nm as in figure 3. Just to clarify, a nanometer is equal to one-billionth (10 to 9) of a meter. It suggests that the technology is being used on a very small scale. Nanoscience and nanotechnologies are regarded as creative approaches in developmental study that focus on understanding and manipulating the behavior of matter at the atomic, molecular, or macromolecular levels. At this scale, the characteristics of substances differ significantly from those seen at larger scales (Madkour & Madkour, 2019).

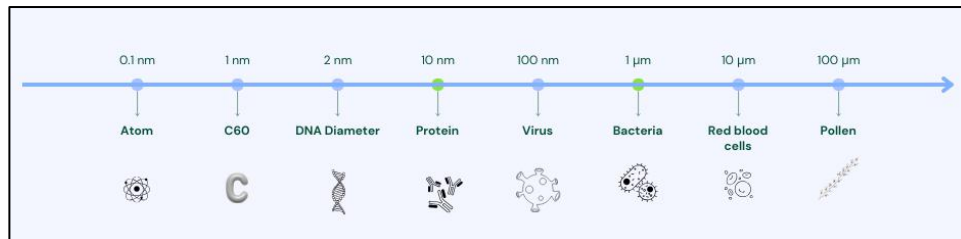


Fig. 3: A pictorial exhibition of things in the “Nano” (<100 nm) and “micro” (>100 nm) size ranges. Where DNA: Deoxyribonucleic acid, C60: Carbon 60.

6.1 Nano-scale Materials and Properties

Nanomaterials are substances that have at least one dimension in the nanoscale range, typically between 1 and 100 nm. Within this size range, the properties of a material tend to differ from its larger-scale counterparts. Nanomaterials can take various forms, including nanoparticles, nanotubes, nano-capsules, nano-spheres, nano-fibers, nano-films, nano-layers, nano-composites, nano-coatings, and nano-sensors (Marcuello et al., 2023). The distinctive characteristics of inorganic nanoparticles frequently arise from their diminutive size, which is less than the mean free path of their electrons (10–100 nm) or the average distance an electron travels before being scattered (scattering length) (Hunyadi Murph et al., 2017). At this particular size, electrons are restricted inside one, two, or three dimensions, and the properties of matter are primarily influenced by quantum mechanical phenomena (Balusamy et al., 2023).

6.2 Nanomaterial in Agriculture

Nanotechnology has shown significant promise in advancing sustainable agriculture. The current advancements in the use of nanotechnology in agriculture mostly focus on enhancing crop productivity and protection as mentioned in figure 5. This involves cleaning up contaminated soils with nano-enabled devices, nano-pesticides, nano-fertilizers, and nano-biosensors. Nanomaterials are essential to many biological and non-biological remediation techniques and play a critical role in determining the fate, mobility, and harmfulness of soil pollutants (Kumar et al., 2023).

6.2.1 Nano Fertilizers

Nano fertilizers improve agricultural. Like vitamins for people, they help plants grow by providing nutrients. Regular fertilizers might waste valuable substances in the air or water. Nano fertilizers keep nutrients where they're needed. They can gently release nutrients, helping plants grow consistently. Nano fertilizers increase crop growth by 18-29%, according to studies. Thus, they may improve farming efficiency and sustainability (Husen & Siddiqi, 2023).

Nano fertilizers aid plants and contain plant nutrients or are nutrients themselves. They ensure crops get what they need for optimal growth without wasting resources. Regular fertilizers may be more expensive and harmful. Nano fertilizers are smart because they store nutrients near plants and release them when needed. Nano fertilizers boost plant health. Recent studies show that nano fertilizers produce crops better than conventional fertilizers, which is great for farmers and the environment (Devi et al., 2023).

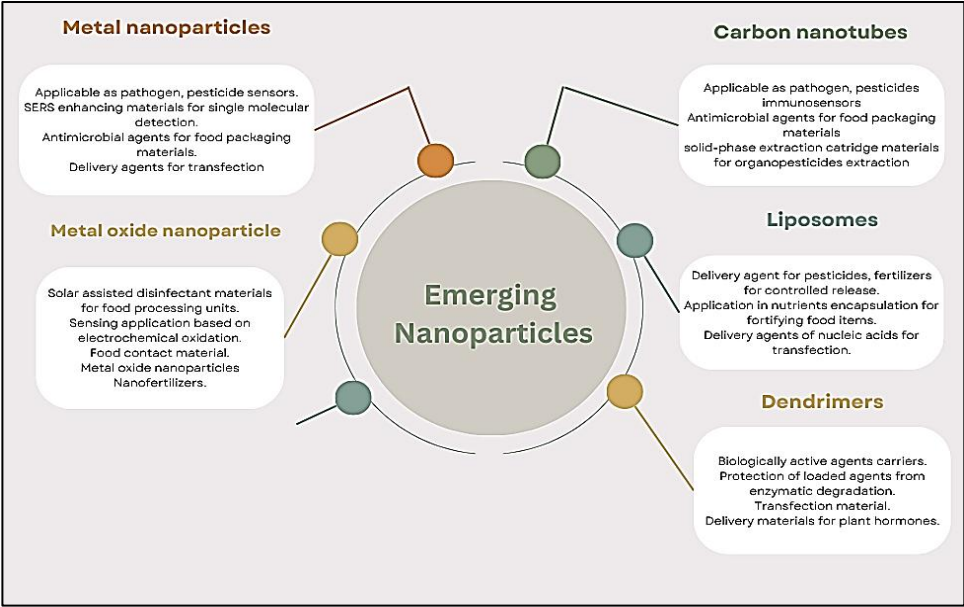


Fig. 4: Major emerging nanomaterials used in agriculture, food, and environment sectors. Graphics of metal nanoparticles, metal oxide nanoparticles, carbon nanotubes, liposomes, and dendrimers are shown along with their potential applications.

6.2.2 Nano Pesticides and Nano Herbicides

Nano pesticides are the solution to overcome the challenges caused due to conventional pesticides in agriculture. Traditional pesticides often cause environmental contamination. These contribute to the development of resistance to pests. It causes risks to humans and the ecosystem (Channab et al., 2024). Nano pesticides provide a targeted and appropriate approach to control pests. In this way it reduced environmental impact, improved efficacy, and improved crop productivity (He et al., 2019).

These Nano-sized preparations act differently from conventional pesticides (Rani et al., 2023). They can decrease the amount and frequency of pesticide application. In this how it is conserving energy and water resources. Additionally, Nano pesticides show better solubility of active ingredients and minimize environmental harm as compared to other chemical pesticides (Yadav et al., 2021).

Nano pesticides against a wide range of pests, including insects, fungi, and weeds. For example, Nano formulations of insecticides like Imidacloprid and permethrin has more efficacy and less environmental impact other than conventional formulations. Similarly, Nano pesticides based on silver, copper, and aluminum shows antimicrobial ability (Xu et al., 2022). Polymeric encapsulated Nano herbicides are far better than conventional herbicides as offer improved efficiency and decrease mobility in soil (Shekhar et al., 2021). The potential health and environmental impacts of Nano pesticides also exist. Nanoparticles can cause hazards to non-target organisms and can kill them. The long-term effects of nanoparticles need thorough evaluation. A detailed risk assessment is necessary to distinguish safe and beneficial forms of Nano pesticides (Dangi & Verma, 2021).

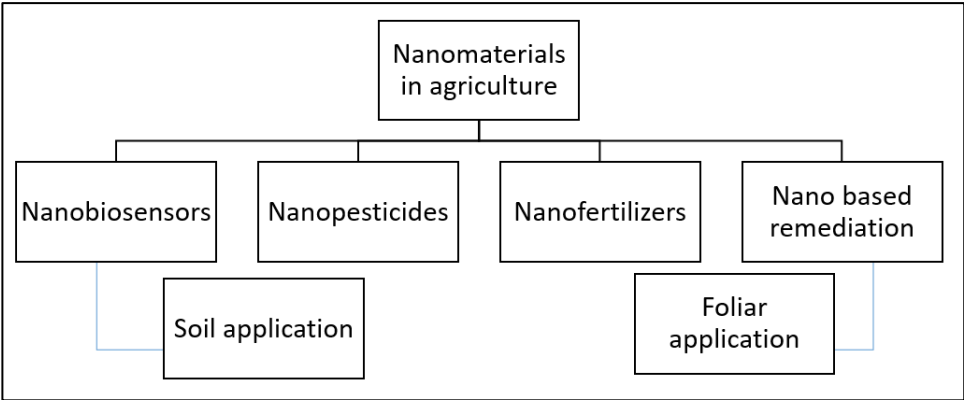


Fig. 5: Nanotechnology's role in agriculture

7 Precision Irrigation

7.1 Evolution of Precision Agriculture (PA)

Precision agriculture (PA) has played a role as a strategic approach to managing variability in farming operations. It has revolutionized agricultural practices since its application in the 1980s (Zurmotai, 2020).

7.2 Integration of GPS and GIS

In the 1980s the advent of the Global Positioning System and Geographic Information System technologies played a significant role (Espig et al., 2020). These technologies have enabled farmers for precise spatial planning and management of agricultural activities (Horstrand et al., 2019).

7.3 Early Applications and Challenges

At beginning applications of PA focused on site-specific operations. Fertilizers application as well as seed selection are the few examples (Espig et al., 2020). The primary obstacles were the limited integration of data and the inadequacy of decision support tools which resulted in decreasing efficacy (Zurmotai, 2020).

7.4 Integration of On-Board Sensor Systems

The integration of onboard sensor systems with computing platforms is used in it. It enabled data collection and modifications to agricultural equipment. In this how many systems are built to improve agriculture against environmental issues (Zurmotai, 2020).

7.5 Enhanced Decision-Making with Biophysical Insights

Precision agriculture solutions use algorithms and biophysical for optimizing agricultural practices. For example variable rate use of fertilizers and spatially variable irrigation management. These are all now based on dereferenced soil sampling and satellite sensor fusion, increasing precision and efficiency (Channab et al., 2024).

7.6 Diverse Stakeholders and Data Sources

Precision agriculture services have a diverse array of stakeholders, from government organizations to private providers and farmer cooperatives (Abioye et al., 2020). Data acquisition sources are public domain to privately held data. Data acquisition requires collaboration and addressing challenges around data standards, sharing them, and ownership (Zurmotai, 2020).

7.7 Nano-scale Water Sensors

Nanosensors are very small platforms designed to get information about measurement and detection at the nanoscale. They can detect biological, chemical, environmental, as well as physical factors. These sensors require the unique characteristics of nanoparticles, such as their surface area-to-volume ratio. This makes them ideal for sensing applications. Nanosensors are used in many areas such as medical diagnostics, food quality sensing, and monitoring water quality having components mentioned in figure 7 (Sadeghi et al., 2024).

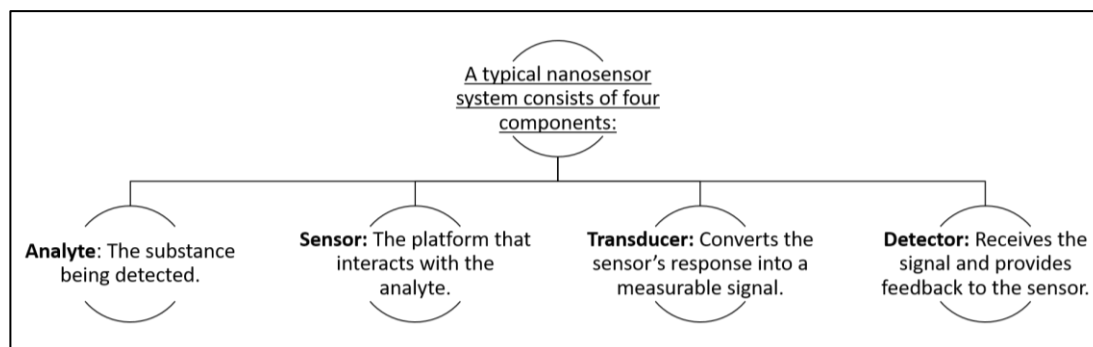


Fig. 6: Components of Nanosensors system

For example, carbon nanotube-based sensors work by detecting changes in conductivity. When specific molecules (e.g., nitrogen dioxide or ammonia) are present, they alter the nanotube's conductivity (Gupte & Pradeep, 2022).

8 Nanotechnology for Food Safety and Preservation

The rapid development of nanotechnology has transformed many domains of food science, especially those that involve the processing, packaging, storage, transportation, functionality, and other safety aspects of food as shown in figure 9.

A wide range of nanostructured materials (NSMs), from inorganic metal, metal oxides, and their nanocomposites to nano-organic materials with bioactive agents, has been applied to the food industry (Ioannou et al., 2020).

8.1 Nanosensors for Food Contaminant Detection

Nanotechnology as a food sensor platform can identify contaminants, notably for food safety and quality applications. Nanomaterial-based chemical and biosensors can be employed online and incorporated into industrial processes and distribution lines as quick, easy, portable, and disposable food contamination sensors (Kuswandi et al., 2017). Pesticide residues, human and veterinary medication residues, microbiological toxins, preservatives, pollutants from food processing and packaging, and other residues can all be found in food.

With their innovative applications, Nanosensors are a new technique that has the potential to identify a wide range of food pollutants, including mycotoxins and several food allergies. The Nanosensors may be combined with wireless technology and utilized online or offline to transmit test findings or contamination warnings in real time to distant servers, enabling quick screening and reporting (Patel et al., 2020).

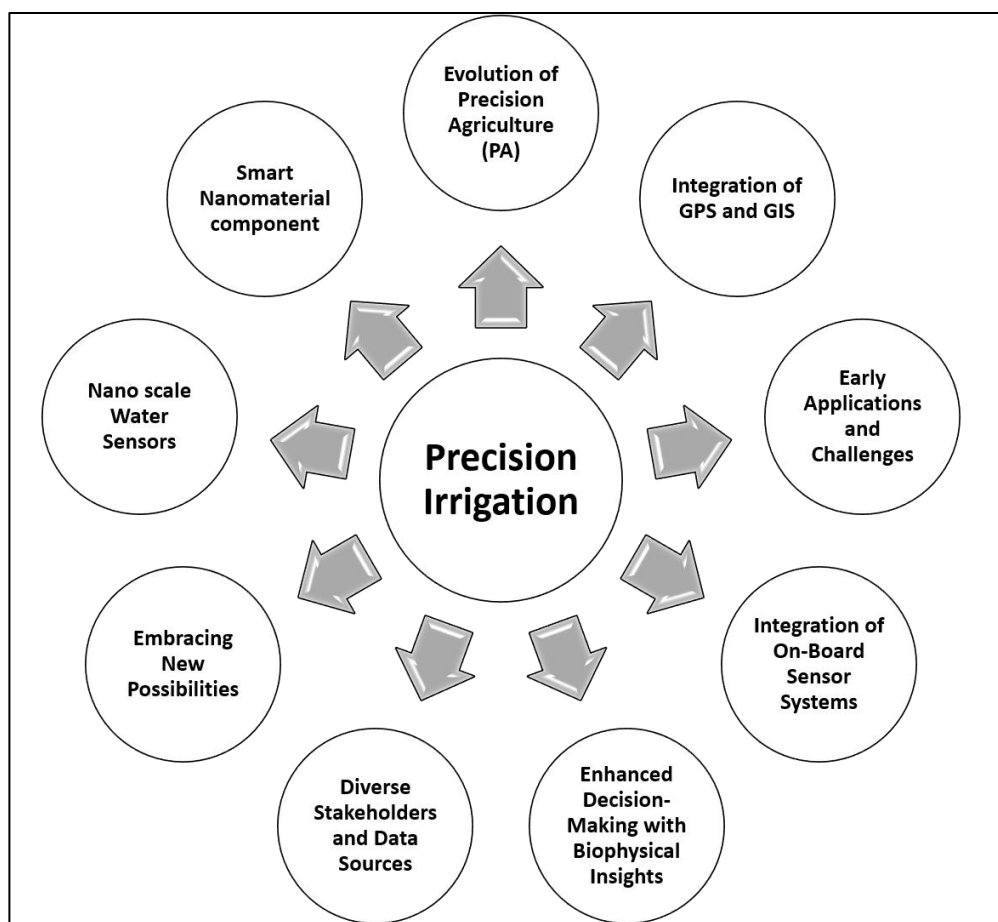


Fig. 7: Precision Irrigation methods

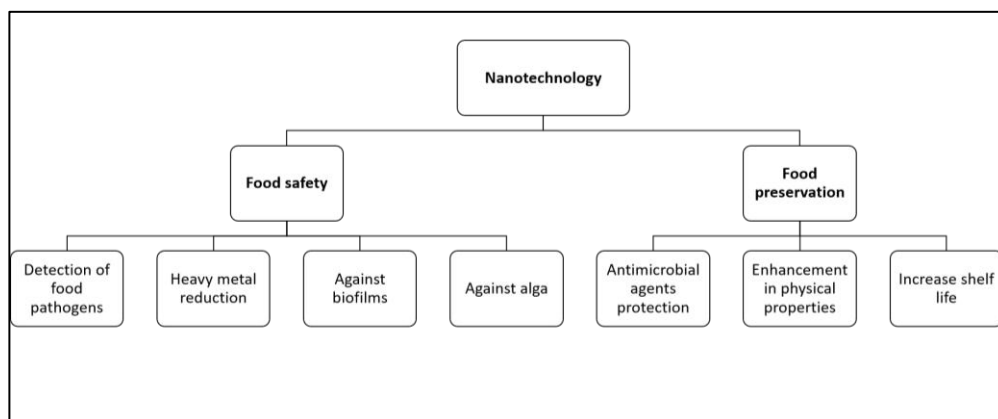


Fig. 8: Nanotechnology role in food safety and food preservation

8.2 Smart Packaging with Nanomaterials

For food preservation and safety following packaging methods are used:

8.2.1 Active Packaging

Active packaging involves the integration of nanomaterials directly into packaging materials to interact with the food contents. These nanomaterials serve various functions such as antimicrobial activity, oxygen scavenging, or UV blocking (Patel et al., 2020). For example, Nano Ag particles show antimicrobial properties. On the other hand, nanoclays increase barrier properties. By nanomaterials packaging actively helps to maintain food quality and safety (Kuswandi & Moradi, 2019).

8.2.2 Smart Sensors

It plays a role in sensing biochemical and microbial changes in food. It facilitates real-time monitoring of food quality. pH sensors also play a crucial role in maintaining food freshness and safety (Kuswandi, 2017). Packaging allows these sensors to provide immediate feedback on food conditions. For example, pH sensors determine acidity levels, while TTIs detect temperature variations. In this how sensors aid in waste reduction and ensure consumer safety (Rai et al., 2019).

8.2.3 Self-Repairing Packaging

Nanomaterials help to develop packaging that can independently repair damage. Nanoparticles containing packaging fill cracks or holes. In this way extending product shelf life and minimizes waste. These self-repairing mechanisms increase packaging lifetime and sustainability. These types of packaging contribute to overall resource efficiency in the food supply chain (Table 1) (Kuswandi & Moradi, 2019).

Table 1: Nanoparticles for application in food packaging.

1	Nanomaterials	Food Packed/Uses	Item Function	References
1	Silver ion and silver NPs	Meats (tuna and turkey)	Food contact paper releases silver ions and nanoparticles (NPs), which have antibacterial properties against Gram-negative bacteria in Turkey.	(Rai et al., 2019; Trbojevich et al., 2020)
2.	AgNPs	Chicken meat	There is no silver in chicken meatballs; microbiological testing revealed no distinction between meatballs kept in plastic bags 2016) containing silver nanoparticles and those kept in control bags.	(Gallochio et al., 2016)
3.	Chitosan and ZnO NPs	For Active food packaging	Compared to pure chitosan, films exhibit high antioxidant action and a considerable antibacterial capability.	(Yadav et al., 2021)
4.	Nanocrystals from Aerogel cellulose	absorbers for food packaging	A porous and uniform structure with a water absorption capacity.	(de Oliveira et al., 2019)
5.	Graphite carbon nitride Nanosheets	Cherry tomatoes	Films have broad-spectrum antibacterial activity and are safe to use.	(Ni et al., 2021)

8.3 Nanotechnology in Food Preservation

There is a lot of promise for nanotechnology to advance sustainability. It encompasses fields of applied sciences including materials processing, medical, food technology, environmental engineering, physics, and medicine. Materials with one or more dimensions of less than 100 nm are the focus of nanotechnology (He et al., 2019). The technology is being considered increasingly because of its many attributes, which include its wide range of use, target-specific nature, gradual release action, and precise action to active locations (Hamad et al., 2018). Nanotechnology's success may be attributed to its promising outcomes, zero emission of pollutants, energy efficiency, and minimal spatial requirements. In addition to these key success elements, nanotechnology has demonstrated a wide range of applications in the fields of food, agriculture, and the environment with regard to safety, toxicity, and risk assessment (Bhuyan et al., 2019).

9 Environmental and Ethical Considerations

Climate change threatens global food systems with vector-borne illnesses, floods, and livestock and fisheries stress. These issues pose food safety and environmental sustainability hazards. Risk-based food safety reduces consumer hazards but increases greenhouse gas emissions and resource waste (Feliciano et al., 2022).

9.1 Ethical Concerns of Nanotechnology in Agriculture

Scientists and governments must balance the potential advantages of nanotechnology in agriculture with the ethical issues caused by a lack of understanding about its negative effects. Global nanotechnology awareness is low (Bhattacharya et al., 2023). Awareness also differs between low-educated and professionally educated persons. How industry and research approach ethical and social concerns and media presentation in connection to the arguments can impact media representation and public cognition, with general public perception a key factor. Public opinion-focused institutions and scholars shape society most (da Rosa Zavareze et al., 2019).

Nanotechnology in agriculture is complicated by nanomaterials, which can harm humans and the environment, and need product labeling, unclear government financing, and public awareness (Shukla et al., 2024). Like genetic modification issues, there may be strong concerns about public health diseases and cautiousness in introducing the technique. Furthermore, rules are crucial to address these issues and boost technological adoption. Neglecting these concerns will backfire and be remembered like earlier scandals (Srivastava, 2023).

10 Challenges and Future Directions

10.1 Current Limitations of Nanotechnology in Agriculture

We must resolve a few issues and restrictions before extensively using nanotechnology in agriculture (Altabbaa et al., 2023). Lack of detailed rules and procedures to manage nanomaterial usage and eradication in farming are nanotechnology restrictions. Classifying and labeling nanoparticles makes safety and environmental impact evaluation challenging. Nanomaterial toxicity, fate, and transport in plants, water, and soil need further study. Nanotechnology costs more than other resources. Nanotechnology demands trained people, advanced equipment, and cutting-edge methods to develop NMs. Nanotechnology approaches are hard and expensive to transfer from lab to field (Periakaruppan et al., 2023).

Furthermore, farmers' acceptance of nanotechnology may be contingent upon their familiarity with and understanding of NMs. The possible dangers and unknowns associated with nanotechnology for the environment and public health. Nanomaterials could vary from each other by bulk counterparts and it might pose anonymous risks to living things. For instance, nanomaterials can pass through biological membranes. They also engage in interactions to cellular constituents, cause oxidative stress, inflammation, or genotoxicity. As a result, more research is required to evaluate the instant and long-term impacts of NMs on human health and the environment (Pathak et al., 2024).

10.2 Emerging Trends and Innovations

The Potential of Nanotechnology in Agriculture One potential use of nanoparticles is to help fertilizers and biochemical enter plant systems. Nano carriers, nanocomposites, nanotubes, nanofibers, and nanoclays are crucial (Panda & Das, 2024). Real-time Nano sensor monitoring is ideal for precision farming and future applications. Wireless field sensing systems enable systematic monitoring and real-time data for precision farming. Climate change issues, nanotechnology can boost photosynthesis and plant development. Chemical technology can create sunlight-absorbing chemicals for plants' leaves and roots. Thus, group photosynthesis can be improved and solar energy transformed into chemical energy that plants can store. Though successful, translating sunlight into chemical energy is one of its key drawbacks (Roy & Hossain, 2024).

Conclusion

The integration of nanotechnology into precision agriculture plays a key role for addressing current challenges in agriculture and food security. Nanotechnology offers advance solutions for increasing crop productivity, improve food safety, and optimize resource utilization. Nanotechnology gives efficient nutrient management and pest control. In this way its leading to increased yields also minimize environmental impact. Moreover, Nano sensors play role in precision irrigation, allowing real-time monitoring and optimization of water usage. It is very important associated with the widespread adoption of nanotechnology in agriculture. Climate change and water scarcity create significant challenges to global food systems and nanotechnology offers potential solutions, careful evaluation of its impact on ecosystems and human health is necessary. Ethical concerns regarding public awareness, safety, and regulatory frameworks must also be addressed to ensure responsible and sustainable deployment of nanotechnology in agriculture. Despite current limitations and challenges, emerging trends and innovations in nanotechnology hold promise for the future of agriculture. Nanotechnology has the potential to make advances for farming practices by offering nutrients, by increasing photosynthesis, and enabling real-time monitoring and management of agricultural systems. By carefully using nanotechnology, we can ensure food security, environmental sustainability, and socioeconomic progress for future generations.

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Toxicological Impacts of Biogenic Vs. Conventional Metal Nanoparticles: Safety Perspectives and Emerging Trends

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Abstract

Although nanoparticles (NPs) have transformed a number of industries, including environmental cleanup and medicine, there are still serious concerns about their safety. This review highlights the effects of conventional and biogenic metal nanoparticles on the environment and human health by analyzing their toxicological profiles. Because of their environmentally benign synthesis and biocompatibility, biogenic nanoparticles which are produced utilizing biological entities like plants, bacteria, or fungi are frequently seen as safer. On the other hand, due to little size, enhanced surface, and residual chemical reagents, ordinary metal nanoparticles that are created by physical or chemical means may be more harmful. Analysis is done on the main mechanisms of toxicity caused by nanoparticles, such as oxidative stress, genotoxicity, and inflammatory reactions. To reduce toxicity, recent developments in the sector have focused on hybrid nanoparticles, surface functionalization, and green production techniques. The analysis examines regulatory structures and challenges in uniform safety evaluations for biogenic nanoparticles, highlighting their potential for safer applications but also highlighting significant obstacles to their scalability and reproducibility. This work underscores the importance of cross-disciplinary approaches that balance innovation and safety to ensure responsible nanotechnology deployment in the future.

Keywords: Nanoparticles, Biogenic, Conventional, Metal nanoparticles, Safety perspectives

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Introduction

Nanoparticles are tiny particles with sizes between 10 and 1000 nm. Drugs can be mixed into, trapped inside, coated onto, or attached to these particles. Depending on how they are made, the particles can be of different types like nanospheres (solid particles with the drug spread throughout) or nanocapsules (tiny capsules with the drug inside) (Langer, 2000). The fabrication of nanoparticles with sizes stretch from 1 to 100 nm using various synthesis techniques, as well as the alteration of particle size and structure, is the field of nanotechnology. These days, Nanoparticles are being used more and more in many fields, such as biology, physics, chemistry, medicine, and material science (Heiligtag & Niederberger, 2013). Particles of bigger bulk material do not exhibit the unique and enhanced characteristics of nanoparticle size reduction, such as, form and size distribution of fine particles (Willems, 2005). The term 'nanoparticle,' is derived from the Greek word 'nano,' meaning 'dwarf or small' A nanoparticle is a particle with one dimension in the size range of 10-9, and 1 nm is equivalent one billionth of a meter (You et al., 2013).

Metallic nanoparticles are often made and stabilized using methods like electrochemical changes, chemical reduction, and photochemical reduction (Chen et al., 2001). The method chosen to make metallic nanoparticles are equally important because their morphology (size and structure), stability and properties of metallic nanoparticles depend on factors like how metal ions react with reducing agents, how stabilizing agents interact with the nanoparticles, and the methods used during their production (Vijayakumar et al., 2013). In many studies on the creation and use of nanoparticles of diverse inorganic metal (silver, gold, copper, iron, platinum, and palladium), scientists have demonstrated their proficiency in metallic nanoparticles, which are currently the focus of much of their research (Azharuddin et al., 2019).

Deposition, sputtering, ball milling, and plasma-based methods are the physical methods to develop nanomaterials (Dhand et al., 2015). Laser and plasma ablation, laser ablation and plasma techniques demand a high energy input. The majority of physical processes are too costly to be used in practical business use due to their range of size distribution, sluggish production rate, waste byproducts, and large energy usage (Seetharaman et al., 2018).

The majority of the chemical approaches that have been proposed for the preparation of nanoparticles such as chemical reduction, pyrolysis, sol-gel, microemulsion, polyol synthesis, hydrothermal synthesis, and chemical vapour deposition are commonly employed to create nanostructured materials (Darroudi et al., 2013). Furthermore, it is fatal for both persons and the environment to use dangerous chemicals and reagents during the compounding process and byproduct formation (Zhang et al., 2019). This can be considered as a reason why these NPs are

not so often employed in biological fields.

Green nanotechnology is a relatively newly developing area of science and engineering that designs new NPs throughout the concept of green chemistry. Synthesis of proteins and enzymes, with natural stabilising and reducing elements, introduces yet another innovative package of biological techniques in the creation of NPs. It is also economical and safe for the environment apart from chemophysical procedures because it lacks any poisonous content (Patil et al., 2020). The bio synthesis of NPs is a bottom up approach that involves utilizing simple single celled to complex multicellular organisms inclusive of bacteria, fungus, actinomycetes, yeast, algae and plant material (Kalishwaralal et al., 2010).

The synthesis and manufacturing of nanoparticles should be easy even though green nanoparticles appear to be an innovative method of developing conventional nanoparticles. Microbes and plants were the bio-resources to be exact available in the universe. However, the use of such bioresources is essential from the standpoint of synthesis and commercialization. In this situation, microorganisms can be used efficiently; however, the synthesis and use of nanoparticles are hampered by the dealing with microbes, increasing production, genetic changes, issues in large-scale growth, processing, and other factors (Patil et al., 2020).

Methods Involve for the Synthesis of Nanoparticles

Following two types of methods are involved in the preparation of nanoparticles:

1. Conventional nanoparticles synthesis
2. Biological-mediated synthesis of nanoparticles

Conventional Nanoparticles Synthesis

Conventional synthesis of nanoparticles two types of processes:

1. Physical Methods of Nanoparticles Synthesis

Physical synthesis of nanoparticles involves following methods:

Ball Milling

Using high intensity ball milling to reduce particle size is the fundamental principle of mechanical milling. The characteristics of mechanical milling depend on the type of powder and the process variables. It is divided into two categories: high energy and low energy milling, which rely on the powder mixture's induced mechanical energy. The most common method for producing nanosized particles is high intensity ball milling (Rajput & Technology, 2015). In this procedure the following numbers of heavy balls are added to a container along with the bulk powder. The second step is the fast spinning of the mixed powder so as to apply force energy on it is achieved. These high-energy mills are attrition ball mills, planetary ball mills, vibrating ball mills, low-energy tumble mills, high-energy ball mills, and more that can reduce the particle size (Rajput & Technology, 2015).

Ion Sputtering

Using an ion beam of inert gas, a solid can be vaporised using the ion sputtering technique. In recent years, some metals have been employed to synthesize nanoparticles employing magnetron sputtering of metal objectives. At relatively low pressures (1 mTorr), the complete process is carried out (Swihart & science, 2003). The process of sputter deposition takes place in an evacuated vacuum chamber with a working pressure of, say, 0.05 and 0.1 mbar, with sputtering gas allowed. In a magnetic control method, a very high voltage is applied to the target (cathode) in a spiralling motion of electrons. This ionises the gas as the sputtering argon atoms are met. This continuous process forms a glow discharge, or plasma, which ignites. The target is attracted to the ball of glowing and positively charged gas ions which keep on hitting it. When this recurs and approaches the target's surface, the gas molecules bombard metal atoms in vacuum and knock the atoms off randomly leaving a cloud on the surface possessing energy exceeding the binding energy, which leads to expulsion of an atom (Vanecht, 2012).

Laser Ablation

By employing laser light the laser ablation method is one which decreases the particle size to the nanoscale. Subsequently, the solid target material coated so that it is thinly coated is irradiated by pulsed laser light. Nd:YAG (neodymium-doped yttrium aluminium garnet) laser at 106 μm output and its harmonic, copper vapour laser, and Ti:Sapphire (titanium-doped sapphire) laser are the main lasers used (Simakin et al., 2004). A material exposed to laser light breaks up into tiny particles known as the nanoparticles. These particles are deposited in the liquid that surrounds the target thereby forming a colloidal solution. The power density and the pulse width define the yield of ablated atoms and particles formed in proportion (Kruis et al., 1998). Several important factors affecting ablation efficiency and the properties of metal particles include laser pulse width, wavelength, ablation period, laser density, along with an effective surrounding liquid media with or without surfactant (Abou El-Nour et al., 2010).

Physical Vapor Deposition

Material is deposited on a surface via the physical accumulation process in the form of nanoparticles or thin films. Material vaporises when subjected to highly regulated vacuum techniques like thermal evaporation and sputtered deposition, and then condenses on a substrate (Pandey et al., 2011). Lanthanum strontium cobalt thin films are typically synthesized using physical vapour deposition methods such pulsed vapour deposition (Park et al., 2017). In pulsed laser deposition, a solid target is hit by a laser, causing it to release a plasma of particles. These particles are then deposited onto a substrate to form a film (Gondoni et al., 2013). This method is commonly used for depositing thin films and metal nanoparticles, especially for carbon nanotubes (Pandey et al., 2011).

2. Chemical-mediated Synthesis of Nanoparticles

Chemical synthesis of nanoparticles involves following methods:

Sol gel Method

Two phases make up the sol gel method of creating nanoparticles: either a) the merging of metal and metal oxide or nanoparticles directly into a prehydrolyzed sol of silica or b) the mixing of preformed colloidal metal (oxide) and a sol which contains the matrix forming species after which gelation takes place. Before hydrolysis, metals reduce and form a complex with silone (Cushing et al., 2004). This method forms a coated gel in the continuum of liquid phase gelatin-matrix colloidal suspension sol. Cationic metal alkoxide and/or aloxysilane is employed as an initiator in colloid synthesis. The two most often used tetramethoxysilanes (TMS) and tetraethoxysilanes to create silica gel. Metal alkoxides are immiscible in water and are the organo-metallic precursors of many different metals, including titanium, aluminium, and silica. Alcohol serves as a reciprocal solvent. It starts a reaction at a fixed pH by incorporating a catalyst within a homogeneous medium of one or more preferred alkoxides. Four significant processes involved in sol-gel are hydrolysis, condensation, particle growth, and particle coagulation (Rajput & Technology, 2015). Low temperature heat treatment is utilized in deposition of metal oxide particles in direct precipitation of metal/metal oxide from silica sol process and thin film preparation is the predominate use for this method (Cushing et al., 2004).

Chemical Reduction

Using chemical reduction technique, several reducing agents are used when a surfactant is present to reduce ionic salt in the correct medium (Guzmán et al., 2009). Metal nanoparticles are formed in aqueous solution by the use of sodium borohydride or another reducing agent. Lai and Mohanty used trisodium citrate (TSC) or sodium lauryl sulphate (SLS) to cap the metal nanoparticles that are formed. At times these two stabilising and reducing agents are combined in one formula. The stability of the metal nanoparticles in the dispersion was measured by the absorbance study (Chattopadhyay & Patel, 2014). Otherwise known as sodium borohydrate (NaBH_4), glucose, ethylene glycol, ethanol, sodium citrate and hydrazine hydrate are used to synthesise silver nanoparticles (Landage et al., 2014).

Hydrothermal Method

Vapours from an aqueous solution interact with a solid to form small particle deposition in the hydrothermal process at elevated temperatures and pressures. In doing so, the cations function as polymeric hydroxide, which promote dehydration of the material a step at a time and thus facilitate the completion of the metal oxide crystal structure. The second metal cation that forms when base is added to the metal salt solution also reduces the formation of complex hydroxide prevents the formation of large number of particles and thus controls the particle generation process (Tavakoli et al., 2007).

Flame Pyrolysis

Flame pyrolysis works by first-hand spraying a liquid precursor into a flame, which forms nanostructures. Initiators with insufficiently high vapour pressure can be delivered in the form of vapour using this technique (Mädler et al., 2002). The precursor is exposed to the flame, allowing it to form nanoparticles as gases (vapor-fed aerosol flame synthesis), liquid (flame-assisted spray pyrolysis: FASP and flame spray pyrolysis: FSP), or solid (Wallace et al., 2013).

Biological-mediated Synthesis of Nanoparticles

There are two kind of naturally occurring biogenic metallic nanoparticle synthesis:

Bioreduction

Microbes and their enzymes convert metal ions into a stable form for biological processes. It is safe to remove the produced metallic nanostructures from adulterated material due to their inert and stable nature (Pantidos et al., 2014).

Biosorption

This novel approach to nanoparticle production involves allowing metal cations in aqueous media to attach to the cell wall of an organism, which in turn causes the development of stable nanoparticles through cell wall or peptide contact (Pantidos et al., 2014).

Nanoparticle Synthesis using Bacteria

Global interest in the suitable application of naturally available resources, like microorganisms, for the synthesis of nanoparticles is constantly growing. Since prokaryotes are abundant in the environment and can adjust to harsh conditions, they have gained attention as a way to make metallic nanoparticles. Some benefits of bacteria include their quick growth and convenience of cultivation and manipulation (Pantidos et al., 2014). Conditions such as temperature, duration of incubation, and oxygenation can be adjusted to influence the growth. According to (He et al., 2007) altering the growth medium's pH during incubation results in nanoparticles with varying sizes and shapes .

Nanoparticle Synthesis using Fungi

Fungi release enzymes and proteins that act as reducing agents to create metal nanoparticles from metal salts. Because of electrostatic contact, metals like silver (Ag) can bind to the cytoplasmic membrane and undergo reduction, which in turn generates silver nuclei and ultimately causes an deposition of both silver nuclei and nanoparticles. Popular fungi for creating nanoparticles include *Trichoderma reesei*, *Aspergillus fumigates*, *Fusarium oxysporum*, and others. The *Fusarium oxysporum* secretes reducing agents that effectively lower these metal ions. Because they require high aseptic conditions to be maintained, microorganism-based nanoparticle syntheses are not practically possible (Pantidos et al., 2014).

Nanoparticle Synthesis using Plant and plant Products

The world has lately expressed interest in the production of plant base nanoparticles (Prathna et al., 2011). The metallic nanoparticles include copper, zinc, silver and gold and these are synthesized with different plant parts and extracts. Secondary metabolites isolated from plants such as phenolic acid, flavonoids, terpenoid, alkaloid, and crude extracts are rich in compounds, which mainly reduce metallic ions to form metallic nanoparticles. Plant redox reactions using metabolic pathways employ both primary and secondary metabolites. These characteristics are applied as capping and reducing agents when synthesizing environment-friendly nanoparticles (Iravani, 2011; Kuppusamy et al., 2016). *Juncea brassica*, *Ilex crenata*, *Sesbania drummondii*, *Clethra barbinervis*, and *Acanthopanax scidophylloides* can advance photoremediation of heavy metals (Iravani, 2011). The bio-reducing agent is next removed from the biological extract and then mixed with aqueous solution of the metal precursor to generate nanoparticles. Spontaneous formation of nanosized particles is observed at room temperature during a number of processes. At times, due to synthesis time constraint, CD is added and heated, or at least, heated. Plant extracts are selected based on availability, ability to produce large quantities of the given extract and the waste produced in the process is ecologically nontoxic (Pantidos et al., 2014).

Safety Aspect \ Advantages

Conventional Method of Nanoparticles Synthesis

The advantages \ safety aspects of conventional methods are as follow:

1. Beneficial for producing high-quality nanoparticles on a large scale at a reasonable cost, with improved solubility of therapeutic components that are indissoluble in water (Ullah et al., 2014; Thamizharasan et al., 2017).
2. It is feasible to produce nanoparticles in liquid media without the need to add surfactant (Simakin et al., 2004).
3. The material that is spat out has the same composition as the target material and is not changed (Kruis et al., 1998).
4. Superior approach compared to evaporation and laser ablation for refractory metals and intermetallic complexes.
5. A viable substitute gas-phase technique for producing metal oxide nanoparticles is flame pyrolysis.
6. It enhances the material's properties by optimizing its composition and grain size (Ullah et al., 2014).
7. The great film endurance of the chemical vapour deposition coating technique is demonstrated (Reina et al., 2009).
8. It is feasible to regulate particle size and shape through methodical observation of reaction parameters (Hasnidawani et al., 2016).
9. Nanoparticles can be prepared to the required size and shape (Tavakoli et al., 2007).
10. Powder that is well-crystallized can be produced.

Biogenic Method of Nanoparticles Synthesis

The advantages \ safety aspects of biogenic methods are as follow:

1. Easily accessible and capable of withstanding harsh environments (Pantidos et al., 2014).
2. Not as pathogenic as bacteria and fungus.
3. The result is somewhat homogeneous nanoparticles (Pantidos et al., 2014).
4. Because of mycelia, nanoparticle synthesis has a huge surface area, is inexpensive, flexible, and easy to scale up for downstream processing.
5. Fungal secretions of proteins surpass those of bacteria in terms of productivity (Pantidos et al., 2014).
6. Non-toxic, environmentally friendly, and biocompatible
7. Toxic chemicals, high pressure, energy, and temperature are not used in green synthesis (Karnani & Chowdhary, 2013).

Toxicity \ Disadvantages

Conventional method of nanoparticles synthesis

The toxicity \ disadvantages of conventional methods are as follow:

1. Large amount of energy required.
2. Prolonged and extensive milling duration.
3. Powder contamination as a result of steel balls.
4. Extended laser ablation causes a large number of nanoparticles to develop in the colloidal solution, obstructing the laser's path and absorbing laser energy into the nanoparticles rather than the target surface. Overall, this causes the ablation rate to decrease (Ghorbani, 2014).
5. The sputtering gas (He, Ne, Ar, Kr, Xe) affects the surface features, composition, texture, and optical properties of nanocrystalline metal oxide films (Chandra et al., 2006).
6. Dangerous chemicals and the creation of harmful final goods
7. Participation in high-energy procedures
8. Process control is a challenging task.
9. Reliability and reproducibility are limited (Tavakoli et al., 2007).
10. Expensive

Biogenic Method of Nanoparticles Synthesis

The toxicity \ disadvantages of biogenic methods are as follow:

1. It can be difficult to precisely manage size and shape.
2. Scaling up can be difficult.
3. Biological sources can vary.
4. Green nanoparticles can penetrate cells and, above a certain limit, cause oxidative DNA damage, cell membrane harm, and disrupt the electron transport chain (Jamkhande et al., 2019).

Future Possibilities

Metal nanoparticles are increasingly used in fields like material science, physics, chemistry, and biology. Their synthesis involves various methods, such as sol-gel, chemical vapor deposition, physical vapor deposition, and green synthesis. Green synthesis is affordable, eco-friendly, sustainable, and free of harmful chemicals. However, more precise methods are needed for commercial applications (Jamkhande et al., 2019).

Conclusion

Nanoparticles hold immense potential across various fields due to their unique properties, with synthesis methods ranging from conventional chemical and physical approaches to green, biologically mediated techniques. While conventional methods offer scalability and control, they often involve high energy demands and hazardous chemicals, posing environmental and health risks. In contrast, biogenic synthesis is eco-friendly and biocompatible but faces challenges in scalability and uniformity. Green synthesis stands out as a promising, sustainable alternative, yet it requires further refinement to meet commercial demands. Balancing innovation, safety, and environmental responsibility is crucial for advancing nanoparticle applications in a sustainable future.

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Treatment of Peripheral Nerve Injury using Mesenchymal Stem Cells

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Abstract

Due to the changing lifestyle in modern times, peripheral nerve injuries (PNI) are becoming more and more common and can arise from trauma, medical diseases, and even sports injuries. Healing these injuries is a prolonged and challenging process. Studies show different PNI rates; lifetime rates range from 2-3% to higher estimates of 13-23 cases per 100,000 people. Six million sciatic nerve injuries in children aged 2020 to 2022 were reported in Pakistan. Although surgery, physical therapy, nerve grafting, and amputation are among the present PNI therapies, these approaches are not always totally successful and may have side effects. Based on degree, PNI can be categorized as follows: nerve entrapment, axonotmesis, and neurotmesis. Recent developments point to mesenchymal stem cells (MSCs) being used in treatment because of their ability to regenerate nerves. Moreover, important for nerve regeneration are neurotrophic elements, which help axon development and microcirculation. Through regeneration and immunomodulation, MSCs show potential in treating PNI; yet, further study is required to fully understand their effects and uses in nerve injury recovery. This book chapter aims at summarizing peripheral nerve injury, its complexity, functional damage and the use of mesenchymal stem cells for treating peripheral nerve injury.

Keywords: Neurotmesis, Nerve regeneration, Schwann cells, Wallerian degeneration, Neurotrophic factors

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Introduction

The fast pace of life in recent years has made peripheral nerve injury (PNI) a major issue. Trauma, accidents, medical disorders, heredity, or signs of other diseases can all be causes of peripheral nerve degeneration (Lopes et al., 2022). Structural problems, natural disasters, conflict, sports injuries, and electric shock can all cause peripheral nerve damage. Because they are complex and time-consuming, PNIs are complex and their healing is time-consuming and challenging. Important aspects of peripheral nerve regeneration are myelin regeneration, axon length, electrophysiological characteristics, Schwann cells, and nerve fibers (Chu et al., 2022). PNI is well-known for its sophisticated care environment targeted at helping patients and their families manage pain, disability, mental illness, life expectancy, hopelessness, and stress (Alvites et al., 2018).

Mesenchymal stem cells (MSCs) have emerged as a promising therapeutic option for PNI due to their unique regenerative capabilities and low immunogenicity. MSCs can be sourced from various tissues, including bone marrow, adipose tissue, and umbilical cord, and possess the ability to differentiate into Schwann-like and neuronal-like cells as shown in figure 1, which are essential for nerve repair. These cells promote axonal regeneration and functional recovery through multiple mechanisms, such as secreting neurotrophic factors, extracellular matrix molecules, and pro-angiogenic factors that create a favorable microenvironment for neuronal survival and growth. Additionally, MSCs modulate immune responses by regulating cytokine expression and macrophage polarization, reducing inflammation at the injury site. Advanced strategies like genetically engineered MSCs, MSC-derived exosomes, and their integration into nerve conduits have further enhanced their therapeutic potential. Despite these advancements, challenges remain in standardizing MSC extraction, cultivation, and application methods to ensure consistent clinical outcomes.

PNIs have a somewhat noteworthy frequency. Different research and approximations yield different PNI statistics and prognostic variables. According to earlier studies, PNI has a lifetime incidence between two and three percent (Martyn and Hughes, 1997). Other studies project 13-23 per 100,000 persons as the PNI prevalence (Hicks and Selvin, 2019). A study particular to Pakistan claims that in 2020-2022 there were 6 million cases of sciatic nerve injury in children (Dave et al., 2025). PNI affects 1-3% of trauma accident sufferers. The shifting PNI data emphasize the relevance of this disorder and the requirement of efficient therapy to guarantee recovery and return to life.

Common treatments for peripheral nerve injuries include surgery, physical therapy, nerve grafting, amputation, limb transplantation, prosthetic limbs, and nerve grafting. All of these treatments have various advantages and disadvantages, but none is 100% effective (Xu et al., 2024). Surgery and suturing lead to the formation of fibrous scar tissue, suture debris, and tissue damage material at the wound site. Other treatments have disadvantages such as organ loss, tissue rejection, organ rejection, toxicity, and immune rejection (Santosa et al., 2020). New strategies that provide enhanced nerve repair and regeneration, such as the use of allografts, mesenchymal stem cells, and biomaterials with minimal side effects, are urgently needed.

Treatment and recovery are closely related to the type of injury, the degree of nerve damage, the extent of the injury, and the nature of the muscles and joints involved (Hussain et al., 2020). For example, in the case of high-energy traumatic injuries, recovery is negatively affected by the severity of the injury. Swelling, scar tissue formation, and adequate axonal and Schwann cell regeneration occur. Neurovascular expansion therapy for space-occupying wounds may have several limitations, including biological complexity, donor site morbidity, short graft distribution, and the need for multiple procedures (Gervois et al., 2016).

From a regenerative medicine perspective, mesenchymal stem cells are used to treat PNI because of their ability to differentiate into neural stem cells (Levorato et al., 2021). This therapeutic approach has the potential to improve treatment outcomes and improve quality of life. Sources of mesenchymal stem cells include adipose tissue, bone marrow, amnion, peripheral blood, cord blood, and muscle (Jiang et al., 2017). All mesenchymal stem cells require proper evaluation and classification before use. This chapter provides an overview of the basics of peripheral nerve injury by mesenchymal stem cells and their use and future efficacy and outcomes.

The main objectives of this book chapter covers a reviewing of PNIs and their treatment using mesenchymal stem cells, prognosis, functional outcomes and limitations.

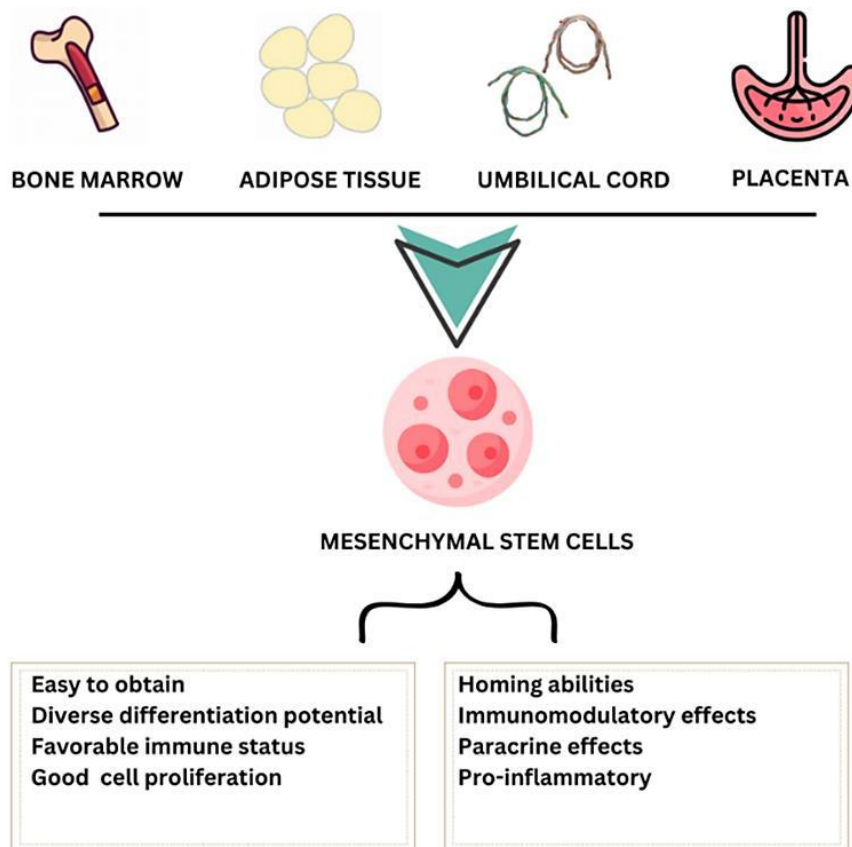


Fig. 1: Derivation and properties of MSCs

What is PNI?

PNI can be defined as any damage to a peripheral nerve that impairs its ability to function. Distal limb atrophy is due to decreased PNI because connections between damaged nerve fibers and organs are negatively affected and sometimes completely lost (Yousefi et al., 2019). Major injuries almost always involve PNI in 1%-3% of patients. The condition has been identified in children who have fallen, as a side effect of treatments such as radiation, chemotherapy, and surgery, and sometimes as a contributing factor to chronic diseases such as cancer and diabetes. PNI can also arise as an iatrogenic injury. Three primary types of conditions lead to PNI: transection, tension, and compression (Brull et al., 2015). Transection is commonly caused by penetrating trauma, tension occurs when the nerve is excessively stretched, and compression can be resolved if the underlying cause of the injury is addressed within eight hours.

Anatomy and Classification of Peripheral Nerve Injury

Neurologists and physicians classify spinal injuries, especially severe ones, into different categories, or schools, to aid in diagnosis and treatment. In 1943, Sir Herbert Seddon developed a classification system based on injury severity, recovery time, and extent of injury, which described three types of injury: nerve entrapment, axonotmesis, and neurotmesis (Warwick et al., 2010).

Neuropraxia (type I) is a rare type of nerve damage that usually results from nerve injury or ischemia. In this case, nerve fibers are blocked at the site of injury, resulting in loss of movement and sensation, while all morphological components of the nerve (including the endoneurium, perineurium, and epineurium) are affected (Fehlings et al., 2016). Since the axon remains connected to the cell body, Wallerian contraction does not occur. Recovery of neurologic function and function is usually rapid, although the time frame may vary from hours and days to weeks or months.

Axonotmesis (Type II) represents a severe injury to a peripheral nerve, usually caused by compression, stretching, or compression (Grant, 2023). In this case, the epineurium remains intact, whereas the perineurium and endoneurium may be damaged. The axon is separated from the cell body, resulting in damage to the axon and its myelin sheath, and Wallerian degeneration of the distal axon stump occurs within 24-36 hours after injury. Visual and motor impairments were observed, and nerves were unable to reach the site of injury (Fox et al., 2017). The surrounding matrix helps the axons remain continuous with the underlying tissue and allows for repair if the damaged nerve stump remains attached to the tissue. The diagnosis of axotomy is greatly influenced by the proximity of the tumor to the target organ. However, self-renewal is rare and requires appropriate treatment.

Neurotmesis (stage III) is caused by nerve entrapment or neurotoxins and is the most severe type of nerve injury. In a neurotome, the entire nerve trunk, including the endoneurium, perineurium, and epineurium, is completely severed. This damage can lead to the destruction of axons, myelin, and connective tissue and can significantly affect cognition. In 1951, Sunderland expanded Seddon's classification (particularly axonal loss) to five levels (Sheaths, 2021). Sunderland grade 1 injuries represent the mildest type of nerve injury, similar to the Seddon nerve. Sunderland diseases 2, 3, and 4 are similar to Seddon axonotmesis. In Sunderland grade 2 injuries, the endoneurium, perineurium, and epineurium are intact despite damage to the axons. Sunderland grade III injuries involve axotomy at the site of injury with loss of continuity of the endoneurium and perineurium. In a Sunderland type IV injury, only the epineurium is intact, whereas the axon, endoneurium, and perineurium are damaged. Sunderland's type V injury met Seddon's definition of neurotmesis, a severe traumatic injury characterized by complete loss of neurological function resulting in complete transection (Radic et al., 2018). Large nerve root injuries with wide gaps require nerve grafting rather than nerve resection to avoid severe compression.

Changes at the Molecular and Cellular Level

Several changes occur at the cellular and molecular level following PNI. In severe transection injuries due to penetrating trauma, pathological changes occur in the damaged proximal and distal nerve trunks. Damaged axons undergo "Wallerian degeneration" at the distal stump, transforming into granular debris that is eventually cleared by macrophages. While activated Schwann cells switch to a regenerative phenotype and proliferate in the distal stump to form longitudinal columns known as "Büngner bands" that are important for guiding growing axons, the proximal stump also first returns to the nodes of Ranvier before attempting to reach the distal stump by releasing the growing axon (Wang et al., 2019). The slow rate of axonal regeneration, which varies by region but is usually expressed as 1 mm/day, almost always defeats this process and results in a lack of active SC force, abnormal axons, and target organ attenuation due to long-term axonal loss. - the term axonal loss remains within. However, the above events and the secretion of neurotrophic factors by SCs create an ideal environment for axonal sprouting.

Treatment Methods

The gold standard approach to treating transection injuries involves surgical fusion of the proximal and distal nerve stumps. However, a nerve graft or nerve conduit is required to bridge the gap if the gap is too large to repair without nerve fiber extension. Cell transplantation has been proposed in recent years as a way to enhance peripheral nerve regeneration (Lam and Leung, 2024). As mentioned earlier, SCs activated in response to nerve injury are critical for Wallerian degeneration and the development of Büngner bands. These properties make SCs the best choice of cells for transplantation; however, other important characteristics of SCs include their high immunogenicity, poor culture growth, and difficulty in harvesting.

Biomaterials and Surgical Techniques

Because the sural nerve is the most common sensory and vascular donor used for autotransplantation, it is not a suitable choice for repairing a nerve with combined motor and sensory or motor components. Given the problems with nerve expansion, researchers have focused on finding alternatives that can fill large gaps without damaging the nerves. Canals have been made from various absorbable biomaterials, with authors worldwide reporting varying results. Canals can be synthetic or natural. Early studies demonstrated the effectiveness of scaffolds engineered nerve conduits, which avoided issues like mechanical incompatibility and nutrient exchange limitations by relying on fibroblast monolayers and neural stem cells to promote axonal growth and functional recovery. Later, nanofiber-based conduits, such as self-assembling peptide nanofiber scaffolds (SAPNS), were shown to enhance motoneuron protection, axonal regeneration, and remyelination in sciatic nerve defects, achieving promising functional outcomes. Regardless of the positive results, autologous drainage, like venous drainage, may include plasma components containing muscle or platelets. These channels require a donor area for collection. Despite great advances in surgical techniques and equipment, further research is needed in this area to establish the best combination of root canal-compatible cells and neurotrophic factors to improve clinical outcomes.

Neurotrophic Factors in PNI

Although activated SCs must localize rapidly to maintain their functional state, axon sprouts grow very slowly and, in the worst case, take a long time to reach the distal stump. Neurotrophic therapies and growth factors that can accelerate this process have therefore attracted attention (Wan et al., 2024). After nerve injury, brain-derived neurotrophic factor (BDNF) is critical and has been shown to promote axonal growth. In addition to increasing SC motility, nerve growth factor (NGF) also has a positive effect on the elongation of growing sensory axons. SCs are chemically attracted to glial-derived neurotrophic factor (GDNF). One important transcription factor that is

increased in response to PNI is Sox11. Myelin levels, nerve length, and BDNF levels can be affected by its expression. It can also help neuronal survival through the production of TNF receptor-associated activators (TANKs) associated with NF-κB. Vascular endothelial growth factor (VEGF) can improve nerve regeneration outcomes by improving microcirculation. Insulin-like growth factor (IGF) has been shown to stimulate axonal elongation and SC mitosis (Chernov and Shubayev, 2021). Although there are potential benefits from the shared use of channels and neurotrophins, it remains important to maintain SCs in a functional state, as they rapidly lose their ability. To facilitate the healing process, scientists have developed methods to obtain cell types that can develop into SCs or SC-like cells or to transplant newly activated SCs into the wound site.

Stem Cells in PNI

Stem cells are undifferentiated cells capable of developing into various cell types and producing multiple cell types. The two primary sources of stem cells are embryos, from which embryonic stem cells can be extracted during the embryonic stage, and adult tissues, which contain adult stem cells present in every tissue of the body (Prochazkova et al., 2015). Stem cells are classified based on their ability to differentiate into different cell types. For instance, muscle stem cells and other immature cells can only differentiate into their respective cell types. Myeloid stem cells are a distinct category of oligopotent stem cells. Multipotent stem cells can differentiate into closely related cell types, such as blood stem cells, which can develop into platelets, white blood cells, and red blood cells. Pluripotent stem cells, including embryonic stem cells and those from the ectodermal, mesodermal, and endodermal layers, can develop into nearly any cell type (Kolios and Moodley, 2012). Totipotent stem cells, which include early cells formed during the division of a zygote and the fertilized zygote itself, are unique in their ability to differentiate into all cell types. Mesenchymal stem cells (MSCs) are highly potent stem cells derived from sources such as adipose tissue, bone marrow, umbilical cord, amniotic fluid, and teeth (Costella et al., 2022) as explained in table 1. Morphologically, these cells are characterized by small cell nuclei with large nucleoli and round clear nucleoli. Their cytoplasm contains a Golgi apparatus, mitochondria, rough endoplasmic reticulum, ribosomes, and several elongated cell processes, and they are widely distributed within an extracellular matrix containing small reticular fibers.

Table 1: Summary of Mesenchymal Stem Cells and their use in Peripheral Nerve Injury(PNI)

Type of Source	Differentiation Potential	Mechanism of Action	Clinical Applications	Key Factors Associated	Challenges	References
Mesenchymal Stem Cells (MSCs)						
Adipose-derived stem cells (ADSCs)	Adipose Tissue	Neuronal, Schwann-like	- Promote axonal growth - Immunomodulation - Paracrine signaling - Anti-inflammatory effects	Peripheral nerve injury repair - Diabetic neuropathy	- VEGF - BDNF - NGF - IL-10	Limited availability in older patients - Variability in yield and quality Zack-Williams et al., 2015
Bone Marrow Mesenchymal Stem Cells (BMSCs)	Bone Marrow	Neuronal, Osteogenic	- Differentiation into Schwann-like cells - Secretion of neurotrophic factors - Modulation of immune response	Treatment of nerve injuries in various models - Growth factors	- Neurotrophic factors - Cytokines (e.g., IL-6) - Limited expansion potential in vitro	Invasive extraction procedure - Limited expansion Fernandes et al., 2018
Wharton's-Jelly derived cells (WJ-MSCs)	Umbilical Cord (WJ-)	Neuronal, Chondrogenic	- Immunomodulatory effects - Enhanced angiogenesis and neuronal survival - Secretion of exosomes	Use in acellular nerve grafts - Regenerative medicine applications	- BDNF - NGF - VEGF - HGF	Ethical considerations in sourcing - Limited understanding of long-term effects Guo et al., 2015
Dental Stem Cells (DPSCs)	Pulp Dental Cells	Neuronal, Odontogenic	- Neuroprotective effects - Ability to differentiate into neuronal-like cells - Secretion of growth factors	Potential for nerve regeneration in dental procedures	- Growth factors (e.g., FGF, EGF) - Anti-inflammatory cytokines	Limited availability post-extraction - Variability in differentiation capacity Xing et al., 2023
Mesenchymal Stem cells derived exosomes	Various Sources (e.g., ADSC)	N/A	- Paracrine signaling effects similar to MSCs - Promote nerve regeneration through extracellular vesicles	Innovative therapeutic strategies for nerve repair	- miRNAs (e.g., miR-21) - Proteins involved in regeneration	Stability and delivery challenges - Regulatory hurdles for therapeutic use Fan et al., 2020

Bone Marrow Mesenchymal Stem Cells

The differentiation of bone marrow mesenchymal stem cells (BMSCs) into mesodermal, ectodermal, and endodermal lineages can be induced. By releasing neurotrophic and growth factors such as BDNF, GDNF, and myelin basic protein and regulating SC behavior, they are known to differentiate into SC-like cells, facilitating nerve regeneration (Hopf et al., 2020). Due to certain challenges associated with BMSC

procurement, including the need for invasive and painful procedures that can lead to low cell yields, BMSCs have some limitations in clinical research. BMSCs exert their beneficial effects in a dose-dependent manner.

Adipose-derived Mesenchymal Stem Cells

Adipose-derived mesenchymal stem cells (ADSCs) are an alternative source of multipotent stem cells capable of differentiating into all three germ layers (Berry et al., 2015). In addition, they have been shown to produce a large number of cells compared to other adult tissues. This is achieved using minimally invasive surgical techniques and simple isolation protocols involving irrigation; and enzymatic agents to facilitate reproduction; centrifugation; and destruction of red blood cells (RBCs). This technique produces cell fragments consisting of several cell types. Among these, ADSCs are of particular interest because they adhere to the plastic surface of culture dishes and exhibit rapid proliferation, allowing for direct identification and isolation from other cell populations. Studies have shown that ADSCs can be induced to express glial cell markers such as S100B, GFAP, and the neurotrophin receptor P75 in vitro (Konno et al., 2013). However, it was found that differentiation of ADSCs into Schwann cells in vitro did not lead to significant improvement, likely due to the innate ability of ADSCs to differentiate into SCs in vivo. Furthermore, the researchers reported that ADSCs did not undergo differentiation into SCs in vivo, despite successful differentiation in vitro. Although undifferentiated ADSCs have been shown to produce neurotrophins, this occurs at low levels. Polycaprolactone conduits seeded with mesenchymal stem cells (MSCs) showed improved permeability and function compared to empty conduits (Yarak and Okamoto, 2010). Another research team used collagen conduits filled with collagen gel containing ADSCs, and their results showed that the improvements observed were comparable to nerve transplantation.

Umbilical Cord Mesenchymal Stem Cells

Despite ethical considerations regarding the use of umbilical cord stem cells (UC-MSCs) and limitations associated with their access, there is evidence to suggest their advantages over other adult cells of various origins: First, the stem cells can be harvested in large quantities. Quantities that are not harmful to the donor, as they are obtained from tissue discarded after birth; second, because they are obtained during pregnancy, the risk of genetic damage is significantly reduced (Bongso and Fong, 2013); Third, they have a smaller biological profile than other adult stem cells, allowing them to undergo more mitotic divisions and be cultured to a greater extent; Fourth, although they do not express HLA-II, their immune properties are less pronounced compared to other mature cells. Furthermore, tubular cells that arise from UC-MSC differentiation have been shown to facilitate axonal regeneration (Mebarki et al., 2021).

Immunomodulatory Effects of MSCs in PNI

PNI triggers a series of inflammatory responses in host cells, leading to alterations in cell morphology and immune-related factors. Current immune signaling factors include interleukin-1 (IL-1 α , IL-1 β), IL-2, IL-4, IL-6, IL-10, IL-12, IL-13, IL-17, tumor-induced cytokines (TNF- α), HGF, nitric oxide (NO), human leukocyte antigen G5 (HLA-G5), and prostaglandin E2 (PGE2) (Li et al., 2022). Mesenchymal stem cells can produce a range of immune factors that affect responses to both autologous and allogeneic tissues, in addition to innate immune cells such as natural killer (NK) cells, neutrophils, macrophages, mast cells, dendritic cells (DCs), and immune cells derived from T and B cells. MSCs mediate their immune response through two primary mechanisms: paracrine secretion of cytokines, including IDO (in humans) or NO (in mice), PGE2, IL-4, IL-10, IL-12, IFN- γ , and TNF- α , as well as cell adhesion (Ge et al., 2019). The function of human MSCs (hMSCs) following injury is attributed to their secretion of bioactive molecules such as cytokines, chemokines, and growth factors, rather than their differentiation capability. Numerous studies indicate that many beneficial effects of stem cell therapy may stem from paracrine mechanisms. However, the immunomodulatory effects of MSCs in the context of PNI are still not well understood (Rufino et al., 2023).

Conclusions

To enhance nerve regeneration and improve sensory and motor recovery, the application of stem cells, particularly MSCs, is beneficial. These cells possess the capability to differentiate into Schwann cells in vitro and can also convert directly into SCs at the injury site. Additionally, manipulating stem cells can modulate the function of native SCs, alter inhibitory and excitatory states, promote myelination and cell survival, and enhance neurotrophic functions. In conclusion, MSCs, with their favorable characteristics such as ease of collection (especially adipose-derived stem cells) and low risk of immunogenic reactions, hold significant potential for improving the regenerative process. Consequently, further research may yield crucial advancements in MSCs' role in promoting nerve regeneration.

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Integrating Nanotechnology and Biotechnology into Sustainable Solutions in Healthcare

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Abstract

Nanobiotechnology provides disruptive approaches to diagnostics, medication delivery, surgery, and treatments, transforming healthcare. Innovative tools including nanomedicine, biosensors, and lab-on-nanoparticles offer early illness diagnosis and specific therapies. Nanotechnology additionally improves chemotherapy, surgical accuracy, and regenerative therapies, with advancements such as nanorobotics. Sustainable healthcare solutions use nanotechnology for the purification of water and bioremediation, which promotes ecological sustainability. Nanobiotechnology promotes high-performance, cost-effective goods, however, there are still issues with public acceptability and scalability. Safety regulations and multidisciplinary collaboration are crucial to address toxicological problems and ensure well-being. Considering the challenges, nanobiotechnology has enormous promise to overcome disparities in medical care, promote fitness equity, and propel worldwide health breakthroughs. Nanobiotechnology can optimize societal advantages by combining advances in science with public health policies, paving the way for an increasingly sustainable and accessible healthcare system.

Keywords: Nanobiotechnology, Healthcare, Nanomedicine, Sustainable Solution, Drug Delivery

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Introduction

Nanoscience is a hot issue in the realm of science, the majority of the continuing debates, definitions, and spotlight are centered on nanotechnology. Consequently, it is a wide phrase that embodies the pinnacle of man's insatiable need for knowledge with practical applications (Suhag et al., 2023). The word nanotechnology refers to any kind of technique that operates on the nanoscale and has real-world applications, such as using individual atoms and molecules to create functional structures. There are numerous present and predicted developments in nanoscale research and nanotechnology concerning applications in medicine, agriculture, energy electronics, and so on (Nasrollahzadeh et al., 2019).

Biotechnology, as the name implies, is a blend of biology and technology. Biotechnology, which is based on biological methods and genetic engineering, builds on these accomplishments by utilizing live creatures or their derivatives to develop novel solutions (Naz, 2015). Biotechnology is the combined use of biochemistry, engineering, and microbiology disciplines to accomplish technical or industrial use of the abilities of microbes and produced cells from tissues. The scope of its use covers everything from agriculture (Cropping Systems, Animal Husbandry, Soil Conservation as well as Soil Science, Seed Technology, Plant Physiology, Crop Management, and so on.) to industry (Pharmaceutical, Food Chemical, Textiles, Byproducts, and so on.), Cell Biology, Medicine, Environmental Conservation, and Nutrition, which makes it one of the most rapid expanding fields (Bhushan, 2017).

The combination of biotechnology and nanotechnology provides an exciting opportunity for scientific discovery, providing transformational answers to a wide range of medical concerns. (Patel et al., 2021). Nanobiotechnology has enormous potential in medicine to transform diagnostics, drug delivery, and treatments. Nano-sized materials and gadgets can travel the human body's complex pathways with remarkable accuracy, improving methodologies for imaging, allowing targeted medication administration, and aiding early illness diagnosis (Hassan & Fathi, 2024). In addition, advances in nanomedicine provide individualized therapies suited to specific genetic profiles, resulting in a new age of personalized medicine.

This chapter investigates the synergistic combination of nanotechnology and biotechnology to create novel and long-lasting solutions to healthcare concerns. It stresses how these multidisciplinary areas may help with essential concerns including illness diagnosis, therapy, medication delivery, and customized medicine. It focuses on the fundamentals of nanotechnology and biotechnology, outlining their distinct contributions to healthcare.

Fundamentals of Nanotechnology and Biotechnology

1. Principles of Nanotechnology

Nanotechnology is the field of science and engineering that involves the nanoscale creation, development, and applications of systems,

devices, and structures (Whitesides, 2005). The following are the main components of nanotechnology. Nanoparticles are the particles that have dimensions in between one and one hundred nanometres. They have distinctive physio-chemical properties that are not present in bulk material due to their size (Tang & Kotov, 2005). Localized Plasmon resonance can be considered as an example which allows the gold nanoparticles to display varying hues depending upon their size (Ghosh & Pal, 2007). Nanoparticles are utilized for drug administration, imaging, and diagnostic purposes due to their ability to cross the biological membrane and target specific tissues or cells (Barua & Mitragotri, 2014). Nanomaterials are those materials that have at least one nanoscale dimension and they can be moulded in many forms like films, nanoparticles, nanofibers, and nanowires. As per (Liu et al., 2012), these materials exhibit unusual catalytic, electromagnetic, and mechanical, properties. Carbon nanomaterials, like carbon nanotubes as well as graphene, exhibit unique mechanical, thermal, and electrical, characteristics (Patel et al., 2019). Metal oxide nanomaterials, such as quantum dots and zinc oxide nanomaterial, are used for energy storage, sensing, as well as catalysis (Figure 1) (Concina & Vomiero, 2015).

Nanostructures, such as nanoplates and nanorods, are another significant aspect of nanotechnology. The fabrication of nanodevices for the tasks of energy creation, electronics, and photonics primarily relies upon nanostructure (Yu et al., 2012). Scientists may create new goods with greater durability by manufacturing materials at the level of the nanoscale, and their potential uses include health, electronics, agriculture, and safeguarding the environment (Ragesh et al., 2014).

2. Principles of Biotechnology

Biotechnology is the use of biological materials such as cells and molecules to create technologies and products which help humanity. In the words of (Gvrilescu & Chisti 2005), this discipline is related to molecular biology, genetics, and biology. It includes biological molecules, which are vital in different fields such as bioprocessing and genetic engineering (Bhardwaj et al., 2019). For instance, with the use of Recombinant DNA technology, it is feasible to synthesize insulin by inoculating the insulin gene from humans in a bacterial cell, which produces a large amount of it (Bhoria et al., 2022). This discipline employs cell culture techniques to produce helpful goods such as vaccines and monoclonal antibodies (Javanmard, 2023). Along with this stem cells hold significant beneficiary results in tissue engineering and regenerative medicines (Gomez-Cid et al., 2021). Biotechnology takes control of biological systems to produce useful products (McCarty & Ledesma-Amaro, 2019). For instance, metabolic engineering deals with altering the metabolic pathways of microorganisms to enhance the synthesis of desired products like industrial enzymes, biofuels, and antibiotics (Intasian et al., 2021). Synthetic biology deals with the creation of novel biological elements and systems that have applications in environmental sustainability, agriculture, and medicine. Biotechnology addresses challenges in business, agriculture, and the health sector by utilizing biological processes and living things such as proteomics, metabolomics, and genomes, which accelerates the field's development.

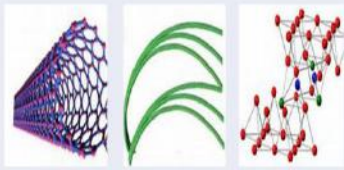
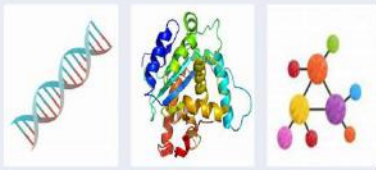
	Nanotechnology	Biotechnology
Scale of Materials	~1 to 100 nm (with a few examples in the 100 to 300 nm range)	Modification of: biomolecules (0.3 to 15 nm) Engineering of: viruses (100s of nm), bacteria (1 to 3 µm), animal and human cells (10 to 25 µm), plant cells (10 to 100 µm)
Materials		
Applications	Medication and drugs, nanofabrics, energy, cosmetics, nanobiotechnology, optical engineering, defense and security	Medical diagnosis, fermentation technology, pharmaceuticals, agriculture, improvement in food technology, environment and energy management, recombinant DNA technology

Fig. 1: Difference between biotechnology and nanotechnology (Mehta, 2013).

3. Intersection of Nanotechnology and Biotechnology: Nanobiotechnology

A new multidisciplinary field called nanobiotechnology has evolved by combining nanotechnology and biotechnology. This field of study combines biological elements with nanoscale materials, systems, and methods to bring novel approaches to agricultural, environmental, and healthcare issues. Nanobiotechnology is primarily concerned with the manufacture and application of nanoscale chemicals to regulate, modify, and analyse biological processes (Singer et al., 2018). This method allows researchers to create hybrid systems with improved functionality and features (Castillo et al., 2017). Nanobiotechnology applications include nanoscale devices for drug delivery (Dendrimers, liposomes, and polymeric nanoparticles), as well as biosensors for the engineering of tissues as shown in Figure 2. These strategies enable controlled release, minimal side effects, and optimal medication absorption. Doxil (liposomal doxorubicin), a type of nanocarrier employed in cancer therapy, targets tumor cells while protecting healthy tissues (Kaasgaard & Andresen, 2010). Gold nanoparticles and quantum dots serve as biosensors for detecting environmental contaminants, diseases, and biomolecules. Diseases can be detected early using nanomaterials. In lateral flow assays (like the COVID-19 rapid tests), gold nanoparticles are utilized to visualize test results. (Huang et al., 2020).

Polymers, ceramics, and composite materials are utilized to synthesize nanostructured scaffolds that allow cell growth, proliferation, and differentiation by engaging with extracellular matrix. This field is also necessary to form 3D-printed tissues and organs (Rana et al., 2017).

Nanoscale and nanorobots are examples of nanoscale materials that are used to address diseases at different levels of cellular organization. Like gold nanoparticles are used in photothermal therapy to kill cancerous cells (Vankayala et al., 2014). By modulating the nanocarriers to target specific cells or tissues, harmful effects can be lessened, and therapeutic efficacy can be increased. According to (Morais et al., 2014), nanomaterials offer more effective electro-mechanical and optical qualities which help in the synthesis of revolutionary biomaterials, devices, and techniques.

However, nanobiotechnology has revolutionized medical research but this field has some safety, ethical, and environmental issues too. Therefore, is essential to carefully examine the toxicity level of these nanomaterials along with their effects on mankind and the environment. For this purpose, regulatory frameworks are being developed (Ahmadi & Ahmadi, 2013).

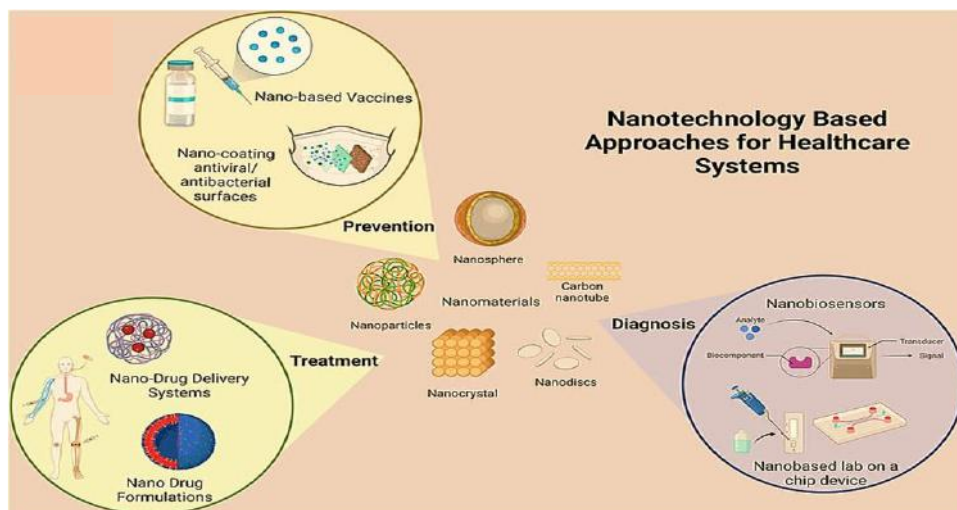


Fig. 2: Diagrammatic representation of nanotechnology-based approaches for healthcare sustainable solution systems (Pokrajac et al., 2021). The figure was created using the Bio Render online tool.

Applications of Nanobiotechnology in Healthcare

Nanobiotechnology has a vast impact on different healthcare sectors. Nowadays, scientists are trying to employ nanoparticles in diagnostics, drug delivery or development, and therapeutics (Table 1).

1. Nanotechnology and Surgery

Researchers are developing nanorobotics (NRBTs) in surgery to improve surgical performance. NRBTs are nanoscale devices that can perform surgery with more accuracy. Surgical nanorobotics is the creation and use of small robots or nanorobots capable of performing surgical operations with great precision and efficiency (Yoon & Kim, 2020). NRBTs may carry out cellular surgeries on a neuron and single dendrite without compromising neurons in a complex network. The well-controlled nano-scissor functionality of NRBTs was confirmed in an animal model (Mazumder et al., 2020). Similarly, nano-bioelectric medicine (NBOE) has been incorporated into surgery. NBOE uses electrical impulses to boost the body's healing systems. NBOE may be used in cancer, cardiovascular diseases, and other problems in the body (Zhang et al., 2022). Implantable medical nanogenerators (IMNGs) were recently brought to the market. IMNGs are nanosensors that use mechanical power from body motions to produce electrical energy. Implanted IMNGs may power a wide range of medical devices, including medication delivery systems, pacemakers, and neurostimulators (Malik et al., 2023).

2. Nanotechnology and Cancer

Nanoparticles (NPs) can carry hundreds of specific anti-cancer compounds to tumor sites. When investigating the links between the usage of NPs and cancer, it is necessary to investigate the tumor diagnosis and treatment strategies linked with nanotechnology (Souri et al., 2022). The focus is on improving chemotherapy medicines' pharmacokinetics and pharmacodynamic properties, as well as their tumor-targeting efficacy. Similarly, NRBTs can be coupled with many gene therapies against cancers (Chouhan & Rangi, 2023). Several innovative nanomedicines have been authorized by globally known health agencies, such as the Food and Drug Administration and the European Medicine Agency (EMA) (Kumar et al., 2021). Figure 3 further summarizes several applications of nanotechnology and biotechnology in healthcare.

Sustainable Solutions in Healthcare Using Nanotechnology and Biotechnology

1. Environmental Sustainability

Bioremediation is the process of utilizing living organisms like fungi, bacteria, and plants to reduce the toxicity of soil. It is a green as well as cost-effective methodology for the treatment of polluted environments. This methodology can enhance its efficiency by integrating with nanoparticles. It has been found that nanoparticles have the efficacy to enhance the remediation process (Usman et al., 2020). Nano-remediation is a sustainable method that helps reduce contaminants within the soil using different mechanisms present in the nanotechnology discipline. For example, various types of nanoparticles such as iron oxide and nano zero-valent iron (nZVI) have been highly employed in bioremediation due to their high action towards the strength of very strong pollutants even including chromium Cr (VI) because of their higher activity (Luo et al., 2021). The use of nanocomposites like Fe₃O₄/biochar neutralizes harmful contaminants by boosting this process with the dehalogenation and dichlorination of organic pollutants (Usman et al., 2020). The

bioremediation process also played a great role in water purification. The utilization of nanoparticles removes pathogens and organic pollutants. For instance, magnetic nanoparticles can remove dye effectively, and nano-absorbents, such as activated carbon and silica gel, provide very cost-effective solutions for water purification (Ali et al., 2020).

Table 1: Applications of Nanobiotechnology in the Healthcare sector

Application	Examples	Explanation	Reference
Diagnostics	Biosensors	Highly sensitive biosensors that can identify even trace amounts of biomolecules in physiological fluids like blood and urine have been made possible by nanotechnology, which can help with early illness identification and treatment.	(Malik et al., 2023).
	Nanopore sequencing	An innovative technique that detects DNA or RNA molecule sequences using nanopores, enabling quick and precise diagnosis of genetic illnesses and cancer.	(Y. Wang et al., 2021).
	Nanomedicine	It can be utilized in both in vitro (via nanodevices at the subcellular level, with samples prepared from human tissue, cell culture, and body fluids) and in vivo diagnostics. In vivo diagnostics, the nanomedicine approach is being used to develop devices capable of working, responding, and modifying within the human body with the sole purpose of early diagnosis of any irregularities in the human body that could lead to toxicity or tumor development events.	(Malik et al., 2023).
	Lab-on-nanoparticles	Tiny devices that can perform multiple functions (drug delivery and diagnostics). These tiny devices are made up of nanoparticles that can detect changes in the body.	(Welch et al., 2021).
Pharmaceuticals	Nano-based drug delivery systems	Nanoparticles can deliver drugs to target sites; they can also enhance in vivo drug stability, solubility of drugs, and absorption/distribution of drugs in the body.	(Oroojalian et al., 2020; Sahu et al., 2021).
	DNA-based drug delivery systems	DNA guns and DNA vaccinations are two examples of DNA-based medication delivery systems that have been developed in recent years. These DNA-based systems enable molecules and nanostructures to self-assemble, improving therapeutic targeting and lowering the toxicity of drugs.	(Liu et al., 2023).
Therapeutics.	Gene therapy	Polyplex micelles are advanced self-assembled nanoscale structures of two cationic polymers containing small interfering RNA (knockdown genes) or plasmid DNA (carry therapeutic genes). Pancreatic adenocarcinoma is among the tumors for which these polyplex micelle-based therapeutic approaches have been studied.	(Salameh et al., 2020; Uchida & Kataoka, 2019).
	Bone regeneration	Nanoparticles can be utilized to make scaffolds that resemble bone structures, which can help direct the formation of new bones and promote bone regeneration. Similar research is being done to create prosthetic joints and nanoscale coverings for knees and hips that imitate collagen and work to stabilize the osteoblasts' process of forming new bone.	(Z. Wang et al., 2021; Wen et al., 2023).
	Regenerative medicine	Nano assemblies' potent tissue regeneration capabilities have significantly improved tissue repair. These technologies are focused on mechanical processes that start tissue regeneration, such as cellular adhesion, migration, and differentiation.	(Malik et al., 2023).

This bioremediation process is also utilized for the treatment of wastewater in which solid waste causes pathogenic organisms to flourish in it due to a rich quantity of carbohydrates and proteins. Efficient microorganisms such as lactic acid bacteria can make wastewater break down fast by triggering mechanisms of fermentation and composting, and this technique becomes extremely powerful in treating wastewater (Shahcheragh et al., 2022). In addition to this, *Streptomyces* sp. Z38 has been identified as an effective agent for the degradation of heavy metals and biodegradation of organic pollutants through the production of silver nanoparticles that help in the bioremediation process (Costa et al., 2020). Besides, water purification is also boosted by the improvement of filter efficiency such as graphene-based carbon nanotubes and carbon channels that help enhance water permeability besides improving the rate of removal of pollutants (Lohrasebi and Koslowski 2019). Copper nanoparticles play a very crucial role in the purification of wastewater if combined with other materials like Polyethylene Terephthalate filters and Polyacrylonitrile nanofibers. They are antimicrobial in nature and offer significant synergistic effects (Bashir et al., 2021). In nanotechnology, these advancements represent a very important step toward more sustainable, efficient, and cost-effective remediation processes.

2. Economic Sustainability

Various sectors of the economy such as energy, medicine, manufacturing, nanotechnology, and biotechnology have the potential to drive significant improvements by enhancing the performance of products along with reducing costs. As a consequence, there is an increasing requirement for quantitative data to evaluate the economic impact of nanotechnology to direct policymakers, decisions, and investment strategies. The integration of nanostructures and the fundamental understanding of applying nano methodologies to technological innovations can direct the establishment of more reasonable products with greater performance (Zucker and Darby, 2005). However, the economic implications of this field remain underexplored, as most economic insights into nanotechnology are based on experiences with earlier technologies. While new applications of existing technologies often have higher initial costs, they are eventually offset by enhanced performance and cost reductions in the long term. The implementation of nanotechnology is expected to follow a similar pattern, where substantial

investments in new production facilities, equipment, and raw materials will lead to higher initial costs, which will decrease as economies of scale are achieved. Furthermore, evaluating nanotechnology's economic impact goes beyond traditional research metrics, such as the number of published papers and patents, to include factors like job creation, manufacturing cost reduction, and the development of new products and services. These factors are important in understanding how nanotechnology can play a great role in the growth of the economy and industry (Morse, 2012).

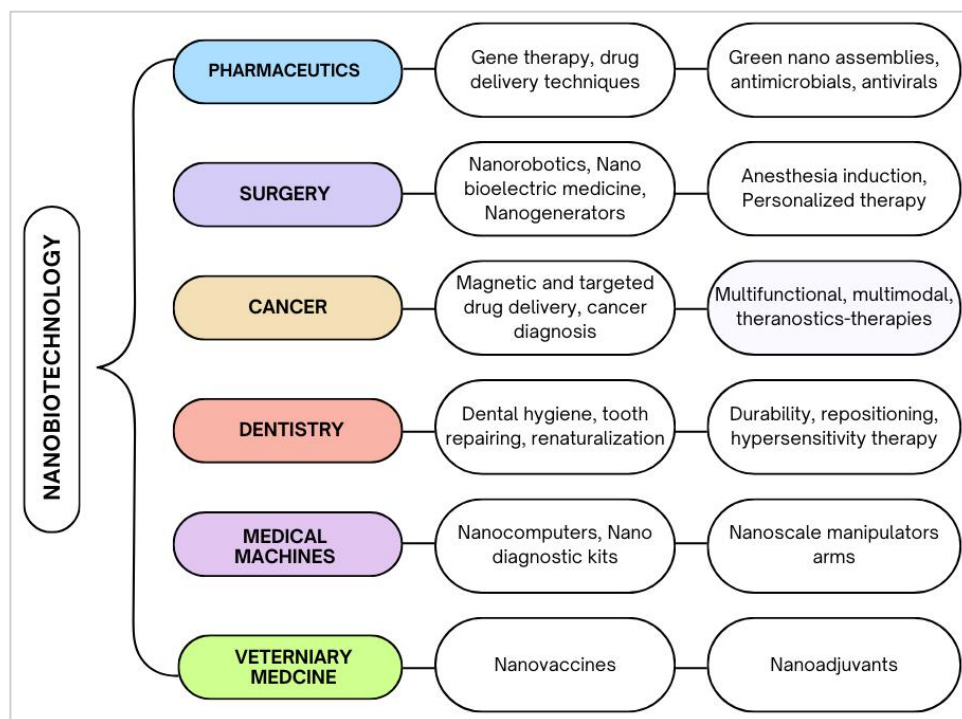


Fig. 3: Flowchart displaying a summary of several applications of nanobiotechnology

In the advancement of nanotechnology, public investment is crucial as it supports fundamental research and addresses societal challenges like environmental and healthcare concerns. It accelerates the commercialization of novel techniques. However, there are many challenges in evaluating the economic impact of nanotechnology. This includes the versatile nature of technology, the challenge of isolating its contributions from other different technologies and its contributions from those of other technologies, and the complexity of collecting correct data because of the established information of business (Babatunde et al., 2019). Moreover, the longer cycle between investments and returns hinder the analysis of the economic value of nanotechnology. To overcome these problems, a proper combination of quantitative and qualitative measures like life cycle analysis, cost-benefit analysis, and markers of research along with developmental investment are necessary for the analysis of the economic impact of nanotechnology. Above that, public acceptance is of great importance in the realization of nanotechnology applications wherein there is a possibility that their commercialization could be stifled by the lack of public trust and interest not only for high-value low-risk products but also beyond. Therefore, proper strategy assessment of nanotechnology has to be undertaken to ensure that it will share significant economic and societal gain throughout its lifetime (Zucker and Darby, 2005).

3. Social Sustainability

Safety in nanotechnology is a very serious issue. There is widespread uncertainty around the possible risks and benefits of nanomaterials, particularly in environmental and medical settings. This uncertainty extends across various sectors, complicating the evaluation of risks associated with new technologies. Unlike more traditional fields, where risk calculations can be more precisely made such as in toxicology, where dose effects are measurable, nanotechnology involves risks that are harder to quantify. Many of these issues, including concerns about the safety of nanomaterials, may only be fully understood through large-scale population studies, such as longitudinal cohort studies or big data analyses, which can help clarify long-term effects (Oluwoye, 2015). As nanotechnology advances in sectors like agriculture (Pramanik et al., 2020), water purification (Sahu et al., 2021), healthcare (Patel et al., 2015), and environmental bioremediation, its potential to improve lives is clear (Babatunde et al., 2019). Even though these innovations also come into existence with great responsibilities for private sectors, governments, and the public to guarantee their secure and moral consumption.

The societal controversy surrounding the development of new technologies, such as GMOs, has historically impacted on the commercialization of these products. Fears of unplanned consequences and public debates on following the introduction of GM crops, have directed to refusal or slow implementation of such technologies in various regions of the world (Dale, 2004; Hall, 2007). Likewise, the safety concerns of nanotechnology products including nutritional supplements, cosmetics, and drugs are expected to influence their approval. For successful commercialization, the understanding of societal responses to nanotechnology is very important. As with previous technologies, factors including demographic variables (age, education, gender, income), level of awareness, and concerns about safety, health, environmental impact along with sustainability play major responsibility in determining public discernment and acceptance (Gupta et al., 2015; Rahim et al.,

2015; Ganesh Pillai and Bezbaruah, 2017). To facilitate the responsible introduction of nano-biotechnologies, stakeholders must address these concerns by providing transparent information about potential risks and benefits ensuring that public safety remains a priority (Figure 4).

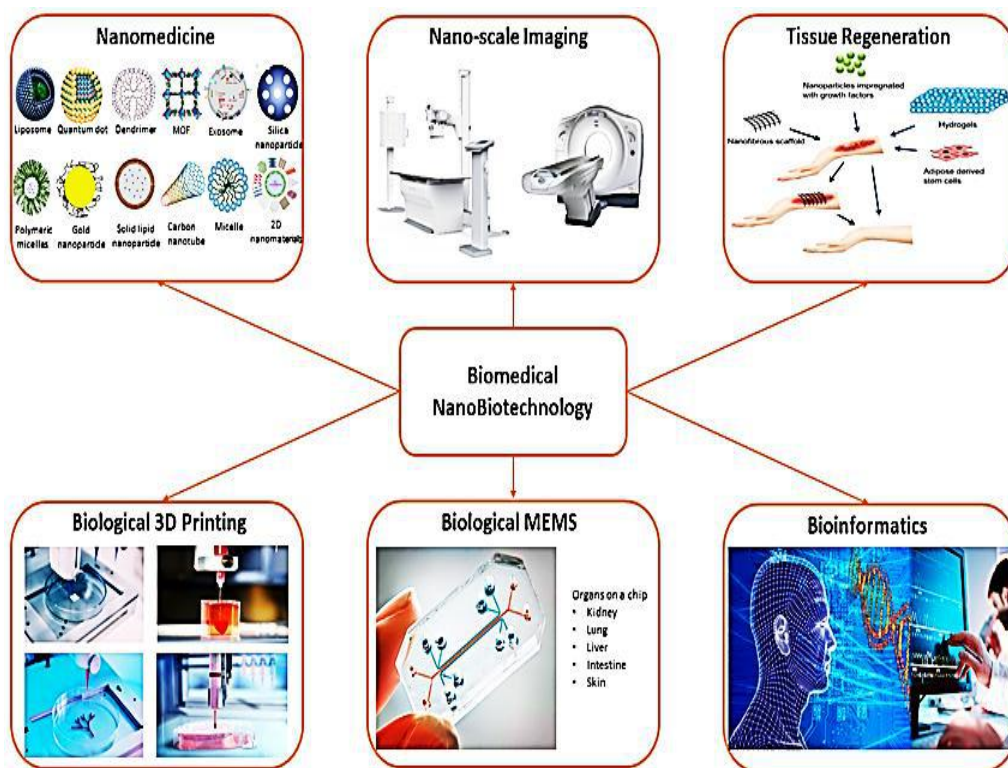


Fig. 4: Sustainable solutions of nanobiotechnology in the healthcare system (Al Sharabati et al., 2022).

Challenges and Future Directions

In recent decades, nanotechnology has received a lot of attention due to its groundbreaking and omnipresent nature. Despite the massive government-aided investment in nanotechnology-based goods, the concurrent industrialization of these systems is not gaining the same momentum. The technology, nevertheless, addresses the unfulfilled requirements of the pharmaceutical sector, such as modifying the formulation of medication to enhance their bioavailability, solubility, or toxicity profiles, to be evidenced by the broad range of outstanding research publications that appear across different scientific newspapers and journals (Kaur et al., 2014). The primary obstacles in promoting of these nanotechnology innovations may be classified as:

1. Insufficient system of regulation
2. Lack of appreciation and acceptability from the public, physicians, and industry
3. Developmental challenges include scalability, repeatability, characterization, quality assurance, and appropriate translation.
4. Toxicological concerns along with safety profiles
5. Lack of interdisciplinary platforms
6. Inadequate intellectual property security

Despite encouraging breakthroughs in experimental animal models, the clinical implementation of nanomedicines is still a lengthy, biased, and frequently unsuccessful process. Specified methods are absent, and the identification of materials and biological processes, as well as statistical evaluations that are frequently used, are typically insufficient. Furthermore, the wide and considerable variability of models used, refusal to share data, and inaccuracies in research design have impeded the advancement of nanomedicines into the final clinical investigation phases. In contrast, contradictory results discovered between published and industry-obtained information along with the difficulty in locating acceptable commercial collaborators owing to the problematic voids in translation have led to the abandonment of future investigations. The overall success rate in cancer clinical studies reduces from 94% in phase I to 48% in the second stage and 14% in the third phase. The practical use of nanomedicine is heavily reliant on the thorough and painstaking evaluation of related characteristics, as tiny modifications to chemistry or manufacturing procedures can cause significant modifications in tolerability and biodistribution (Đorđević et al., 2022).

The United States regulatory assessment procedure for nanotechnology and biotechnology goods works in tandem. The two systems contain data controls, security endpoints, as well as actors regulated by comparable or identical groups, laws, and rules. In both nanotechnology and biotechnology, the industry is frequently the primary developer and broadcaster of safety research for regulatory bodies as well as the general public. This might result in skewed information, whether intentional or not, indicating an infringement of integrity. The pre-market research is frequently not necessary, notably for genetically altered foods (per FDA policy) and nanomaterials with similar molecular formulae to existing chemicals. If no obligatory pre-market regulatory clearance procedures exist, negative health impacts from nanoparticles are unlikely to be evaluated. This absence of need could give rise to a violation of equality, as vulnerable communities are, by definition, disproportionately impacted by harmful health impacts (Kuzma & Besley, 2008).

Multidisciplinary groups creating nanomedicines by linking material science, novel platform evaluation, and models of disease more

effectively akin to desired medical conditions, whereas influencing the present regulatory structures according to science-based norms, will undoubtedly produce the data needed to grant marketing approval for the disruptive innovations demanded to address the world's remaining gaps for treatments and health care (Đorđević et al., 2022). The possibilities for using nanomedicine to enhance health are endless. Incorporating public health skills is critical for maximizing benefits in both population and individual health. This effect on nanomedicine research will aid in identifying the most pressing areas for technical innovation, determining how to optimally allocate resources, and shaping policies to safeguard both the environment and humans. Adopting an integrated approach to nanotechnology education and research will effectively enhance the status of the knowledge, leading to a higher return upon investment benefiting the general population. The study and creation of innovative nanomedicine uses, linked with wellness concepts, will revolutionize the wellness of people worldwide (Pautler & Brenner, 2010).

Conclusion

The combination of nanotechnology and biotechnology transforms healthcare by introducing inventive, novel, and sustainable solutions. Nanobiotechnology blends precision and biological variety to provide personalized therapies, enhanced treatment, and early detection. Biodegradable nanoparticles reduce trash and toxicity, improving sustainability. Expandable solutions improve accessibility, hence promoting wellness equity. Scalable solutions offer a link to global medical professionals and other stakeholders. However, ethical problems, legislative barriers, and future safety implications must be addressed. Collaboration among policymakers, researchers, and stakeholders is critical for overcoming these obstacles and realizing the full promise of nanobiotechnology.

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The Role of Nanotechnology and Biotechnology to Reduce Male Infertility: Novel Solutions for Complex Challenges

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Abstract

Infertility is the failure of a couple to conceive after a year of unprotected sexual activity. Male infertility is the failure of a male to conceive a female after at least a year of consistent, unprotected sexual activity. There are various causes of male infertility. Males may be the only cause of infertility in 20% to 30% of cases, with a 50% overall contribution in couples. Some infertile couples are still able to conceive if they do not receive treatment. Various treatments for male infertility include lifestyle changes, oral medications, hormonal therapies, gonadal treatments, and other options. The VF and ICSI treatments for male infertility primarily target sperm malfunction but often overlook underlying genetic, epigenetic, or physiological issues. However, advances in biotechnology and nanotechnology have opened new avenues for more effective and targeted therapies. Biotechnology is essential to developing gene therapies, regenerative medicine, and diagnostic tools to provide individualized treatments for male infertility. With its exceptional capacity for molecular-level interaction, nanotechnology has the potential to improve medicine delivery, minimize adverse effects, and improve sperm function. This chapter examines how these state-of-the-art technologies can be used to diagnose, treat, and possibly cure male infertility, emphasizing these technologies' difficulties and therapeutic uses.

Keywords: Male infertility, Biotechnology, Nanotechnology, Sperm function, Gene therapy.

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Introduction

Infertility is the inability of a couple to conceive after a year of consistent, unprotected sexual activity (Practice Committee of the American Society for Reproductive Medicine, 2020). In the United States, infertility upsets almost 15% of couples (Thonneau et al., 1991; Louis et al., 2013). Male infertility refers to the failure of a male to achieve pregnancy with a female partner after at least a year of consistent defenseless intercourse. Male factors are the cause of about 20% of infertility cases and contribute to an additional 30–40% of cases (Hull et al., 1985; Agarwal et al., 2015). Overall, male factors account for around 50% of all infertility case's (Schlegel et al., 2021). The WHO defines normal semen parameters, as outlined in Table 1 (Cooper et al., 2010).

Table 1: Normal semen parameters in accordance with WHO

Parameters	Values	95% CI
Volume	1.5 mL	mL 1.4–1.7
Sperm Morphology	4% Normal	3–4
Sperm vitality	58% alive	55–63
Concentration of Sperm	15 M spermatozoa/mL	12–16
Number of sperm/ejaculation	39 M spermatozoa	33–46
Progressive motility	32%	31–34
Progressive and nonprogressive sperm motility	40%	38–42

1.1 Etiology

Male infertility can arise from various causes. Primary testicular defects, including irregular sperm parameters, account for 65% to 80% of cases. Endocrine disorders, typically resulting from hypogonadism, contribute to 2% to 5%, while sperm transport disorders represent about 5%. Idiopathic infertility, where the male has normal semen parameters but remains infertile, makes up 10% to 20% of cases (Winters & Walsh, 2014).

1.2 Epidemiology

Globally, around 13% to 15% of couples experience infertility, with 1 in 5 couples unable to conceive within their first year of trying (Esteves et al., 2011). However, even without specific treatment, nearly half of young couples in the United States who do not conceive through their initial year of sexual activity will be able to conceive within the following year (Evers, 2002). Male factors are the sole cause of infertility in 20% to 30% of cases and contribute to about 50% of infertility cases overall (Agarwal et al., 2015).

1.3 Pathophysiology

Male infertility can be classified into the following categories:

- Pre-testicular causes: These include chromosomal abnormalities, genetic factors, retrograde ejaculation, anejaculation, hypogonadotropic hypogonadism and erectile dysfunction.
 - Testicular syndromes: Examples comprise orchiectomy, primary testicular dysfunction, cryptorchidism, and atrophic testes.
- Post-testicular causes: These involve seminal tract obstructions, post-vasectomy complications, congenital lack of vas deferens, premature ejaculation, erectile dysfunction, plus the usage of condoms or diaphragms (Leslie et al., 2024).

Treatment

Some infertile couples can still achieve pregnancy without treatment (Figure 1). Research shows that 23% of infertile pairs conceive within two years without intervention, and this percentage increases to 33% after four years (Matorras et al., 1996).

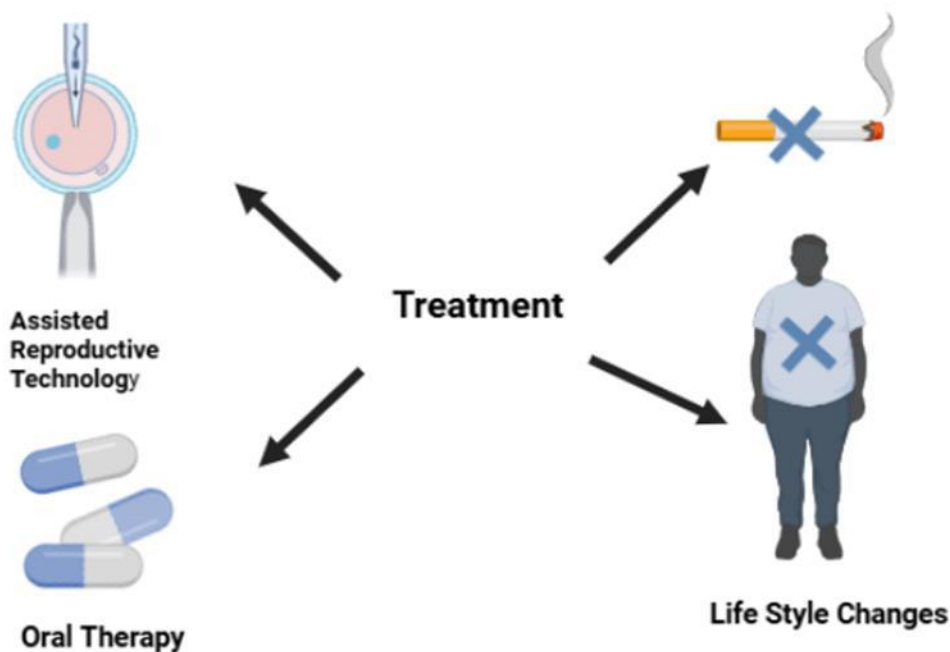


Fig. 1: Ways of Treating Male Infertility (Biorender)

2.1 Lifestyle Changes

Lifestyle changes that may improve male fertility include leaving smoking, decreasing or eliminating alcohol drinking, adopting a healthier diet, losing weight if overweight, increasing physical activity, avoiding harmful artificial lubricants throughout intercourse, decreasing stress, stopping recreational and illegal drug usage (such as marijuana), limiting prescription medications, and minimizing contact to pesticides, heavy metals (like boron, mercury, lead, and cadmium), and excessive chemicals (Penzias et al., 2018). While the exact impact of these factors on male infertility remains uncertain, it is reasonable to assume that maintaining a healthy lifestyle can enhance overall male fertility (Sharma et al., 2013).

2.2 Oral Therapies

In addition to being cost-effective, these therapies may provide psychological benefits. There is sufficient evidence suggesting potential advantages to justify clinical exploration for infertile men who cannot afford alternative treatments or are not suitable applicants for them. Such cures also allow physicians to offer a form of "treatment" while giving the pair more time to achieve a natural pregnancy (Whitten et al., 2006; Chua et al., 2013). Oral treatments are deliberated optional and are categorized into nutrition-based, antioxidant-based, and hormonal therapies.

While some studies present conflicting results, reducing oxidative stress on sperm and semen through antioxidant therapy appears to be a promising approach for treating male infertility (Qamar et al., 2023). However, in a three-year, multi-institutional trial involving 174 infertile men across nine reproductive centers, antioxidant therapy without L-carnitine did not lead to important improvements in semen parameters or pregnancy rates over a six-month observation period (Steiner et al., 2020). Despite this, additional key findings support using antioxidants in male infertility treatment.

The most extensively considered vitamins, antioxidants, and minerals, include coenzyme Q10, lycopene, N-acetyl cysteine, folic acid, L-carnitine, vitamin C, vitamin E, selenium, and zinc. Hormonal therapies, which are considered optional, include clomiphene, tamoxifen, and aromatase inhibitors.

2. 3 Sperm Abnormalities and Suggested Treatment

2.3.1 Standard semen analysis or Normospermia (15 million sperm/mL)

Men with standard semen analysis may also have an infertile spouse or idiopathic male infertility. In these cases, assisted reproductive technologies like IVF combined with ICSI should be used (Sunder & Leslie, 2022).

2.3.2 Low Motility or Asthenozoospermia

N-acetyl cysteine and L-carnitine can considerably increase sperm morphology and motility. Other cures include condom use to decrease exposure, immunity suppress steroid treatment for both spouses, and specific sperm processing for direct use in IUI (Sunder & Leslie, 2022).

2.3.3 Low Morphology or Teratozoospermia

N-acetyl cysteine and L-carnitine improve the morphology of isolated sperm. IVF with ICSI, may also be viable cure options (Sunder & Leslie, 2022).

2.3.4 Low sperm count or Oligozoospermia, (<15 million sperm/mL)

Hormone levels, including FSH, testosterone, LH, and prolactin, should be assessed. Low testosterone go along with by high LH and FSH may indicate Klinefelter syndrome, particularly if both testes are small. In these cases, karyotyping is suggested. If karyotyping results are normal, ART, including IVF with ICSI, should be used (Sunder & Leslie, 2022).

2.4 Gonadotropic Therapy

Gonadotropin therapy for men with idiopathic infertility remains a topic of debate. A meta-analysis of six randomized trials showed higher pregnancy rates with this therapy related to placebo (Finkelstein et al., 2013). While FSH promotes Sertoli cell action and sperm manufacture, its effectiveness is limited when used alone (Santi et al., 2015).

Effective gonadotropin therapy typically involves a combination of HCG, LH, FSH, GnRH, and HMG. For men with idiopathic hypogonadotropic hypogonadism (IHH), exogenous testosterone supplementation is discontinued. Treatment for male infertility in IHH has been successfully achieved using groupings of HCG, FSH, GnRH, and HMG.

Medications to accelerate the recovery of spermatogenesis are recommended in cases of delayed or prolonged recovery, older patients, individuals with azoospermia, and those with extended testosterone use. HCG, FSH, and SERMs are commonly used to stimulate the testes to produce endogenous testosterone naturally. Amongst these, as clomiphene in aiding sperm recovery, tamoxifen may not be as active.

2.5 Assisted Reproductive Technologies

Assisted reproductive technologies (ART), like as in vitro fertilization (IVF), intrauterine insemination (IUI), and intracytoplasmic sperm injection (ICSI), deliver traditional solutions for male infertility. These practices efficiently manage conditions like oligospermia and azoospermia, and poor sperm motility. For azoospermia (obstructive and non-obstructive), surgical sperm retrieval methods enable the usage of viable sperm.

Cryopreservation, artificial gametes, nanotechnology-based sperm organization, and gene-editing technologies improve ART's achievement. Together with hormonal treatments, antioxidant supplementation, and lifestyle adaptations, these improvements offer targeted treatments for male infertility, improving effective conception while decreasing the emotional burden on affected individuals (Jain & Singh, 2025).

3. Limitations of Male Infertility Treatments

IVF and ICSI treatments for male infertility primarily address sperm dysfunction but often fail to address underlying genetic, epigenetic, or physiological factors. Invasive sperm retrieval methods, such as TESE, do not resolve genetic abnormalities in sperm, which may compromise embryo quality and pose risks to the health of offspring. Hormonal therapies can be costly, have side effects, and require multiple cycles, making them emotionally and physically demanding for patients (Mehta et al., 2016).

4. Application of Nanotechnology in Treatment of Male Infertility

The fascinating multidisciplinary topic of nanotechnology is concerned with altering specific, size-dependent qualities at the nanometer scale (1–100 nm). Their ability at nano scale to manipulate and alter matter's behavior is unparalleled. Proper material control can be used to manage and improve solubility, targeted release, and other important features. The development of nanoscience has had a significant impact on several scientific fields, most notably medicine.

Nanoparticles (NPs) offer a treatment for infertility in couples due to their long and load-carrying ability. They have shown promise in reproductive medicine, preserving fertility, diagnosing and treating infertility, puberty, menopause, STIs, and reproductive tract malignancies (Baig et al., 2021).

4.1 Nanoparticle-mediated L-carnitine Transfer

Male infertility impacts 40% of couples, and L-carnitine (LC) is considered a potential treatment. However, traditional LC supplementation faces limitations due to absorption issues. This study examines the usage of nanoparticles to enhance the transfer and efficiency of LC in male

fertility treatments. While there are challenges related to safety and scalability, nanoparticle-based LC delivery shows promising potential for future clinical applications (Moghadam et al., 2024).

4.2 Antioxidant Nanoparticles

Antioxidant nanoparticles can improve sperm function and male fertility. Cryopreservation increases oxidative stress in sperm cells, which decreases the capacity for fertilization. Cerium oxide (CeO₂) NPs can act like reactive oxygen species (ROS) and accumulate oxygen keep sperm viability in cooling. This improves motility, enhance sperm velocity, and keeps both plasma membranes and DNA integrity protected, boosting efficiency in small sheep farms that use liquid-cooled semen (Khalil et al., 2018).

Nano-selenium (SeNPs) has also been utilized as a ROS scavenger to defend sperm cells from oxidative stress. It increases semen quality subsequently thawing and decrease oxidative damage in semen of rooster. Oral supplementation of SeNPs defends spermatogenesis from oxidative stress due to an anticancer drug, cisplatin (Safa et al., 2016).

4.3 Transfer of Functionalized Materials through Sperm-transported Nanoparticles

Nanotechnology is progressively being used to develop Nano platforms for transferring biological materials to cells or particular tissues. These treatments hold important potential for improving assisted reproductive technologies in farm animals. The distinguishing features of sperm cells, including their motility, limited intracellular uptake, and capacity to interlink with various compounds, have enhancing research into using nano carriers to effectively load sperm with proteins and nucleic acids. Studies have confirmed that polyvinyl alcohol (PVA)-Fe₃O₄ and PVA-Eu₂O₃ nanoparticles can be burdened into bovine sperm cells devoid of affecting their motility or acrosome integrity. Moreover, mesoporous silica nanoparticles (MSNPs) carrying fluorescent nucleic acids or proteins can interrelate with sperm membranes while preserving normal function. These results could pave the way for generating diagnostic and therapeutic tools targeted at enhancing sperm quality and treating male fertility issues (Ben-David Makhiluf et al., 2006; Makhiluf et al., 2008; Barkalina et al., 2014).

4.4 Controversies Surrounding the Usage of Nanotechnology in Reproductive Medicine: Environmental Effect of Nanoparticle Dispersal and Reprotoxicity"

Metal oxide nanoparticles (NPs), are gradually used in everyday life, including electronics, cosmetics, and food packing. There are ecological worries about their dispersion and distinctive biological effects on living organisms. Zinc oxide NPs have been revealed to apply cytotoxic action on murine testicular germ cells, affecting the maturing procedure of sperm in the epididymis (Talebi et al., 2013). Silver NPs are a possible cytotoxic cause for sperm cells, causing oxidative stress and reducing the achievement rate of in vitro fertilization (Yoisungnern et al., 2015). Exposure to TiO₂NPs can cause decrease in sperm production, testicular toxicity, and sperm lesions in mouse testes (Hong et al., 2015). AgNPs and Gold are widely used metal NPs, with the administration of AuNPs in mice causing an important decline in motility and normal morphology of sperm, chromatin remodeling, increased DNA damage, and lower chromatin stability. TiO₂NPs can cause DNA damage in male mice and affect the potency of male offspring after maternal exposure. Other metal NPs, CeO₂NPs, and dimercaptosuccinic acid-coated maghemite do not affect ram or bull sperm function or structure when added *in-vitro*.

4.5 Additional Challenges in the Practical Application of Nanoparticles

Nanoparticles (NPs) have limitations in in vivo drug delivery, targeting, and immune clearance. However, strategies like protein corona and PEGylation have been developed to improve targeting. This approach has not been broadly used for male infertility cure but has shown potential in testicular functions. Understanding the mechanisms of NPs' uptake and intracellular fate is vital for optimizing their planned functions. Further study is needed to translate this technology into effective in vivo products (Baig et al., 2021).

5. Application of Biotechnology in the Treatment of Male Infertility

In 1919, Hungarian engineer Karl Ereky introduced the term Biotechnology. Biotechnology uses live creatures or the parts of them to produce novel products. It is an integration of bio science with engineering through which live cells are used to produce novel products (Gupta et al., 2017)

5.1 Applications in Medication

Biotechnology has become vital tool in medicine, driving remarkable progress in health. Some medical applications are mentioned below:

5.1.1 Gene Therapy

Gene therapy is the delivery of specific genes to the cells to cure diseases. This can be done by various methods, such as viral or non-viral techniques. Applications of gene therapy have targeted conditions such as cystic fibrosis, muscular dystrophy, and certain cancers (Sayed et al., 2022).

5.1.2 Recombinant Protein Production

Biotechnology has facilitate the large-scale synthesis of recombinant proteins used as therapeutic agents. By genetically modified bacteria, or mammalian cells, these systems produce specific proteins for medical use. Examples include insulin for diabetes management, growth hormone for treating growth deficiencies, and clotting factors for hemophilia patients (Huang et al., 2012).

5.1.3 Genome Editing

The capacity to modify genetic code has revolutionized medicine. Advanced techniques like CRISPR-Cas9 enable precise gene editing in cells or organisms, paving the way for potential treatments for genetic syndromes, cancer, and contagious (Kolanu, 2024).

5.1.4 Personalized Medicine

Biotechnology advancements have led to the emergence of modified medicine, which tailors cures to an individual's genetic profile. This approach employs techniques like genetic testing and pharmacogenomics to evaluate how a person's genes disturb their reaction to specific medications (Imran, 2024).

5.1.5 Stem Cell Therapy

Stem cells are unique in their ability to alter into various cell types, making them a capable option for addressing numerous diseases and injuries. Advances in biotechnology have facilitated the large-scale production and modification of stem cells, which enables their specific application in therapeutic treatments (Zweigerdt, 2009).

5.2 Role of Biotechnology in Male Infertility

Louis Ignarro in 1992 showed that nitric oxide (NO) has an important function in human male penile tissue and that the inhibitor of cyclic GMP degradation potentiates the effect of release neuronal NO (2). This work aided in the creation of very effective remedies for men who suffer from the condition (ED) (Goldstein et al., 1998).

5.3 Gene Editing Techniques

5.3.1 Microarray

Microarray a laboratory techniques that make us in analyses of thousands of gene expression simultaneously. The use of this technique is increased in identification of genes related with human male infertility. After creation of cDNA microarray for human testis, Chen and his colleagues discover *tsMCAK* a novel testis-specific gene that is homologous to *HsMCAK*, this gene encodes human testis-specific mitotic centromere-associated kinesin (Cheng et al., 2002).

In testes *tsMCAK* gene was found to be expressed with spermatogenic arrest at spermatocyte stage. However, this gene is absents in patients that are suffering from sertoli-cell-only syndrome and also in patient with spermatogenic arrest at spermatid stage. This shows that *tsMCAK* have a critical role in the later phases of spermatogenesis, and absence of this gene might cause male infertility.

These results show that microarray technology is an important tool in gene identifications associated with male infertility. This technique provides molecular markers for future diagnosis and therapeutic application. it help in the discovery of novel genes their pathological mechanism of action, and their role in human male infertility (García-Giménez et al., 2017).

Microarray technology allows a quicker, more accurate diagnosis while also permitting the advancement of better treatment methods for various diseases. This progress is of great benefit to researchers and clinicians aiming to enhance diagnostic procedures and develop new therapies for various reasons for male infertility. So far, many of the known and new genes were analyzed using microarray technologies as possible causes of male infertility, they were made both in mice and humans and it gives hope for diagnosis and treatment.

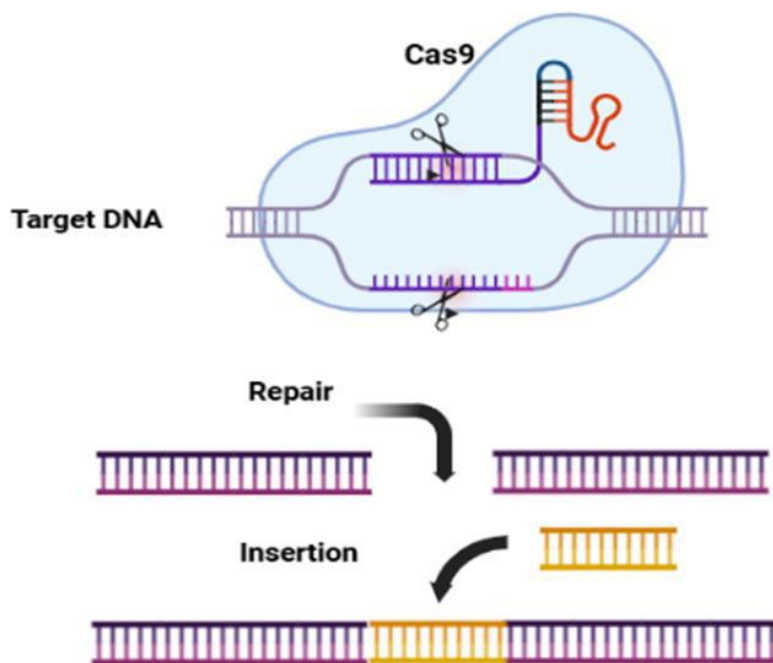


Fig. 2: Mechanism of CRISPR in Gene Editing (biorender)

5.3.2 CRISPR/Cas9

The procedure of cutting external viral nucleic acids in clustered repeatedly interspaced short palindromic repeats (CRISPR) has revealed its potential for gene editing. An RNA-guided tool, the CRISPR/Cas system is designed to modify specific DNA sequences. It functions through Cas proteins and includes CRISPR clusters, leader sequences, repeat regions (tracers), and a conserved set of CRISPR linked genes (Cas genes) (Liu et al., 2022).

The CRISPR/Cas system, especially CRISPR/Cas9, became highly popular among researchers soon after its debut in 2013. This technology has transformed genetic manipulation, making it easier to delete, insert, and substitute genes in various organisms, as illustrated in Figure 2.

In 2013, Yuxuan Wu and his team laid the groundwork for using CRISPR/Cas9 to repair genetic defects (Wu et al., 2013). By 2015, they had successfully used CRISPR/Cas9 to edit the *Crygc* gene in mouse spermatogonial stem cells (SSCs), effectively repairing genetic issues in mice (Wu et al., 2015). This innovative use of CRISPR/Cas9 for homology-directed repair (HDR) in SSCs offered a new beneficial approach to tackle male infertility linked to genetic problems in germ cells. In 2019, Xiaoyu Li and his colleagues applied CRISPR/Cas9 in vitro to correct a point mutation in the SSCs of Kitw/Kitwv mice (Li et al., 2019). Later being displaced back into the testes, these corrected SSCs effectively restored the normal fertility of the mice.

Conclusion

The combination of nanotechnology and biotechnology in addressing male infertility offers a promising strategy for treatment. Nanotechnology enables targeted drug delivery systems, accurate imaging, and biomimetic environments that enhance spermatogenesis, thereby improving both the effectiveness and safety of treatments. On the other hand, biotechnology drives innovations in gene editing, stem cell therapy, and assisted reproductive technologies. Recent developments, such as CRISPR-Cas9 for gene editing and nanoparticles for localized drug delivery, highlight the merging of these disciplines. Nonetheless, challenges such as ethical issues and regulatory obstacles persist. To fully leverage these technologies, collaborative efforts in research, clinical trials, and policy-making are essential.

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Nanoparticles - Emerging Replacement to Antimicrobials

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Abstract

Nanoparticles (NPs) generate interest as substitutes for traditional antimicrobials because of their distinct physicochemical properties and wide-ranging effectiveness against fungi, viruses, and bacteria. NPs destroy microorganisms by disrupting membranes, producing Reactive Oxygen Species (ROS), interfering with enzymatic processes and DNA replication, and dissolving biofilms. Gold NPs (Au NPs) have been used in various fields, from engineering to medicine, in recent years. Au NPs' biocompatibility allowed them to be utilized in antibacterial treatments, cancer treatment, and arthritis treatment. Silver NPs (AgNPs) have potent antibacterial effects by breaking bacterial membranes and interfering with enzyme functions through the generation of ROS. Ag, Au, zinc oxide (ZnO), and titanium oxide metal NPs (MNPs) have special antibacterial properties. Their most intriguing feature is their ability to administer medicines in the intracellular space where the infection is located. As a result, they enhance medication stability, boost drug circulation, improve target delivery, and boost therapy efficacy. They also improve the antibacterial spectrum, reduce toxicity and side effects, reduce the duration of treatment, and reduce the dosage of necessary medications. In nanomedicine, the active substance is transported and released at its pharmacological target by the use of nanovectors. Therefore, adjusting the pharmacokinetic route and bioavailability improves the effectiveness of medications and reduces their side effects.

Keywords: Nanoparticles, Silver, Gold, Polymers, Metal Oxide, Antiviral, Drugs, Antibiotics

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Introduction

Antibiotics are drugs that have the ability to either kill or inhibit microorganisms (Baquero & Levin, 2021). Antibiotics are categorized as antiviral, antifungal, and antibacterial depending on their target population. The majority of antibacterial substances are commonly referred to as antibiotics. Antibiotics have supported a variety of medical procedures, such as chemical therapy and organ transplantation, and have been used since ancient times for both prevention and treatment of infections. Protein and RNA synthesis, membrane structure breakdown, inhibition of enzymes, and DNA disruption are the well-known antimicrobial pathways of antibiotics. Antibiotics have been created in a variety of groups or classes, depending on how multi-drug resistance develops. Therefore, it is nearly impossible to envision a world without antibiotics (Muteeb et al., 2023). Unfortunately, this might come to pass as a result of microbes becoming more resistant to antibiotics. Drug resistance in bacteria is directly caused by the misuse of antibiotics, high dosages of medications that increase toxicity, prolong hospital stays, and raise mortality, as well as by their widespread use in agriculture and the lack of new antibiotic research. Furthermore, the accessibility with which products and infected individuals can now travel around the world contributes to the unprecedented spread of infections. Antibiotic resistance to pandemic infectious illnesses is a significant public health concern in addition to the negative socioeconomic effects. Antimicrobial resistance (AMR) has been identified by the World Health Organization (WHO) as one of the main public health concerns. Antibiotic resistance in microorganisms can be prevented by decreasing the use of antimicrobial agents and improving drug release, changing the targets of antibiotics, creating medications that break down or modify the enzymes of microorganisms, creating a biofilm coating that includes the bacteria, and limiting exposure to antibiotics (Tang et al., 2023).

These changes will eventually result in less drug accumulation in microbial cells or a brief intracellular presence of medications that are

unable to reach therapeutic concentrations efficiently therapeutic concentrations. But at this time, larger dosages and frequent drug administration are common, which greatly increases the possibility of negative side effects in both humans and animals. Numerous antibiotics that are often used to treat harmful germs have caused resistance (Uddin et al., 2021). In addition, the process of developing and promoting new antibiotics is expensive and time-consuming, involving the production of novel chemicals, several clinical trials, and licensing. There is a chance that bacteria would quickly become resistant to entirely novel antibiotics, which would reduce antibiotic use and sales and worsen the state of the economy and public health. Therefore, the failure of antibiotic treatment would eventually lead to a greater chance of infection-related death. Modern remedies are therefore essential for overcoming these barriers. The most significant advancement in recent years, nanotechnology, has revolutionized medicine. The market for products that use nanotechnology is growing steadily. The advanced field of nanotechnology will influence initiatives to improve human health. Medical experts have looked into NPs' lifespan, efficacy, resilience, adaptability, and special physicochemical characteristics (Bhardwaj et al., 2023).

They are used in many therapeutic techniques, including tumor identification, prognostic visual assessment of therapy, and targeted drug delivery. NPs were produced using several traditional methods, including chemical processes like photo-reduction, sol-gel, thermolysis, and micro-emulsion, as well as efficient methods like physical vapor deposition, laser ablation, sputtering, and mixing. These methods have the potential to make NPs unstable, cause dangerous substances to adhere to their surface, and produce dangerous byproducts. Biogenic NPs are made using environmentally friendly processes. Stable NPs, the use of a biomass-based coating on the surface that offers larger surface areas for biological interaction, the avoidance of hazardous byproduct formation, and more stabilizing or reducing factors that ultimately make the process cost-effective are some of the benefits of green synthesis. However, prolonged exposure to NPs at work could provide unexpected health risks to people. Additionally, breathing in NPs in the form of air pollutants might result in secondary exposure to NPs. Systemic health problems can arise when these inhaled NPs pass the immune system and spread throughout the body (Saratale et al., 2022). The antibacterial and antiviral properties of nanoparticles, such as AgNPs, AuNPs, quantum dots (QDs), carbon dots (C-dots), graphene oxide (GO), silicon materials, polymeric NPs, dendrimers, and polymers, are generally quite strong.

Role of Silver NPs in Antimicrobial Action

When AgNPs are exposed to bacteria, they have a tendency to assemble at the bacterial membrane, causing perforations that ultimately result in cellular death (Tripathi & Goshisht, 2022). The mechanisms of action between AgNP surfaces and biological elements also interact with different sizes (ranging from 1 nm to several 100 nm), as particle size may significantly suggest their action strategy without a secondary component. By inactivating bacterial enzymes and generating ROS, AgNPs produce cytotoxic activity. Ag⁺ species are given a prominent role by some other methods. In contrast to (metallic Silver Nanoparticles) Ag⁰ Nps, some systems that contain originally Ag (+1) species, such as salts, zeolites, or ionomers, release ROS through ion exchange and dissolution (Varier et al., 2019). NPs serve as a reservoir for the monovalent Ag species, which turns into an antibacterial agent. The Ag ions are attracted to organic compounds, particularly phosphates, amines, and thiols, with which they establish a quasi-covalent bond (around sixty-five kcal/mol is the Ag-S binding energy).

Although these compounds are rather rare in the biological world, Ag⁺ has an equivalent affinity for selenol groups. Several substances, including cofactors, membrane-bound or intracellular peptides, and DNA, have been determined to be the ions' targets in the dying bacterium (Godoy-Gallardo et al., 2021). Any high-affinity moiety will be readily adsorbed by Ag⁺ ions unlike antibiotics that target a single component of the bacterial life cycle; therefore, it is unlikely that multiple pathways are impacted, leading to cellular death. Ag binds to a wide variety of sites in a non-specific manner, disrupting multiple elements of cell metabolism at once and ultimately causing cell death, which is far more likely. Some of the impacted pathways are extremely susceptible to even small amounts of Ag species. The antibacterial action of Ag NPs against a wide range of microbes may be explained in part by their capacity to interfere with a wide range of paths. Comparing Ag⁺ activity with and without oxygenic respiration revealed that more than half of the antibacterial activity was mediated by ROS (Kędziora et al., 2021).

Ag⁺ ions in nanoparticulate systems were also produced by oxidation and the discharge of ions that have been chemisorbed at the surface of particles. The antibacterial properties of *Urtica dioica*'s phytosynthesized AgNPs against a variety of harmful microbes were investigated. Compared to the controls, which were AgNO₃ solution and leaf extracts, the AgNPs showed more activity. Furthermore, the increased concentration of AgNPs was observed to enhance the antibacterial properties. Compared to the controls, which were AgNO₃ solution and leaf extracts, the AgNPs showed more activity. Furthermore, the increased concentration of AgNPs was observed to enhance the antibacterial properties. Both biological and environmental systems include large amounts of chloride, which precipitates as the somewhat soluble compound AgCl (Sarvarkar et al., 2024).

Role of Gold NPs in Antimicrobial Action

Au NPs have been used in a wide range of fields, from engineering to medicine, in recent years (Hu et al., 2022). Au NPs' biocompatibility allowed them to be utilized in antibacterial treatments, cancer treatment, and arthritis treatment. Au NPs can detect cell receptors, tumor metabolites, and endocytosis under dark-field light-scattering microscopy. Additionally, biosensors, disease indicators, toxic metals, pesticides, and blood glucose measurements have all benefited from the usage of green-synthesized Au NPs. Additionally, Au NPs may be able to cleanse and break down harmful contaminants. Because of their reduced size, polyvalences, distinct surface chemistry, and photothermal nature, NPs also enhance a wide range of gene expressions associated with redox reactions that lead to microbial death. When Au NPs react with bases that include sulfur or phosphorus, they inactivate enzymes called NADH dehydrogenases (Mikhailova, 2021). These enzymes disrupt respiratory chains by producing a lot of free radicals, which kill cells. The composition of the cell wall also affects the antibacterial action. Compared to Gram-positive bacteria, Au NPs showed more activity. In addition to the structure of the bacterial cell wall, the antibacterial activity is also influenced by concentration, purifying techniques, and surface alteration (capping or coating materials). Antibiotic coatings, particularly aminoglycoside antibiotics, can increase the effectiveness of Au NPs in antibacterial activity. The fact that green-synthesized Au NPs exhibit effective antibacterial activity against specific bacterial strains when compared to chemically synthesized Au NPs is fascinating and could be the

result of the synergistic interaction between Au NPs and extracts (El-Borady et al., 2020).

Role of Metal Oxide NPs in Antimicrobial Action

Recently, ZnO has been employed for piezoelectric nanogenerators and nanoscale optoelectronics in addition to being a semiconductor with a broad bandgap (3.36 eV) that has a range of nanostructures and possible electronic uses. They are effectively employed to combat microbes. According to certain findings, the production of ROS on the surface of CaO, MgO, and ZnO exhibits significant antibacterial activity, as determined by a conductometric approach. After ZnO breaks down the cell membrane, ZnONPs securely adheres to the deceased bacterium's surface, blocking additional antibacterial activity and releasing peroxides into the medium with strong bactericidal efficiency. Another study's findings showed that a smaller particle size increases activity because of its high surface area-to-volume ratio (Gökmen et al., 2024).

Role of Polymeric in Antimicrobial Action

Polymeric NPs, which are colloidal solids with a diameter of 10–1000 nm, are the most prevalent type of organic nanoparticle (Shrestha et al., 2020). Higher amounts at target places may result from the tiny size's ability to enhance capillary penetration and cell absorption. When delivered through polymeric NPs made of poly(ethylene glycol)-block-poly(lactide-co-glycolide) (PEG-PLGA), diphyltin, a vacuolar ATPase blocker, proved more successful than diphyltin alone in preventing feline infectious peritonitis (FIP), which is brought on by a mutant feline CoV. Mice also showed greater tolerance to NPs loaded with diphyltin. Consequently, a polymeric nanoparticle-based nanoformulation showed promising antiviral efficacy against FIP. Because of their flexible molecular structure and lengthy chains and branches, polymers have a strong antiviral potential. It is possible to develop polymers according to arbitrary requirements based on their viricidal properties. They can be utilized as co-factors for the management of viral infectious illnesses in addition to being effective antiviral medications. Antiviral drug-carrying polymers effectively increase the solubility of antiviral medications, extending their retention period and improving their cell uptake efficiency. Organotin compounds, for instance, were made according to the requirements of universal viral agents. By preventing viral reproduction, cisplatin and organotin-like polymers efficiently destroy viruses. Oligo-phenylene ethynyls (OPE) and cationic conjugated polyelectrolytes (CPE) based on polyphenylene ethynylene (PPE) make up the polymers. When exposed to UV-visible light, the π bonding structure in the compound's backbone produces singlet oxygen species, which is how they work as antiviral medicines through the mechanism of oxidative stress. Proteins, RNA, and DNA are among the macromolecules that are harmed by oxidative stress (Thakur et al., 2024).

Expandable and water-soluble polymers comprise Polymeric nanogels that are created by joining hydrogel particles that readily break down into smaller pieces that are eliminated by renal clearance. By binding to the heparan sulfate proteoglycans on the surface of the host cell, these polymers can stop virus particles from entering the cell. These pliable nanogels are effective HSV-2 viral infection inhibitors.

Role of Liposome in Antimicrobial Action

Liposomes are spherical and typically range in size between twenty and thirty nm (Has & Sunthar, 2020). They are composed of a phospholipid bilayer enclosing an aqueous core. Liposomes are safe and biocompatible. HIV-1 production was stopped when liposomes containing antisense RNA targeted at T-cell receptors were contained in the HIV envelope region. By lowering cellular cholesterol, polyunsaturated fatty acids included in these PLs demonstrate independent antiviral action. One of the prospective goals of many viral systems, such as HCV, HBV, and HIV, is to target the manufacture of cholesterol within infected cells. In HCV, HBV, and HIV infections, PLs dramatically reduced viral production and infectivity. Without active medicinal components preloaded, stearylamine (SA)-loaded cationic liposomes reduced viral infectivity. Many mammalian cell lines, particularly A549 cells, showed reduced baculoviral infectivity when exposed to SA liposomes. By lowering cholesterol levels, the non-toxic SA liposomes may enhance their antiviral properties, which become more pronounced as they adhere more firmly to the cell membrane. SA liposomes are associated with the antiviral medication acyclovir and enhance the entrance of virus fragments into host cells (Pradhan et al., 2021).

Antiviral Mechanism of NPs

Nanoparticle antiviral mechanisms need to focus on virus adhesion, penetration, replication, and budding. Depending on the form and nature of the NPs utilized, potential mechanisms include limiting viral replication, preventing viruses avoiding adhering to host cells, and directly or indirectly inactivating the virus (Alavi et al., 2022). By changing the capsid protein's structure, NPs typically prevent the aforementioned processes and ultimately reduce virulence, which is associated with both physical and chemical strategies to reduce the amount of active virus. Broad-spectrum, non-toxic NPs can combat dengue, lentivirus, RSV, HSV, and human papillomavirus. Effective viral prevention was demonstrated by the scientists using a set of antiviral NPs with long, flexible linkers that resembled heparin sulfate proteoglycans, the highly repetitive focus of viral attachment ligands. The VAL repeating units were effectively bound by the virus, simulating a strong and multivalent binding. Local-field action against virus surface receptors is one of the primary and immediate mechanisms of the NPs-mediated antiviral effect (Zare et al., 2021). The membrane potential can be significantly changed in this process by the NPs deposited on the cell surface. In contrast, NPs' indirect antiviral method involves preventing the virus from entering the cell by altering the membrane potential.

According to these reports taken together, the primary mechanisms of nanoparticle antiviral activity include binding to the plasma membrane, inactivating viral particles before entry, binding competition between double-stranded DNA and viral particles, interference with viral attachment, reduction of virus-host cell adhesion and penetration, and the relationship with the virus and NPs for the host cell. The interaction between MNPs and viral particles prevents the virus from replicating. Viral replication is inhibited and viral particle release into host cells is prevented by the potential antiviral action of non-toxic NPs like Au. NPs can inhibit the neuraminidase enzyme, that breaks the connection between the hemagglutinin on the descendant virus and the recipient cell's sialic acid receptor (Chakraborty & Chauhan, 2024). NPs stop this cleavage process, obstruct the release of virus offspring from infected host cells, and stop the infection from spreading. Thus, suppression of hemagglutinin and neuraminidase activity may be the potential antiviral mechanism. Additionally, Au NPs prevent viruses from adhering to host cells.

Advantages

In nanomedicine, the active substance is transported and released at its pharmacological target by the use of nanovectors (Abou Bakr et al., 2023). Therefore, adjusting the pharmacokinetic route and bioavailability improves the effectiveness of medications and reduces their side effects. Ag, Au, ZnO, and titanium oxide MNPs have special antibacterial properties. Their ability to administer medicines in the intracellular space where the infection is located is their most intriguing feature. As a result, they enhance medication stability, boost drug circulation, improve target delivery, and boost therapy efficacy. They also improve the antibacterial spectrum, reduce toxicity and side effects, reduce the duration of treatment, and reduce the dosage of necessary medications. The most promising strategy to fight antibiotic medication resistance is to use them because of all these benefits. Bacterial infections predominantly caused by intracellular bacteria can be treated with nanobiotics, the next generation of antibiotics. Noble metals, mainly Cu and Ag, are used in daily life and have long been recognized for their antibacterial properties (Qin et al., 2021). For example, door handles in several hospitals have Cu coatings added to them to lessen the spread of bacteria in the medical setting. Antimicrobial properties against MDR species, including, *Acinetobacter baumannii*, ESKAPE pathogens (*Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterobacter*), have been demonstrated in vitro via nanoparticle studies. A study demonstrated the dose-dependent antibacterial efficacy of Ag Nps against enterobacteria such as *Klebsiella pneumoniae* and *Escherichia coli*, with an honorable MIC of about 1.4 µg/mL. Additionally, the antibacterial activity of cefotaxime, gentamicin, and meropenem against these species was enhanced when Ag Nps were present at the same time (Malawong et al., 2021). Other research has shown that it is effective against both Gram-positive and Gram-negative bacteria both in vitro and in vivo. Additionally, it can be a substitute for the treatment of tuberculosis, a serious illness that affects millions of people globally. Treatments for MDR TB include chemotherapy and second-line drugs like ethionamide (ETH), which can result from the misuse of first-line medications. However, patients frequently struggle to follow treatment plans that call for high ETH dosages. Synergistic medications could be encapsulated in the NPs, significantly streamlining treatment and improving patient compliance. Additionally, it can be a substitute for the treatment of tuberculosis, a serious illness that affects millions of people globally. MDR TB, which is managed with second-line drugs like ETH or chemotherapy, can result from the misuse of first-line medications. However, patients frequently struggle to follow treatment plans that call for high ETH dosages. Synergistic medications could be encapsulated in the NPs, significantly streamlining treatment and improving patient adherence. Antimicrobial medications (antibiotics, antivirals, and antifungals) can be made with the NPs. The most well-documented combination is with antibiotic compounds; they are known as nanobiotics. The MNPs are utilized because they are inexpensive, simple to synthesize, and straightforward to employ. The MNPs are based on several metals, primarily CuO, iron oxide (Fe₃O₄ or Fe₂O₃), ZnO, titanium dioxide (TiO₂), Au, and Ag. Because of their special optical, biological, and catalytic qualities. Ag NPs are used in the veterinary and human sectors in addition to research labs (Hajra et al., 2024).

The main advantage of AuNPs, which are thought to be the least hazardous MNP, is their ease of manufacturing and alteration by one or more thiol ligands with distinct chemical properties. MNPs facilitate the delivery of antibiotics to the cell surface because they function as drug carriers. The concentration of antimicrobial medications is increased at particular sites on the cell membrane as a result of the interaction between the antibiotics and NPs. In particular, AgNPs and AuNPs' affinity for sulfur-containing proteins in bacterial cell membranes enhances their interactions with cells and increases the permeability of the membranes. The antibiotics can enter the cell more easily as a result (Tripathi & Goshisht, 2022).

Limitations

NPs pose a health danger to people with their many benefits and wide range of uses. MNPs have limited applications both in vivo and in vitro, and research has indicated that they can enter cells and result in DNA damage, inflammation, organ toxicity, and oxidative stress. NPs pose a health danger to people with their many benefits and wide range of uses (Khan et al., 2021). The primary characteristics of MNPs have been linked to their toxicological effect as a result of their ability to penetrate the two hundred nm blood-brain barrier and their rapid penetration into human cells. NPs smaller than ten nm frequently have strong antibacterial action together with high cytotoxicity, agglomeration facilitates deposition and delays NP diffusion, increasing effective doses. Protein binding to NPs, cellular absorption, oxidative stress, autophagy, inflammation, and apoptosis are all regulated by surface charge. MNPs can be made less harmful to people. For maximum effectiveness, the size can be adjusted, and capping agents can be employed to improve ion release, minimize agglomeration, and stop unwanted NPs from oxidizing. polyacrylic acid, Oleic acid, polyvinyl alcohol (PVA), polyethylene glycol (PEG), and polyvinylpyrrolidone (PVP) are capping agents that are frequently employed (Liu & Tang, 2020).

Conclusion

NPs have distinct processes that include altering bacteria membranes, enzyme activity, and DNA synthesis, they present a promising option to control AMR. They are better than conventional antibiotics because of their tailored delivery, which increases efficacy while lowering dosage and adverse effects. Liposomes, polymeric NPs, Ag, and Au have all exhibited exceptional antibacterial properties. Ag NPs and gold Au NPs are two of the most notable nanoparticles due to their strong antibacterial properties and outstanding biocompatibility. Other metal-based nanoparticles, like ZnO further enhance the antibacterial arsenal and titanium oxide, which can efficiently target intracellular pathogens. Beyond their antibacterial qualities, nanoparticle-based treatments have further benefits. Nanoparticles maximize therapeutic drug pharmacokinetic profile and bioavailability by facilitating targeted drug distribution, increasing circulation time, and boosting drug stability. This lowers the necessary dosage and length of therapy, minimizes toxicity, and lessens adverse effects. The ability of nanoparticles to improve healthcare is highlighted by nanomedicine's novel method of medication delivery and its capacity to solve current problems in antimicrobial therapy. Therapeutic options for combating infectious diseases and antibiotic resistance that are more efficient, secure, and sustainable are probably going to be made possible by ongoing studies and research in this area.

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Nanoparticle-based Treatment for Respiratory Disorder

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Abstract

Every year, the increase in respiratory problem instances around the world impacts the well-being and standard of life of millions of individuals. Since chronic respiratory diseases (CRDs) are the leading cause of hospitalizations and deaths, sophisticated treatments that allow for the regulated delivery of medications to specific target sites are required. To address this demand, a variety of nanoparticles (NPs) has been studied, including carbon-based, dendrimers, polymeric, liposome, and quantum dots. The use of NPs as drug delivery vehicles can improve the efficacy of commercial drugs due to their advantages in targeted effects, prolonged drug release, and patient compliance. The use of nanotechnology as drug delivery systems to treat respiratory tract diseases, such as asthma, lung cancer, lung infections, and chronic respiratory disorders (CRDs), is covered in this chapter.

Keywords: Nanoparticles, Respiratory, Disorder, Chronic, Polymers

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Introduction

In 2016, respiratory disorders led various impairment and at least 9 million deaths globally reported by World Health Organization (WHO). A little over 15% of the fatalities were caused by these illnesses (Horváth et al., 2017). The most common respiratory conditions are common cold, bronchitis, pneumonia, TB, pharyngitis, laryngitis, and lower respiratory infections, and obstructive lung illnesses such as lung cancer, asthma, and the chronic obstructive pulmonary disorder (COPD). Air pollution and hereditary characteristics and bacterial and viral infections are the primary causes of the respiratory illnesses. Airborne illnesses and the infections could easily infect the lower respiratory airways, affecting them and result in acute respiratory infections (Thorlund et al., 2020). Severe respiratory infections can be caused by the newly discovered COVID-19 corona virus, as well as avian influenza A (H7N9) and severe acute respiratory syndrome corona virus (SARS-CoV). Genetic problems and air pollution are the causes of chronic respiratory diseases and such as lung cancer, cystic fibrosis (CF), asthma, COPD, and hay fever. Healing and restoring the respiratory system's functions is the primary treatment objective in the order to enhance patients' standard of life (Thorlund et al., 2020). The primary objectives of the respiratory diseases treatment are to reduce the number of deaths and the casualties, improve standard of life and lessen drug adverse effect, and provide an appropriate therapy for symptom relief.

The need for the new treatments that can get past issues like drug resistance and poor drug efficacy and side effects and expense might make using medications based on nanotechnology more acceptable. The development of nanomedicine and nanotechnology in recent years has created opportunities for treatment of respiratory disorders. The surface to volume ratio of nanoparticles (NPs) is extremely high due to their nanoscale size (Yazdi et al., 2021). With the right designs this characteristic makes it possible to attach numerous ligands to the surface, enhancing the chances that multiple covalent connections will be formed, and can be used simultaneously in the targeted treatment (Ghorani-Azam et al., 2022). Additional features of nanoparticles include enhanced chemico-biological stability, the potential to bind to hydrophilic and hydrophobic medications, and the ability to be administered by injection or inhalation (Deng et al., 2021), depending solely on the reagents' chemical structure and the nano-carrier's physicochemical properties. One of the widely utilized medicine delivery methods for both respiratory and non-respiratory conditions is aerosol delivery (Bianco et al., 2021). Because they are functionalized for targeted distribution, have greater biocompatibility, and have fewer side effects, nanosystems may be more effective than traditional

medications (Mousavi-Kouhi et al., 2021). Various kinds of nanoparticles, such as inorganic and organic ones, were accessible for biological applications; these should be discussed in further detail in order to build new nano-systems for particular uses. In order to provide fresh concepts for more practical future drugs, the NPs utilized to treat respiratory conditions were discussed in this chapter.

Respiratory Disorders

Chronic Respiratory Diseases (CRDs)

Numerous hospital stays, countless costs, and, in the most severe situations, fatalities are all caused by CRDs, which also lower many patients' quality of life. The most well-known CRDs include lung cancer, cystic fibrosis, asthma, allergic rhinitis, and chronic obstructive pulmonary disease (COPD) (Sleurs et al., 2019). The most prevalent non-communicable disease (CRD), asthma affects over 300 million people worldwide (Papi et al., 2018a). Its symptoms, which include coughing, chest tightness, and shortness of breath, call for long-term treatment and, in certain situations, endless periods (Strzempek et al., 2019). With upper respiratory system infections, pollen exposure, and air pollution, the intensity of symptoms might fluctuate over time and result in respiratory failure (Lambrecht et al., 2019). When an overactive immune response is triggered by exposure to airborne environmental allergens, asthma with allergies is the most common type of asthma. Bronchodilators and anti-inflammatory medications are inhaled as part of the treatment to lessen airway blockage and inflammation. Traditional therapies, however, primarily address asthma symptoms rather than the underlying cause of the condition. Under this method, the patient must take medication for the duration of their lives (Givens et al., 2018).

Another severe form of CRD, COPD, affects around 64 million people, accounts for 10% of deaths in the over-40 age group, and is the third leading cause of mortality globally (Barnes et al., 2018). Toxic particle exposure, like that seen in smoking, is the main cause of risk for COPD (Papi et al., 2018a). The conditions that make up COPD include emphysema and chronic bronchitis, however most individuals have both phenotypes. Chronic exposure to the compounds in cigarette smoke triggers reactive oxygen species (ROS), which leads to apoptosis and inflammatory-oxidative stress. Consequently, alveolar gap widening causes lung tissue to deteriorate, leading to emphysema.

About 70 000 people worldwide suffer with cystic fibrosis (CF), a hereditary condition caused by a malfunction in a protein that transports substances called the cystic fibrosis transmembrane (CFTR) (Stephenson et al., 2017). The secretion of chloride ions into exocrine glands is controlled by the CFTR protein. The absence of chloride ions impairs the mucociliary clearance and damages the airway mucosa by making gland secretion more viscous. Chronic pulmonary infections are thus characterized by the persistent colonization of bacteria and fungi, particularly *Pseudomonas aeruginosa* and *Candida spp.*, in the endobronchial region (Schwarz et al., 2018).

Acute Respiratory Infections (ARIs)

The primary cause of death for children under five is acute respiratory syndromes (ARIs), also referred to as ARSs. ARIs are among the world's leading causes of death, accounting for approximately 4 million deaths per year (FoIR et al., 2017). A common cold, pneumonia, laryngitis, bronchitis, pneumonia, and tuberculosis are illnesses caused by lower respiratory tract infections, which are mostly caused by viruses and bacteria. With the advent of new virus-related illnesses like the novel corona virus, COVID-19, the severity of ARIs rises annually. According to reports since the middle of the 1960s, there are seven reported human corona viruses that cause 15% of cases of the common cold (Yang et al., 2020).

The severe acute respiratory syndrome corona virus (SARS-CoV), the Middle East respiratory syndrome corona virus COVID-19 are the corona viruses that cause the greatest number of deaths in the human population. Initially identified in Saudi Arabia in 2012, MERS-CoV caused around 2494 cases and 858 fatalities across 27 nations. China was the first place where SARS-CoV and SARS-CoV-2 were isolated. In 32 different countries, SARS-CoV caused 8422 cases and approximately 919 fatalities in 2002 and 2003. Since its discovery in December 2019, the most current coronavirus-driven ARI, COVID-19, has attacked 54 075 995 individuals and killed 1 313 919 people in nearly every nation on Earth (as of November 16, 2020) (Dashboard et al., 2020). The lower respiratory tract is primarily impacted by COVID-19, and early symptoms in afflicted patients include fever, exhaustion, dry cough, and dyspnea. Additionally, the condition compromises important organs like the heart, liver, kidneys, and gastrointestinal tract, which results in a number of organ issues (Chauhan et al., 2020).

The avian influenza A (H7N9) viruses, which initially surfaced in China in 2013 and have since resurfaced every year as winter-spring epidemic waves, are another important source of ARIs.³³ The H7N9 virus infected a significant number of people worldwide during 2016 and 2017, leading to 54 481 000 illnesses and 145 000 fatalities (Chavez et al., 2021). According to certain research, bacterial pneumonia, another significant ARI, was much more common during viral pandemics (Golda et al., 2011). The symptoms of pneumonia, which can be brought on by bacteria or viruses, include chills, fever, chest pain, coughing, sputum production, and dyspnea. Many hospital admissions among people 65 years of age or older are due to pneumonia, which is referred to be the "special enemy of old age (Metlay et al., 1997). Due to the negative toxic effects of small molecule antibiotics (like vancomycin) and their poor efficacy against strains of pneumonia that are resistant to multiple drugs, there is potential for improvement in the present treatments (Kim et al., 2018).

Tb is an ARI associated for the death of more individuals than any other microbiological pathogen, with roughly 1.5 million deaths recorded in 2018 (Okram & Singh, 2024). TB is a poverty-related disease, impacting the most disadvantaged and marginalized groups, therefore its elimination at a worldwide level is still not feasible. Night sweats, high temperatures, weight loss, coughing, and chest pain are the main signs of this illness (Sulis et al., 2014).

Asthma

Over thirty million individuals worldwide suffer from asthma, the most prevalent non-communicable disease (Papi et al., 2018b). Coughing, chest tightness, and shortness of breath are among its symptoms, which call for ongoing treatment—sometimes for an indeterminate amount of time (Strzempek et al., 2019). When upper respiratory system infections, pollen exposure, and air pollution are paired with symptoms that fluctuate in intensity over time, respiratory failure may result (Lambrecht et al., 2019).

Reversible airway blockage, bronchial hyper responsiveness, and persistent airway inflammation are the hallmarks of asthma, an inflammatory lung disease. An inflammatory reaction brought on by prolonged exposure to irritants damages lung tissue and narrows the tiny airways. Nanoparticles' anti-inflammatory properties have already been demonstrated in a number of inflammatory conditions (Yang et al., 2019). By making it easier for the medication to reach the target area and enhancing its deposition in the lungs, nanoparticles enhance the therapeutic impact (Yang et al., 2019).

Lung Infections (caused by Parasites, Fungus, Bacteria and Viruses)

A number of major lung infections can be fatal, including viral lung infections, pneumonia, and tuberculosis. Lung infections affect the majority of air sacs and, to a lesser extent, the airways that carry air to the lungs. Although a range of therapies and diagnostics have been employed to treat lung infections, therapy has become more challenging due to the rise of bacteria that are resistant to drugs and the negative consequences they cause once they enter the lung environment (Muhammad et al., 2022). More than ever, there is a need for innovative approaches to regulate bacterial activity. The application of nano material science can be a potential method in this area, and the growing body of knowledge in the synthesis of nanomaterials should be viewed as a worldwide approach.

Lung Cancer

Lung cancer is the most prevalent kind of cancer worldwide, and nanomaterials are crucial to cancer treatment. Uncontrolled cell development in lung tissues is the hallmark of lung cancer, which continues to be a significant and unsettling cause of death and widespread illness (Figure 1) Regenerative medicine and nano therapy have advanced in treating lung diseases and lung biology (Sanaei et al., 2022).

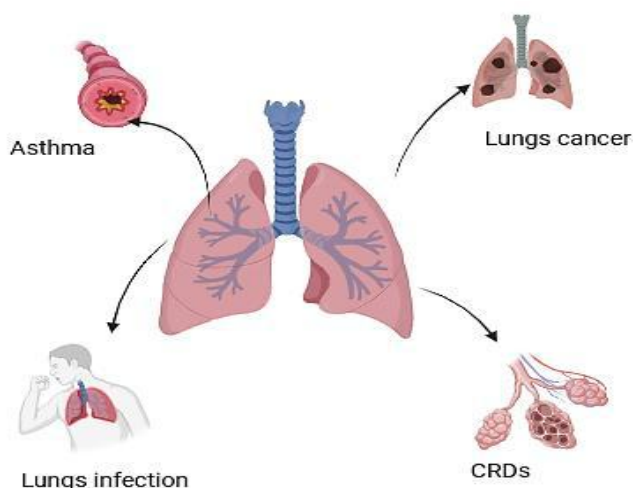


Fig. 1: Respiratory disorder illustration (Retrieved from BioRender)

Limitations for Treating Respiratory Diseases

The standard of life is significantly reduced by the negative impacts of the lack of creative tactics for fighting CRDs and ARIs, particularly for senior patients. The use of nanotechnology may help to partially solve the primary challenges commonly encountered in the treatment of respiratory diseases (such as multidrug-resistant strains, a lack of creative ideas, early detection challenges, failure therapy trials, side effects, and high cost) (Rodrigues et al., 2019). By using nanostructures, nanotechnology breaks down the boundaries between materials science, biology, and physics. Materials with particle sizes ranging from 1 to 100 nm are referred to as nanomaterials. Because of their huge surface area, these materials have special qualities. Accordingly, nanomaterials have been extensively researched in nanomedicine science for their potential use as drug delivery systems, biosensors, micro fluidics, and fillers for tissue engineering (Patra et al., 2018). Because of their direct targeting impact, ability to increase treatment efficacy, and ability to decrease side effects, NPs (nanoparticles) are more effective than some conventional approaches. This can lead to a sensitive decrease in toxicity and negative effects (Lombardo et al., 2019).

Furthermore, drug delivery with NPs is typically non-invasive, offers simple and inexpensive production techniques, strong being biodegradable and long-term stability (Zhou et al., 2018). Drug loading into nanoparticles can occur through covalent bonding, adsorption, or encapsulation among the drug and the surfaces of the nanoparticles. The outermost layers of the particles are altered to guarantee precise targeting of the various body parts. Typically, oligosaccharides, polymers, proteins, peptides, and other compounds are employed for this purpose (Popielarski et al., 2005). Following inhalation, Brownian diffusion deposits the nanoparticles into various areas of the respiratory system. The region of the respiratory tract where the deposition will take place is determined by the dimension of the nanocarriers. The nose, pharynx, and larynx are the best upper airways for smaller nanoparticles (B1 nm). While particles with a dimension of about B20 nm will mostly deposit into the deeper alveolar areas of the lungs, those with a size of about B5 nm exhibit excellent deposit into the trachea and bronchial regions. The way the nanocarriers and cells interact in aerosolized drug delivery nanoparticles are a better non-invasive way to access the respiratory tract while treating respiratory disorders (Oberd et al., 2005).

Where the nanocarriers are deposited in the body determines how they communicate with cells in the respiratory tract. Receptor-mediated endocytosis is often responsible for the nanoparticles' intracellular uptake. According to this method, certain biomolecules (including protein molecules, glycoprotein's, which and glycolysis) precipitate on the surfaces of nanoparticles to produce a complex that macrophage receptors can recognize. Through pseudo pod extensions, these biomolecules attach to the receptors of macrophages, facilitating the uptake of nanoparticles. Depending on the parts involved in the particle production and the interaction of the membrane, the endosomal material may take distinct routes at this step. The endosome may occasionally change into acid vesicles and merge with lysosomes. These structures can use enzymatic and hydrolytic processes to break down the drug delivery capsule (Rothen-Rutishauser & Blank, 2009).

Nowadays, a wide range of NPs are being investigated as drug delivery methods for the treatment of respiratory illnesses. Nanocarriers are often classified as either organic or inorganic. Their compositions, sizes, forms, surface characteristics, and manufacturing processes can all affect their physicochemical and biologic qualities.

Treatment of Respiratory Disorders with Nanoparticles

Different respiratory conditions have been treated using a variety of nanoparticle medication kinds.

Carbon-based Nanoparticles

Carbon-based materials, such as a) new industrial carbon like carbon fibers, b) conventional industrial carbon like activated carbon, and c) novel carbon nanomaterials like graphene and carbon nanotubes, are crucial to the development of material science. While macro carbon material lacks an appropriate band gap, making it difficult to function as an effective fluorescent material, primary research and applications of carbon-based substances are widespread in transdisciplinary disciplines (Liu et al., 2020). Carbon nanotubes and carbon nanodiamond are robust, lightweight, extremely conductive, and multipurpose. These nanoparticles' drug delivery mechanisms may be functionalized to provide reliable diagnostic instruments (Chauhan et al., 2020). Although carbon nanotubes are inhaled, they pose health hazards, including inflammation and lung fibrosis (Maiti et al., 2019), thus they are not appropriate for treating respiratory conditions. In recent years, a variety of newly developed carbon-based nanomaterials have been modified and used extensively in pharmacology, medicine, and biology due to their significant features (Poulsen et al., 2018).

Dendrimers

Due to the tree-like branching structures, the word dendrimer was taken from the Greek word Dendron, which meaning tree. Based on their physicochemical properties and dendrons arms that originate from the central core of make up a dendrimer (Ambekar et al., 2020). Dendrimers are widely utilized in the gene editing and pharmacology and drug delivery and antibiotics (Liu et al., 2023). These days a variety of the dendrimers including PAMAM, polyethylene glycol and polylysine, are frequently employed as the nanocarriers to cure disorder (Yousefi et al., 2020). To circumvent dendrimers' cationic toxicity, dendrimers-based nanocarriers must be functionalized with the biomolecules which is simple to do because dendrimers have large amino groups (Ambekar et al., 2020).

Polymeric Nanoparticles

Solid colloidal particles that are known as the polymeric nanoparticles and they are ideally composed of the polymers that can be obtained naturally or artificially (Yazdi et al., 2020). Polymeric micelles and the polymersomes are examples of the last three kinds of the polymeric nanoparticles: hydrogels and nanospheres and nanocapsules. In the order to the chemically or physically absorb a lot of the water or dissolved medications hydrogels polymeric materials with a large number of the linked hydrophilic groups have a three-dimensional network. Medicines and other substance that are inserted into a matrix of the polymers in nanosphere polymeric nanoparticles (NPs) whereas the therapeutic ingredients is contained inside a polymers capsule shell in nano capsule polymeric NPs. Polymeric nano particles are useful for the treating a variety of disorder because they deliver the medication to the precise locations and in a precise quantity (Sur et al., 2019).

Liposome

Liposomes (LPs) are the packets made of the concentric lipid bilayers also known as the lamellae that develop on their own when they specific lipids are hydrated in the water. Lipid bilayers are used to create LPs which resemble self-assembling colloidal polymeric nanoparticle. Lipids can form spherical and oval shaped structures because of their hydrophilic and hydrophobic sides (Saraf et al., 2020). Solid lipid nanoparticles and micelles and phytosomes and nanoemulsions are the nanoparticles that resemble themselves as liposomes. More precisely liposomes are the ideal for encasing the hydrophilic medications due to their watery core. The phagosomal form of the hydrophobic medicines may also be positioned between the bilayer of lipids of cell membrane (Kumar et al., 2020).

Lipid Nanocarriers

Liposomes may be most porous and safe nanocarriers that are in the body since lipids make up narrowly permeable cell membranes. Liposomes are basis for the majority of FDA-approved nanoparticles albeit they have significant drawbacks. Continuous exposure to the aqueous solutions and the bodily fluids can cause liposomes to oxidative degrade and the leak drugs (Thompson et al., 2017). Since solid lipid nanoparticles and the nanoemulsions cover a wider spectrum of the medications and are the less expensive drug delivery methods they might be better options than liposome (Roy et al., 2022). Due to their poor water solubility lipid-based nanocarriers may be able to overcome the challenges of limited availability for the oral treatment. Because of the lipid nanoparticles (NPs) are the nanosized and lipid soluble, they are more pharmacokinetic and the biocompatible and less toxic and can be scaled up for the industrial manufacturing (Dumont et al., 2018).

Quantum Dots

A breakthrough in nanoscience quantum dots (QDs) is the semiconductor of inorganic crystals with varying quantities of electrons that inhabit specific and well-defined quantum states (Reshma et al., 2019). Both the organic and inorganic classifications apply to common QDs composed of carbon, graphene, phosphides, Cd or zinc chalcogenides, and indium arsenide (Ruiyi et al., 2020).

Others

Researchers are favoring nanoscale materials with promising research and application opportunities for respiratory medication administration, and more and more nanoscale drug-carrying devices are being created for respiratory drug delivery. Bilosomes, also known as bile bodies, are vesicular structures derived from bile salts that are more stable and effective at encapsulating drugs than conventional liposomes (Zakaria et al., 2013).

To increase its bioavailability and solubility, resveratrol was loaded into PEGylated bilosomes. The results demonstrated that the nanoparticles suppressed the Mpro enzyme of the severe acute respiratory syndrome corona virus type 2, which may be used as a medication

carrier to treat respiratory illnesses. Another new approach to the delivery of inhaled biologics is the use of nanosomes. Natural pure heavy-chain antibodies are extracted to create nanosomes, which are tiny therapeutic proteins (~15 kDa). Their brief half-life across the bloodstream made them a good fit for pulmonary administration. A nanosome called ALX-0171 is made for targeting respiratory syncytial virus (RSV)-specific proteins at sub-nanomolar concentrations. The results showed that when administered by dispersion in a rat model, both nostril and lungs RSV titers were significantly reduced (Detalle et al., 2016).

Conclusion

Acute and chronic respiratory conditions contribute significantly to the global health burden by lowering the quality of life and increasing mortality rates. Conventional therapy approaches are useful for controlling symptoms, but they have side effects, such as low bioavailability, expensive costs, and drug resistance. The high surface area volume to ratio, functionalization potential, and nanoscale size of NPs provide improved drug delivery capabilities. Nanoparticle-based medication delivery systems offer innovative approaches that have the potential to completely transform respiratory healthcare by removing hurdles associated with drug resistance and ineffective treatments. Nanomedicine has demonstrated exceptional promise in treating tuberculosis, Asthma, lung cancer, COPD, and viral infections. For example, inhalable nanoparticles make direct medication deposition into the lungs possible, which improves therapy results at lower dosages. But issues like long-term toxicity, obtaining regulatory permits, and mass production must be resolved. Future studies should focus on improving targeted treatments, guaranteeing biocompatibility, and perfecting nanocarrier compositions.

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Nanotechnology in Agriculture: Enhancing Crop Yield and Sustainability

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Abstract

Nanotechnology is a major advance in agriculture that helps solve big problems in food production and sustainability around the world. Using nanotechnology, agriculture can improve its accuracy, efficiency and commitment to the environment. Nano-fertilizers, nano-pesticides and nano-sensors are used to improve the use of resources, decrease waste of chemicals and help preserve soil and water. Nanotechnology improves plant resistance to environmental problems by altering their genes and cells which increases their ability to take in light and withstand stresses. They help farmers to get better harvests and follow sustainable methods by lessening harm to nature and protecting different species. Even so, using nanotechnology in real life requires dealing with problems such as risks to the environment, people's health, the ability to be used on a large scale, cost and regulation. If handled properly, nanotechnology can help feed the world, protect the environment and reduce the negative effects of climate change on agriculture.

Keywords: Nanotechnology, Sustainable Agriculture, Nano-fertilizers, Crop Resilience

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Introduction

People have depended on agriculture for a long period to obtain what they need for food, clothing and bioenergy. As the world's population increases and the climate changes, farmers have to find new ways to make farming both more productive and sustainable. Nanotechnology, by working with small materials at the nanoscale, provides new answers to these issues. Because of it, farmers can make things that are very precise, so interventions can be used to enhance various parts of farming (Shang et al., 2019).

Nanotechnology can change farming methods to make them more efficient, better for the environment and sustainable. The use of nanomaterials lets farmers handle nutrients and pesticides more efficiently, use less and keep a close eye on the soil. Furthermore, nanotechnology can be applied to create smart ways to transport drugs, biosensors and materials that help crops withstand different environmental problems (Gupta et al., 2023). The increase in world population and the need for more food bring problems to agriculture such as lower yields, issues from pests and diseases, climate change and a lack of water. With nanotechnology, nanoparticles contribute to nutrient delivery, pest control and stress management because of their unique shape, size, form and electrochemical features. The large surface area and strong structure of nanomaterials make them better for agricultural use than regular materials. Metal-based engineered nanoparticles have attracted notice for their adjustable properties (Zulfiqar et al., 2024).

Nanotechnology assists in saving the environment by helping to produce clean air and environmentally safe products. But there are worries that nanoparticles can be toxic because they may change how cells interact with their environment, absorb nutrients and carry out their metabolic processes. Because of these risks, companies must take steps to evaluate and control them (Klaine et al., 2008). Using nanotechnology in farming makes resources more efficient cuts down on contaminating the environment and helps crops grow better by applying just the right number of pesticides and fertilizers. Precision farming and monitoring crop health in real time help build a food supply that will last for years to come (Lead et al., 2018).

This chapter examines the transformative role of nanotechnology in agriculture, exploring its applications, benefits, and challenges in building a sustainable agricultural framework.

2. Nanotechnology in an Agricultural Context

Nanometer is equal to one-billionth of a meter; it is too small for most humans to imagine. At this level, the properties of materials are quite different from those you see in larger pieces. At this size, quantum effects are noticeable; the ratio of surface to volume increases and materials may have unusual reactivity and interaction abilities. Nanotechnology in agriculture uses nanomaterials, nano-sensors and nano-devices to boost productivity make farming more efficient and help it be more sustainable. Due to their special physical, chemical and biological traits, nanoparticles are suitable for many uses, including farming and conserving the environment. Nanoparticles key features such as a great deal of surface area, increased responsiveness and ways to interact with biological substances that are not seen in larger particles (Nasrollahzadeh et al., 2019).

In agricultural applications, nanotechnology in farming helps farmers focus their actions more accurately. Unlike before, nanoscale technologies make it possible to manage certain biological activities with great accuracy. Because of this, farming is more efficient, sustainable and friendlier to the environment (Shang et al., 2019).

Agriculture has consistently been the most important industry since it sends raw materials to both the feed and food industries (Velasco-Muñoz et al., 2021). Because there are more people on our planet and fewer natural resources, growing food must be productive, successful and protect the environment. Much of objectives for future will depend on our transformation taking place (Mukhopadhyay, 2014).

2.1 Current Agricultural Challenges

With the world's population increasing, global agriculture must discover how to produce more food without harming the environment (Duro et al., 2020). The amount of farmable land is shrinking, there is less water and climate change is making it much harder for traditional farming to meet food needs (Ingrao et al., 2023). Environmental pollution can happen because of the many chemicals, water pollution and greenhouse gas emissions from traditional farming (Chataut et al., 2023). Conventional approaches for fertilizing and handling pests can damage the environment and lead to extra resources being wasted (Shanmugavel et al., 2023).

2.2 Nanoscale Materials: A Comprehensive Solution

Nanotechnology is helping farmers manage nutrition, water supply, pests, diseases, the environment and crop strength. They can address global agricultural issues and sustainably help people get food (Shang et al., 2019).

2.3 Improved Nutrient and Water Delivery

A good way to deliver nutrients and water is essential for healthy crop growth. The usual way of adding fertilizers and watering plants often allows nutrients to escape which both reduces the size of harvests and harms the environment. By using nanoscale fertilizers, farmers get better results from using less fertilizer, as their plants better absorb essential nutrients. The approach helps to cut down waste and pollutants and protects the environment (Yadav et al., 2023). Nano-hydrogels and nano-clays are being added to soils to help them keep water. Their ability to hold water, nano-hydrogels help soil soak up about 40% more water and are valuable in places with less water. Also, when irrigation uses nano-based technology, less water evaporates and less runs out. These innovations improve the way we use water and protect agriculture in places where droughts could occur (Zaib et al., 2023).

2.4 Nano-fertilizers: Precision Nutrient Delivery and Improved Absorption

Nano-fertilizers are revolutionizing plant nutrition by providing nutrients with remarkable precision. Plant nutrition is being improved by the accurate supply of nutrients with nano-fertilizers. Using typical fertilization techniques often means adding too much fertilizer and a lot of it is wasted. Unlike other fertilizers, nano-fertilizers are made to pass straight into the cells of plants, offering nutrients exactly as they need them (Kumar et al., 2021). There is less waste since nutrients are not released as fast like with conventional agriculture. Assuming studies, introducing nano-fertilizers into farming may result in nutrient efficiency improving to 80% which is a useful improvement for farmers (Easwaran et al., 2024). Nano-fertilizers are flexible enough to be adapted to fit the needs of every plant. Nutrients in soil can be made available by soil pH, temperature or moisture. Plants can get the nutrients they need most during important growth stages, so their yield is high and they require less frequent fertilizing. Using nano-fertilizers in precision agriculture systems improves both the usefulness and the benefits they provide to the environment and the economy (Iqbal, 2019).

Many traditional ways to apply fertilizer led to large amounts of nutrients being lost and the environment being polluted. Nano-fertilizers help solve the problems that traditional techniques can't address. These advanced materials are designed to give plants nutrients more exactly, making plant nutrition management better (El-Saadony et al., 2021).

Nano-fertilizers have the ability to make nutrient use more efficient. Conventional fertilizers are spread everywhere and can be wasted, unlike nanoparticle-based fertilizers which are designed to work with plant cells (Das & Das, 2019). Both silicon dioxide (SiO₂) and zinc oxide (ZnO) nanoparticles are known to help improve how the body uses nutrients and its metabolic functions (Zafar et al., 2024).

Nano-fertilizers have many different advantages. It has been demonstrated that nano-fertilizers can improve nutrient absorption by as much as 80% which means crops grow better and there is less harm to the environment. In addition, nano-fertilizers make it possible to release nutrients in a controlled way. Nano-fertilizers are different in that they can be set up to release nutrients slowly which fits the plant's schedule and helps avoid losses. This helps your body use nutrients better and also reduces harm to the environment (Ayenew et al., 2024).

Nano-fertilizers are able to overcome important agricultural issues. These new methods help crops by cutting back on chemicals and improving how nutrients are given, creating a more sustainable way to feed them. It has been found in field trials that using nano-fertilizers can cut fertilizer use by half without affecting or increasing crop yields (Goswami et al., 2024).

2.5 Nano-pesticides: Targeted Pest Control with Reduced Environmental Impact

Broad spectrum conventional pesticide use is usually with chemicals that can harm 'beneficial' organisms and disturb the functioning of ecosystems. On the other hand, however, nanotechnology includes new pest control technologies that are specific and effective. Long lasting efficacy results from their sustained and controlled release mechanisms yet these do not harm non target organisms. The nano-pesticide, for example, could be engineered to degrade after it targets the insect, thereby, reducing residual contaminant (Yousef et al., 2023). In addition, nano-particles are able to 'target' delivery of active ingredients to pest sites thereby increasing efficacy at lower concentrations. In addition, nanotechnology allows biodegradable carriers that minimize environmental persistence and, in turn, reduce long term ecological effects. More recently, new development includes smart nano formulations that will only release active ingredients under appropriate environmental conditions, i.e. presence of pests. In addition to optimizing effectiveness, this also minimizes waste, just as well as global efforts to minimize chemical dependence and to adopt curiosity for sustainable crop protection practices (Zainab et al., 2024).

In addition to pest management, nanotechnology holds promise in disease control through nanoscale delivery of antimicrobial agents and vaccines. These treatments can prevent diseases from developing and curtail the spread of pathogens, significantly reducing crop losses (Biswas et al., 2023). This targeted approach also reduces the risk of pests developing resistance to pesticides.

Gacem et al. (2022) research showed how effective nano-pesticides are. For example, inhibition of agricultural pests like a wide range of insects was shown by copper oxide nano-particles. These nano-formulations represent an important asset as they allow more targeted pest control with much less environmental persistence than with conventional pesticide formulations (Gacem & Chaibi, 2022).

The critical benefits afforded from nanoscale pesticides are due to their distinctive features. As a result, their small size makes them better able to enter directly into plant tissue for improved pest control. Additionally, nanoparticles can be modified for sustained, controlled release and the quantities of chemicals that need to be administered for successful pest control are greatly reduced. A reduction in chemical usage of 40-65% while maintaining or improving pest control efficacy has been shown in studies of nano-pesticides. It's a big step toward sustainable agricultural practice aimed at eliminating the use of chemicals that contaminate and harm the environment (Zhang et al., 2023).

2.6 Soil Health Monitoring and Improvement

Sustainable crop production requires healthy soil which however experiences degradation by soil erosion, nutrient depletion and contamination. One-way nanotechnology can enhance soil health is by offering tools to will allow you to monitor soil conditions — such as pH, moisture and nutrient levels in real time. Furthermore, the use of nano-materials can help improve soil quality; elevating microbial activity, increasing nutrient availability and decreasing the incidence of harmful pollutants. For instance, certain nano-particles can link to extra metals or solids in the soil to make them more easily extracted and seem less dangerous (Yadav et al., 2023).

3. Nano-sensors: Real-time Crop Health Monitoring and Early Disease Detection

Innovations in nano-sensors have helped to revolutionize the way crop health is looked after in agricultural monitoring. These small sensors can quickly monitor plant physiology without harm, giving farmers new ways to take care of crops. Ibrahim and others (2024) built sensors using carbon nano-tubes that show very good sensitivity for plant pathogen detection. Such nano-sensors monitor soil nutrients, plant stress, initial signs of disease and environmental changes all at the same time (Ibrahim et al., 2024).

Nano-sensors allow us to spot agricultural risks early, well before any damages become noticeable. Traditional approaches to crop monitoring which depend on visual examinations after much of the damage has appeared are different from nano-sensor methods which give fast and correct data needed for action beforehand (El-Abeid et al., 2024). According to Khattak et al. (2024), nano-sensors are able to detect gentle changes in plant metabolism, how they handle nutrients and their reactions to stress accurately. By using real-time data, farmers are able to deal with issues before they get too serious, turning reactive habits into predictions (Khattak et al., 2024).

Teaming up nano-sensors with advanced data analytics raises their ability to solve problems. Farmers can learn about possible crop health problems in real time, so they can take quick action. After finding molecular signs suggesting the presence of pathogens, they can warn those in agriculture about possible hazards early on. The ability to spot risks early on greatly improves how we protect our crops (Shaw & Honeychurch, 2022). Nano-fertilizers, nano-pesticides and nano-sensors all work together to transform agriculture, as can be seen in Table 1. They provide new, precise ways to deal with issues farmers have for a long time faced which can make food production more efficient and friendly to the environment (Singh et al., 2024). Monitoring agricultural conditions in real time is needed if proactive management is to work. With nano-sensors, farmers can track nutrients in their soil, look after the health of their crops, observe for diseases early on and test for drought or salt conditions. Because the sensors give information instantly, farmers can make the right choices to save their crops and use resources efficiently (Alam et al., 2024).

4. Genetic and Cellular Interventions

With nanotechnology, interventions can be done accurately at the gene and cell level to drive new developments in crops. The use of nanotechnology supports gene transfer to make plants more tolerant of drought, less vulnerable to pests or better at using nutrients. Adding coatings to seeds made from nano-materials improves their ability to grow and ensures a strong beginning to crop growth (Kumari et al., 2023).

Zinc oxide nano-particles have demonstrated that they may help crops resist stresses and improve their yields. With nanotechnology, scientists are able to address targeted changes to crops by delivering their genetic material. With such progress, we now have more opportunities to grow crops that are adaptable in situations facing climate change (Inam et al., 2024).

5. Enhanced Water and Nutrient Use Efficiency

Scarcity of water is a serious problem all over the world, since water generation is heavily used in agriculture. Nanotechnology provides new answers for this challenge using nano-engineered water storage materials, advanced irrigation methods and nano-membranes for water reuse (Muhammad et al., 2025).

These hydrogels in soil improve its ability to hold water, so crops continue to get the moisture they need, even when drought occurs. Their use can lead to as much as 40% more soil retention on site, providing a lasting way to handle water challenges. Also, incorporating nano-materials into drip irrigation helps spread water more evenly prevents wastage and supports good farming techniques in dry and semi-dry areas (Vedovello et al., 2024). Nano-enabled filters also help purify polluted water so it can be used for irrigation and means less reliance on fresh water. As a result of these technologies, we can address water challenges and there is a continuous supply for irrigation. Nutrient use efficiency is also enhanced by nanotechnology. Nano-fertilizers can increase nutrient absorption by 80% than conventional methods (Pramanik et. al, 2020). The significant advantage of these advanced nano-formulations for modern agricultural practice is being able to deliver nutrients precisely to the plants. They are unlike conventional fertilizers in that they reduce loss of nutrient through leaching, holding the essential elements available to crops for longer time. Further, their nano-scale size promotes uptake of nutrients at the cellular level leading to healthier, more efficient plant health and growth. The key mechanism is that nano-particles (SiO₂ and ZnO) interact directly with plant cellular structures driving better nutrient uptake and metabolic processes (El-Saadony et al., 2022).

Table 1: Nano-fertilizers and Nano-pesticides: Key Characteristics, Applications, and Environmental Impacts with Nanoparticle Examples.

Category	Aspect	Details	Nanoparticles	Findings	References
Nano-Fertilizers	Precision	Nanoparticles enable direct	ZnO NPs, Fe ₃ O ₄ NPs	NPs, Nano-fertilizers improve	(Abdel-Hakim et
	Nutrient	nutrient penetration into plant	Carbon-based NPs	absorption efficiency by up to	al., 2023)
	Delivery	cells.		80%.	
		Nutrients are released gradually	Chitosan	NPs, Responsive release based on soil	(Shaghaleh et al.,
		based on environmental triggers.	Hydroxyapatite NPs	pH, moisture, and plant growth	2022)
				stages.	
Targeted Pest Control		Nano-fertilizers minimize nutrient loss through leaching and volatilization.	TiO ₂ NPs, Silica NPs	95% reduction in nitrogen runoff compared to traditional methods.	(Xia et al., 2020)
		Higher bioavailability of nutrients for plants.	ZnO NPs, Calcium Phosphate NPs	Improved crop yield and reduced need for reapplication.	(Hammerschmitt et al., 2021)
		Nanoparticles enable precise delivery of active ingredients to pest-affected areas.	Silver NPs (Ag NPs), Graphene Oxide NPs	Quantum dots release active compounds in response to pest activity.	(Ibrahim et al., 2021)
		Active ingredients are released only under specific environmental conditions.	Copper NPs, Chitosan NPs	Moisture-sensitive pesticides that activate during high humidity levels.	(Huang et al., 2018)
		Nano-encapsulation enhances stability and prolongs the activity of pesticides.	Polymeric NPs, Carbon Quantum Dots	Longer-lasting pest control compared to conventional formulations.	(Sarmah et al., 2024)
		Nanopesticides reduce the likelihood of pest resistance development.	Titanium Dioxide NPs, Silver NPs	Gradual and controlled release decreases exposure to sub-lethal doses.	(Pan et al., 2014)
		Reduced impact on non-target organisms and ecosystems.	Zinc Oxide NPs, Silica NPs	Lower toxicity to beneficial insects and soil microbes.	(Rashid & Chung, 2017)

6. Chemical Usage Reduction through Targeted Nano-interventions

For a long time, the industry has struggled against the environmental harm caused by overuse of pesticides and other agrochemicals. Large-scale use of chemicals on farms normally causes problems for the environment and wastes many resources. Nanotechnology creates a new way to deal with these challenges by offering precise treatment methods (Gallardo, 2024). Targeted intervention at the nano level was found in experiments to help reduce chemical use. Such chemicals deliver nutrients and pesticides extremely well, enabling farmers to treat problems in specific areas rather than many open areas. Using this strategy reduces negative impact on the environment and increases performance. As reported by Saritha et al. (2022), the use of nano-based agriculture might help reduce chemicals used by up to 60-75%, compared to traditional techniques. Experimentally, zinc oxide nano-particles outperform in pest control and planting; the solutions they provide are narrowly designed to safeguard the environment from further contamination (Saritha et al., 2022).

7. Sustainability Improvements: A Deeper Dive into Nanotechnological Innovations

7.1 Advanced Mechanisms of Chemical Reduction

Agriculture for decades has required great amounts of chemicals, leading to major environmental damage. Nanotechnology gives a precise means to use less chemical, ensuring greater effectiveness. The use of nano-encapsulation in chemicals reduces chemical leaching by about 90% and sharply lowers pollution (Sharma et al., 2023).

Nano-particles built for agriculture are designed using technology that includes smart changes to their surface, ways they release their content and the ability to connect with specific materials. As an example, by setting up certain requirements in the soil, quantum dot nano-

particles will only deliver the nutrients or pest control products that are required. Precision application in farming eliminates waste and harmful excess use of agricultural chemicals (Mittal et al., 2020).

7.2 Advanced Solutions for Water Management

Farmers everywhere are struggling with drought, but nanotechnology offers solutions that are beyond traditional options. If we immerse nano-hydrogels in water, they turn into reservoirs that release moisture to plants over time (Shemer et al., 2023). They guide the water to where it's needed, stop it from slipping out and offer plenty of moisture to the roots. Because of this technology, less water is used and crops are better able to handle different environmental problems. Because they use less traditional watering methods, nano-hydrogels improve the management of water resources (Vundavalli et al., 2015).

7.3 Broader Ecological Implications

Apart from boosting productivity, nanotechnology affects the way we manage agricultural ecosystems. Introducing these measures raises biodiversity, toughens ecosystems and reduces the amount of chemicals entering the environment. So, new farming methods are allowing us to address problems stemming from climate change and a lack of resources (Ezeonu et al., 2012).

8. Technological Mechanisms Driving Nanotechnological Innovations

8.1 Nanoparticle-Mediated Genetic Material Transfer

The innovations made possible by nanotechnology are really changing how we look after our farms. A highly useful application of nanoparticles is their ability to deliver DNA into plant cells more precisely than any other technique. By using this approach, cells are modified efficiently and plant integrity is protected as little cellular disruption takes place. Also, the genetic material enclosed in nanoparticles becomes more stable and precise, cutting down the chance of unplanned genetic changes. Unlike earlier genetic engineering, using nanotechnology produces crops that are more productive, genetically improved and can last longer, with less impact on the environment (Mmbando, 2024).

8.2 Controlled Release Systems for Agrochemicals

The usual use of agrochemicals is known to cause ineffective use and environmental damage since too much is often spread not only targeted. Advanced controlled-release systems developed using nanotechnology address these problems by increasing both accuracy and sustainability. Nano-agriculture has developed a key feature where nanoparticles react to pH, moisture or temperature changes, so that agrochemicals are released only in suitable weather or soil. Using this technique increases the timing and purpose of the active ingredients and also significantly cuts down the possibility of these ingredients seeping into surrounding areas. By targeting the chemicals only to where they are needed such systems increase their effectiveness and help decrease the effect on the environment (Kumar et al., 2021)

8.3 Nano-encapsulation for Enhanced Protection

Applying nano-encapsulation to agrochemicals makes them resist damage from the environment and stay stable. The use of herbicides improves the application rate and reduces waste. Furthermore, as a result of this technique, agrochemicals can remain active for a longer time, so less needs to be applied, lessening harm to the environment (Pateiro et al., 2021).

8.4 Integrated Technological Mechanisms

The greatest benefits of using nanotechnology in farming appear when its various techniques are combined into one system. When we mix genetic material transfer, controlled-release technologies and nano-encapsulation, we have the potential to handle more than one agricultural complication. With this strategy, there's better use of resources, an improvement in productivity and crops become abler to withstand environmental problems. Besides, it greatly lowers the environment's burden from farming which in turn helps to maintain sustainability and boost efficiency (Mahra et al., 2024).

Conclusion

Overall, nanotechnology could greatly benefit agriculture, though the main issue is how to tackle problems of scaling, expense, access fairness and public reaction. Working to ensure that smallholder farmer's gain from these advances means making nano-solutions practical and inexpensive. At the same time, strict laws, informing people and close teamwork make sure smart technology is used safely. In this way, nanotechnology can help build an agricultural field that is both eco-friendly, efficient and withstands problems.

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Nanobiotechnology in Cancer Therapy: Targeted and Personalized Treatments

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Abstract

The field of nanobiotechnology is changing how cancer is treated by joining nanotechnology with biology to deliver treatments that target individuals. Combining various techniques makes it possible to accurately deliver medicines, fight many drugs growing resistant, enhance immunity and cut the overall harmful side effects for the patient. Targeted delivery of drugs is achieved with specialized nanoparticles, using either passive or active strategies known as liposomal doxorubicin and polymeric nanoparticles. Nano-biosensors are used to discover biomarkers and nanocarriers are developed to deliver CRISPR/Cas9 and siRNA for genetic editing in this area. Theranostic systems that diagnose and treat at the same time, together with lights-based therapies called photothermal and photodynamic, give patients effective and less invasive treatments. Spite such challenges as toxicity, policies and ethics, new technologies such as smart nanoparticles, artificial intelligence and sustainable nanotechnology, are bringing good progress to oncology and encouraging wider and more effective use of their applications. Nanobiotechnology is expected to help more precisely treat cancer and benefit patients worldwide.

Keywords: Nanobiotechnology, Targeted Drug Delivery, Precision Oncology, Theranostic systems, Photothermal, Photodynamic

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Introduction

Cancer is still one of the toughest problems facing modern medicine, due to its biology, complex nature and malignant cells' willingness to adapt. Although chemotherapy, radiation therapy and surgery are central to cancer treatment, they usually have many disadvantages (Chu et al., 2024). Such drugs have limited specificity which harms the body's healthy cells, can lead to resistance and so reduces treatment success and living standards for patients. Since cancer is being discovered in more people worldwide, new strategies that address these challenges are needed quickly (Jacquemin et al., 2022).

The field of nanobiotechnology now provides important new treatments for patients dealing with cancer. The field combines deep knowledge in nanotechnology and biology, using the special features of very small materials to work with living systems at their smallest parts (Chehelgerdi et al., 2023). Because of their strong features such as large surface-area, adjustable size and more reactions, these nanomaterials are suited for new cancer treatment methods. Precision and versatility, nanobiotechnology supports new targeted, individualized and gentler methods for treating cancer (Mosleh-Shirazi et al., 2022).

The treatment of cancer around the world underlines why new innovations are required. WHO data reports that cancer caused about 10 million deaths around the globe in 2020, placing it as the second most common cause of death (Cao et al., 2024). As a result of this high number, we need to explore new treatments that offer more than existing approaches. Increasing numbers of cancer cases are partly due to older people, changes in how we live and greater contact with carcinogens, calling for attention to effective and patient-friendly approaches (Denburg et al., 2019).

Nanobiotechnology is already making major changes to oncology by helping to resolve some of the main problems seen in regular treatments. Making use of nanotechnology makes it possible to administer medication to certain body parts, offering controlled drug discharge and lowering toxic effects or side effects. Besides, when these diagnostic and treatment functions are merged in a single platform,

known as theranostics, it provides a convenient way to care for cancer. This way, the results from treatments can be checked as they happen and diseases can be noticed earlier, guiding better and more flexible reactions (Patra et al., 2018).

By involving several areas of science, nanobiotechnology is a big step forward in the fight with cancer. Improving effectiveness, reducing negative effects and merging diagnostic tools with treatment make it vital to future oncological care. Accepting these developments, health professionals are overcoming the issues of traditional methods and giving millions of patients' new reasons to hope (Ma et al., 2024).

2. Targeted Drug Delivery Systems

Targeted drug delivery systems are among the biggest contributions of nanobiotechnology to treating cancer. Unlike regular chemotherapy that shares drugs all over the body, these systems permit more local use of drugs, cutting down on the risks and boosting treatment at the tumor site. Nanotechnology enables doctors to send medications right to cancerous tissues, sparing the healthy ones, so the treatment works well and causes less harm (Yao et al., 2020).

2.1 Precision Drug Delivery Mechanisms

Nanotechnology for drug delivery depends mainly on passive and active targeting principles. Essentially, passive targeting is due to the EPR effect which allows nanoparticles to collect more in tumors than in healthy tissue because tumor blood vessels are abnormal and lymphatic drainage is reduced. With blood vessels having holes of 100 to 800 nm, large nanoparticles are able to enter and build up in tumor areas. Furthermore, slow lymphatic drainage in tumors stops the removal of nanoparticles, keeping them longer and allowing them to do their therapeutic work. Using this technique is most successful for nanoparticles sized 10–200 nm, because they slide past the kidneys and properly enter the tumor cells.

Targeting drug delivery more precisely is possible by loading nanoparticles with molecules such as antibodies, peptides, aptamers or other tiny molecules that adhere to the overabundant receptors known to be on cancer cells. Example: Nanoparticles decorated with antibodies for HER2 receptors bind only to cancer cells that over express HER2 and boost how effective the therapy is with much less damage to other cells (Yoo et al., 2019). In the same pattern, folate-attached nanoparticle systems target the increased presence of folate receptors in cancer cells from ovarian and lung tissues. With ligands attached to them, nanoparticles target cells accurately, enhancing the ability to carry out receptor-mediated uptake into cells (Anarjan, 2019).

2.2 Nanocarriers: Enhancing Drug Delivery Efficiency

Targeted drug delivery systems greatly rely on the use of nanocarriers. For instance, liposomes, dendrimers, polymeric nanoparticles and micelles are valuable due to the unique drug-encapsulating and delivering properties they all have. Phospholipid bilayers form spherical liposomes that include hydrophilic drugs in their inner aqueous region and hydrophobic ones in the surrounding layer (Alshawwa et al., 2022). Because of their increased solubility, better stability and more consistent bioavailability, chemotherapeutic agents in liposomes are considered safe and effective for drug delivery. PEG modification keeps the liposomes from being taken up by the MPS for longer because it reduces opsonization (Lu et al., 2021).

The tree-like structure of dendrimers and the large number of functional groups on their surface give them an ability to load drugs and adjust their surface chemical properties. Being extremely small and carefully made, these carriers accurately deliver substances where needed for treatment. As an example, PAMAM dendrimers are frequently examined for carrying cancer drugs such as methotrexate and doxorubicin (Mittal et al., 2021).

Polymeric nanoparticles with polylactic acid (PLA) and poly (lactic-co-glycolic acid) (PLGA) as biodegradable polymers ensure that drugs are released in a controlled pattern. They secure the drugs from early degradation and give a structural base for attaching targeting agents to the nanoparticles' surface. Both the paclitaxel and EGFR-targeting peptide on PLGA nanoparticles have increased the effectiveness of lung cancer models (Bhardwaj & Jangde, 2023). Self-assembled micelles, created by amphiphilic block copolymers, include both a core for hiding insoluble drugs and a surrounding layer for greater stability and solubility in aqueous solutions (Attia et al., 2011). These systems strongly support delivering paclitaxel and docetaxel which are hydrophobic chemotherapeutics. Transferrin-functionalized micelles were found to deliver drugs right to glioblastoma cells because transferrin receptors are overexpressed in these tumors (Gaucher et al., 2005).

2.3 Integrated Treatment Approaches

Today, cancer treatment relies on combination therapy to increase the power of drugs and overcome ways cancer cells become resistant. Combination therapy includes several types of therapy, including chemotherapy, therapies based on RNA and those that alter the immune response, by administering all of them together in one treatment. The problems with pharmaceutical incompatibility, poor absorption rates and harmful side effects in typical combined therapies are minimized, leading to better therapeutic results (Mokhtari et al., 2017).

2.4 Combining Multiple Therapeutic Agents

Nanocarriers have the flexibility to deliver many kinds of therapeutic agents, mainly chemotherapeutics, small interfering RNAs and some immunomodulators. Treatments that target cancer cells when they divide such as chemotherapy can also include siRNA to shut off important genes that make cancer cells resistant to treatment. This combination helps make the treatment even more successful and counteracts reasons for failure (Subhan & Torchilin, 2019).

Doctors and scientists regularly depend on polymeric nanoparticles and liposomes for combination therapy. Using these nanocarriers, it

is possible to contain and deliver both hydrophilic and hydrophobic drugs in the simplest way. Tumor models that were resistant to treatment showed better results when liposomal systems were loaded with doxorubicin and siRNA targeting MDR1. The siRNA knockdown of the MDR1 gene restores sensitivity to doxorubicin in the tumor and helps slow down tumor growth.(Parveen et al., 2023).

Nanotechnology is being used more often to combine immunomodulators which strengthen the immune system, with standard cancer treatments. Nanoparticles with both chemotherapy and anti-PD-1 or anti-CTLA-4 antibodies act in two ways: they harm cancer cells and help the immune system attack cancer. Combining treatments improves how the immune system works and makes it less likely that cancer will come back (Thakur et al., 2020).

2.5 Boosted Effectiveness and Minimized Resistance

It is very useful that nanocarriers can give therapeutic agents at the same time in our bodies. Differences in how drugs are absorbed or eliminated sometimes cause one drug to be delivered at a different time than another in a traditional combination regimen, lowering the effects of the treatment. This problem is addressed by nanocarriers which carry and release numerous agents together at the tumor site (Din et al., 2017). In breast cancer models, the combination of paclitaxel and curcumin in PLGA nanoparticles produced stronger results than those substances used separately. Paclitaxel reduces the functioning of microtubules, while curcumin blocks the NF- κ B way which is a factor in drug resistance. The combination treatments increase cancer cell death and at the same time reduce the risk of inflammation and boost the effectiveness of cancer treatments. Because of these systems, patients take lower doses of medications which lowers the chance of side effects in the body (Baek & Cho, 2017).

In addition, nanocarriers keep therapeutic drugs stable and prevent them from degrading too early. Since enzymes in the blood can quickly degrade RNA therapies, it is especially important for them. Wrapping siRNA into nanoparticles allows it to reach its target and become more effective in therapy. Polymeric nanoparticles containing both cisplatin and surviving-siRNA have helped control tumor growth in ovarian cancer studies. Dual-action nanoparticles show how combination therapy can produce the best possible therapeutic outcomes. These systems work on several cancer biology matters at the same time such as excessive growth, avoiding the immune system and resistance (Zare et al., 2022).

Using gold nanoparticles that absorb light in photothermal therapy (PTT) with chemotherapy is a new way to treat cancers. Activated by near-infrared light, these chemotherapy-carrying nanoparticles make heat around tumors which affects their blood vessels and increases the therapy's arrival to the tumor. Loading doxorubicin onto gold nanoparticles for PTT has led to tumor ablation that is more effective than the use of just one of these approaches (Han & Choi, 2021).

These systems are also used to deliver more than one drug at once. Building polymeric micelles using paclitaxel and bevacizumab has shown that the drug pair works best by addressing cancer growth and the formation of blood vessels. The combination interrupts blood delivery to tumors and encourages tumor cells to die, resulting in better outcomes in glioblastoma testing (Wang et al., 2010).

2.6 Tailored Therapeutic Approaches

Customized therapy for cancer is becoming a reality to considering each patient's personal genetic, molecular and clinical makeup and nanotechnology helps make this happen. Because cancer has many different genetic mutations and markers, doctors must use carefully designed treatments for each patient, especially since these factors differ within a single tumor. With nanotechnology, it is possible to tailor therapies by offering precise testing, directed drug transport and ways to alter DNA. Such nano-sensors are able to recognize particular cancer markers in the body with great accuracy and sensitivity, according to Alghamdi et al. (2022). With the use of sensors, scientists can identify molecules such as DNA, RNA or proteins that indicate cancer in the body which helps to manage both early detection and continual therapy tracking. Carbon nanotube sensors have recently been employed to discover KRAS mutations in colorectal cancer, directing personalized care and leading to improved results (Mikaeeli et al., 2024). Nanotechnology helps to specifically deliver CRISPR/Cas9 and siRNA, two gene-editing tools that are changing how we treat cancers caused by genetic mutations. These nanocarriers stop the medicines from breaking down during their time in the blood and direct them to the required cancerous cells. Lipid nanoparticles have shown to be very useful in getting CRISPR/Cas9 elements to oncogene mutations, both correcting genetic alterations and killing cancer cells. When loaded with siRNA, nanoparticles have been made to block the gene codifying for MDR1, making chemotherapies more effective against drug-resistant cancers. Using these nanocarriers, therapeutic agents go where they are needed most, protecting against wrong targets and harmful side effects (Zhou et al., 2024).

It also helps design a single platform called theranostics that can detect biomarkers and treat them at the same time. Imaging tumor-specific biomarkers, gold nanoparticles also allow chemotherapy or gene editing, so patients can move smoothly from being diagnosed to being treated (Raheem et al., 2023). Using multimodal machines simplifies care, boosts the success of treatments and reduces the number of invasive tests needed. Besides, being able to alter the environment surrounding a tumor is essential for personalized medicine. The use of nanoparticles in the tumor microenvironment changes the environment which can improve both the response to therapy and the activation of the immune system. Personalized nanomedicine has demonstrated the advantage of overcoming common problems with cancer treatment, making therapies both safer and more effective than one-size-fits-all options. Developments in nanotechnology will enable personalized cancer care and help narrow the gap between research and actual use at the patient's bedside (Al-Thani et al., 2024).

3. Development of Theranostic Platforms Combining Imaging and Treatment

The unique traits of nanomaterials, including how easy it is to adjust their size, their high surface area and how diverse their functions are, are used by theranostic platforms to bring together therapies and imaging tools. These platforms serve to give therapy as well as inform physicians about the tumor's location, size and reaction to the therapy. It is important for such work to support precision oncology which means treatments are changed in response to how the tumor behaves at every stage (Kim et al., 2024). Their multifunctionality and ability to

adapt make nanoparticles the main basis of theranostic platforms. Some research teams apply quantum dots for imaging, as well as delivering cancer drugs into the cancerous cells. In addition, polymeric nanoparticles can include substances useful for scanning (such as gadolinium for MRI) and also carry medicines designed to stop cancer growth (like doxorubicin). With these hybrid tools, clinicians can instantly see both the spread and the success of the given treatment within the body (Altinbasak et al., 2024).

Among important advances in theranostics, stimuli-responsive nanoparticles have been developed that release their medicines in reaction to changes in pH, temperature or enzymes. Because they work best only where the environment is acidic and holds enzymes, they are highly valuable in cancer therapy. At the same time, their imaging features let doctors track the therapy immediately, so they can tell right away if the treatment is having the desired results (AlSawaftah et al., 2022).

4. Real-Time Monitoring of Treatment Efficacy

Getting real-time updates on the safety of treatments is one of the greatest advantages of using theranostics. As a result, specialists can recognize how tumors react to treatment and can respond quickly by adjusting therapy, to help patients avoid unwanted side effects. For example, using gold nanoparticles in photothermal therapy helps doctors keep track of temperature in the tumor as treatment goes along, ensuring cancer cells are destroyed without hurting other tissues. Their optical imaging properties, specialized nanoparticles can be used to see a tumor shrink in real time, allowing for quick results (Lee et al., 2020). In a similar manner, using magnetic materials in MRI-theranostics lets clinical staff distribute medicine continually and monitor how the tumor responds. Adding therapeutic agents to tiny magnets helps doctors see how the medicine reaches the tumor and watch the results of the treatment. For patients with metastatic cancer needing to treat several tumors, this type of imaging is very helpful (Gauger et al., 2020).

One new area of theranostics is the use of nanoparticles with molecular probes to find drug resistance when it happens. These systems spot signs of resistance in the cancer, so doctors can treat the patient differently before the cancer grows. Just as an illustration, with HIFs, theranostic nanotechnology targets the regions in tumors where blood is deficient, while delivering and activating medicine that kills resistant cancer cells (Sun et al., 2023).

5. Light-Based Nanotechnology Therapies

Light-based nanotechnology methods are highly modern and are widely used for treating various cancers. Through these techniques, light is used to make nanoparticles or photosensitizers active in the tumor, so cancer cells are eliminated precisely without hurting neighboring healthy cells. By combining these therapies with immune therapy, their potential as therapies for cancer increases through a kind of teamwork (Overchuk et al., 2023).

6. Photothermal Therapy (PTT) with Gold Nanorods and Nano shells

Photothermal therapy relies on nanomaterials that change captured images of light into heat, killing cancer cells. Among all agents, gold nanorods and nano shells have an edge in PTT due to their excellent near-infrared (NIR) light absorption which makes it easiest for light to penetrate tissues. The gold-based nanoparticles, when activated by NIR light, cause the temperature of tumor cells to increase so much that they die. Heat triggers injury inside the cells and also harms the vessels supplying the cancer, making it grow more slowly (Riley & Day, 2017). The aspect ratio of gold nanorods is easy to adjust, making it possible to control how they interact with light. Gold nanorods have been shown in studies to cause hyperthermia in tumors and reduce tumor growth in test models. Similar to other gold structures, gold nano shells (a core with a gold coating) are used in the treatment of breast and prostate cancer with PTT. It has been proven in studies that nano shell mediation of PTT may support treatment either on its own or in cooperation with chemotherapy to help drugs reach the target by widening blood vessels (Yu et al., 2024). Using Nanoparticle Photosensitizers for Photodynamic Therapy (PDT) PDT depends on photosensitizers which, when exposed to light, generate ROS and harm both the cancer cells and the cells around them. Photosensitizers benefit from nanoparticle-based delivery, as it improves their stability, helps them reach the right tissue and enhances their usefulness because of the problems caused by their poor solubility and fast clearance by the body (Zhou et al., 2016).

Many clinicians rely on porphyrin-based photosensitizers in PDT. Their pharmacokinetics and tendency to build up in tumors are greatly enhanced when they are put in nanoparticles. In fact, using liposome-encapsulated porphyrins enhances the tumor-related production of ROS, helping ablate it more than applying normal free photosensitizers may. In addition, when silica nanoparticles are functionalized, they show high efficiency in treating breast cancer in animal models. By co-delivering photo-agents and other medicines, nanoparticles can produce better therapeutic effects. In the case of hybrid nanoparticles joining photosensitizers with chemotherapeutics, the effects on tumor growth are higher because many pathways involved in oxidative damage and apoptosis are activated (Akbar et al., 2023).

7. Synergy of Light-Based Therapies and Immune Activation

A major advantage of light-based nanotechnology therapies is their ability to trigger the immune response which opens the door for better cancer treatments. Immunogenic cell death (ICD) is triggered by each method, making TAAs and DAMPs available to boost response from the immune system against tumor cells. Along with the main cytotoxic effects of light, immune activation extends how long these therapies are effective and decreases the risk of tumor regrowth (Guo et al., 2022). As a result, PTT of tumors leads to TAAs and heat shock proteins which dendritic cells and other antigen-presenting cells detect, prompting the activity of cytotoxic T lymphocytes. Work with gold nanorods indicates that PTT helps more CD8⁺ T cells reach the tumor site, leading to better overall anti-tumor defenses. In the same way, PDT-triggered ROS led to cell destruction and also draw immune cells to where the tumor is located. Nanoparticle-enhanced PDT is able to present TAAs at a better level, encouraging strong T-cell immune responses. Moving on to first-generation treatments, joining PDT with immune checkpoint inhibitors like anti-PD-1 antibodies has led to long-lasting tumor regression in studies done with animals (Zhang et al., 2022).

8. Nanoparticles in Combatting Drug Resistance

Drug resistance is a major problem for cancer treatment, primarily for cancers that grow and return. Several things contribute to cancer MDR such as overactive efflux pumps, changes in drug targets, improved DNA repair and avoiding apoptosis. Because of these factors, chemotherapy drugs often do not work well which causes the disease to continue advancing and treatments to fail. Experts believe that nanotechnology is helping deal with drug resistance by allowing the use of targeted therapy, eliminating pathways that make drugs less effective and restoring the ability of medicines to work (Emran et al., 2022).

8.1 Targeted Delivery of Agents against Resistance Pathways

Nanoparticles help conveniently deliver small interfering RNA (siRNA) and CRISPR/Cas9 gene-editing systems to disregard pathways implicated in drug resistance. siRNA-loaded nanoparticles can efficiently block the MDR1 gene which codes for the P-gp pump and therefore stops the cells from developing drug resistance to therapy. By using lipid nanoparticles, scientists have shown that MDR1-targeted siRNA can restore paclitaxel's effects on ovarian cancer cells and lead to major tumor shrinkage in animal studies (Huang & Xiao, 2022). Using gene-editing tools inside nanocarriers gives a stronger method for handling resistance. CRISPR/Cas9 allows scientists to remove genes that make bacteria immune or repair changes in the genome that cause therapy unwanted side effects. Researchers have found that gold nanoparticles, designed for use with CRISPR/Cas9, disrupt the expression of P-gp proteins in breast cancer cells resistant to many drugs (Xu et al., 2021). Nanoparticles allow apoptosis factors to be sent to frog eggs, overcoming the resistance issue. Polymeric nanoparticles holding Bcl-2 inhibitors have been found to help overcome resistance to chemotherapy in cancer by stimulating apoptosis in cells with strong anti-apoptotic proteins (Yoo et al., 2024).

8.2 Restoring Treatment Sensitivity with Targeted Molecular Interventions

Treatment effectiveness in resistant tumors is improved when targeted drugs act on the nearby cell environment and its inner activity, made possible by nanotechnology. Often, the microenvironment of a tumor protects cancer cells from therapy by offering supportive zones through lack of oxygen, acidic surroundings and joint characteristics of non-cancer cells. Devices consisting of nanoparticles that only release their drug when the tissue has low pH or less oxygen ensure that resistant cancer cells receive the healing agents while healthy tissues are not damaged (Fernandes et al., 2018). In other words, nanoparticles may carry materials that modify cancer metabolism to help fight resistant cancer. Such carriers, when given loads of 2-deoxyglucose, can stop cancer cells from getting the necessary energy, improving the results of traditional therapies. Through focusing on the metabolic adaptations of resistant cells, nanoparticles weaken their ability to keep multiplying during treatment. A strategy that combines both types of drugs shows great promise. Cancer cells' resistance to chemotherapy can be overcome by nanoparticles containing both paclitaxel and HDAC inhibitors which act by changing the cell's epigenetic profile and restoring sensitivity. Targeting both genetic and epigenetic parts of resistance helps cover possible MDR in a single treatment (Wang et al., 2024).

Conclusion

The use of nano particles in cancer treatment helps focus therapy cuts side effects and raises the success rate. Even so, the full potential of nanomedicine in medical practice is kept limited by nanoparticle toxicity, unknown long-term outcomes, complex regulations and high manufacturing costs. Questions about how people should have access to their own treatments and how genetics should be used add more issues to this topic. Continuing with new ideas, advanced particles that react to various signals and using artificial intelligence may solve these issues. Also, greener and cost-effective manufacturing tries to make nanomedicine larger and more sustainable. Because of interdisciplinary efforts and conscious innovations, nanotechnology may make cancer care safer, more successful and accessible to all.

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The Future of Nanotechnology in Biotechnology: Emerging Trends and Innovations

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Abstract

Nanotechnology is greatly improving biotechnology by supplying fresh solutions for medicine, agriculture and environmental sustainability. This study looks at growing innovations and areas for future growth in nanobiotechnology. Targeted use of nanomaterials, improvements in gene therapy and advances in biosensing are making major changes in diagnosing and treating illnesses. Advances in nanomaterials are being achieved more quickly today due to using artificial intelligence (AI) and machine learning (ML) together which is helping create new treatments, diagnoses and solutions for the environment. In addition, there is a new emerging technology called nanorobotics that gives medicine, drugs and industry higher levels of precision and helps clean the environment. Refined nanofabrication and practical biofunctionalization are helping to make biosensors more sensitive and encouraging sustainable methods used in agriculture. Although these advances look good, we must still deal with safety issues, ethical questions and government guidelines. Joining forces between researchers, policymakers and businesses is essential for improving responsible innovation. This concept expects nanobiotechnology to advance health care, increase sustainability and improve many aspects of industry, helping to resolve ecological problems worldwide.

Keywords: Nanobiotechnology, Targeted Drug Delivery, Artificial Intelligence, Biofunctionalization, Policymakers

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Introduction

Nanotechnology is the handling and application of materials at the nanometer level and is making important progress in biotechnology. This work deals with developing, building and applying materials, devices and systems that have special qualities because of their extremely small size. Applying the special features of nanoscale materials enables nanotechnology to solve tough biological challenges and strengthen different biotechnological solutions. The power to work with cells and molecules at the nanoscale has transformed medicine, agriculture and environmental science, so that now nanotechnology is essential for modern biotechnology. For instance, special nanoparticles can target single cells, making sure that drugs go exactly where they are needed and reducing the side effects often found in standard therapies (Saleh & Hassan, 2023).

There are now new types of diagnostics, including nanosensors and biochips, that function quickly and accurately to detect diseases at an early point. They allow us to treat patients more effectively while also giving personalized medicine a new level of support to genetic information. Besides, using nanotechnology, bioengineered materials and organs are easier to develop because it improves the scaffolds used in the tissue engineering process and allows for faster development of new biotechnologies and medical solutions. They demonstrate that nanotechnology connects ideas in science to useful technologies in biotechnology (Malik et al., 2023). Since nanotechnology interacts with biotechnology, experts from different disciplines, including physics, chemistry, biology and engineering, have to collaborate. The interdisciplinary way is essential for handling the scientific and technical problems in nanobiotechnology. In other words, to design and use nanoparticles correctly, one must know much about chemistry and materials science in one area and molecular biology and biochemistry in another. Joining forces allows scientists to create nanomaterials that can serve both as medicines and as tools for diagnosing diseases, a process known as theranostics. How these efforts worked so well points to the gains made when different fields come together (Patel et al., 2024). A schematic illustrating in Figure:1 various sensing technique and the integration of micro- and nanotechnology to enhance their specificity and sensitivity, paving the way for innovative solutions to emerging biomedical and

environmental challenges. The innermost circle depicts core sensing techniques, including resistive, capacitive, piezoelectric, optical, acoustic, and electrochemical sensing. Surrounding this, the middle circle highlights advancements in micro- and nanotechnologies, such as nanoparticles, nanomaterials, microfluidics, and MEMS, which, in conjunction with the Internet of Things (IoT), are being applied to improve the performance of these fundamental techniques. The outermost circle represents biomedical (blue) and environmental (green) challenges that are being addressed through the application of these enhanced technologies.

Nanobiotechnology ethics and rules are greatly helped by the participation of various experts. Because this field is rapidly developing, new and comprehensive ways to check safety, effectiveness and ethics are being formed. Teamwork between scientists, policymakers and ethicists guarantees that nanobiotechnology's growth and use is guided by both society and ethical rules. Because unintended risks are a significant concern in these fields, they must be considered thoroughly. The reason behind these frameworks is to uphold public trust and favor responsible innovation (Souto et al., 2024). Also, having different backgrounds working together in nanotechnology for biotechnology helps create new ideas and solutions. As another example, material scientists and biologists have created nanocarriers that work like the membranes in cells, helping them do their job well inside bodies. Similarly, working together, engineers and clinicians have developed tiny medical devices used for safe operations within the body and for instant monitoring of health. By highlighting these achievements, it's clear that aligning efforts in this area helps push the field forward in nanobiotechnology (Ji et al., 2024)

2. Emerging Trends in Nanobiotechnology

Advances in healthcare, diagnostics and tissue engineering have been made possible by nanobiotechnology's rapid effect on the life sciences. By blending nanotechnology with biotechnology, experts have developed several new approaches to handle tough biological and medical problems. Nanobiotechnology has made progress in three main fields: nanomedicine, targeted drug delivery, advances in diagnostic biosensors and new developments in nano-bio interfaces for tissue engineering. The achievements in this area suggest nanobiotechnology may dramatically transform modern medicine and biotechnology. A big step forward in this area is the creation of ways to deliver drugs more precisely which has changed how treatment is done. Often, standard drug delivery choices result in toxicity spreading throughout the body, restricted absorption and unexpected side effects. For specific cell treatment, scientists often depend on nanoparticles like liposomes, polymeric nanoparticles or dendrimers to ensure the drugs only reach the intended places in the body, leading to a better outcome and fewer negative consequences (Ciftci et al., 2025). Figure 2 demonstrates nanoparticle-mediated drug delivery targeting atherosclerotic plaques in a mouse model. The left panel shows NPs interacting with red blood cells and macrophages in the bloodstream, while the right panel illustrates their accumulation at atherosclerotic plaques for localized drug release. This approach enhances therapeutic precision, reducing systemic side effects in treating cardiovascular diseases.

These systems are designed to stick only to receptors found on abnormal cells like cancer cells after special surface changes are applied. Specific targeting of tumors minimizes harm to normal body cells and helps lead to better health results. First, chemotherapy nanoparticles, including Doxil, have been proven to stay longer in the body and cause less harm than the common chemotherapy. Second, using nanoparticles that release directly when there are changes in pH, temperature or these factors allows for precise medicine (Elumalai et al., 2024). Nanomedicine has helped to develop new treatments for difficult diseases such as those affecting the brain and infections. Nanoparticles are able to penetrate the blood-brain barrier and carry medical substances to the brain. As a result, nanomedicine has great potential for treating diseases like Alzheimer's and Parkinson's and for blocking drug-resistant bacteria (Furtado et al., 2018).

3. Advances in Biosensors for Real-Time Diagnostics

Detection and measurement of biological molecules in samples are made possible by biosensors which blend biological components with transducers. Biosensor technology has changed a lot because of nanotechnology which has made them more sensitive, more specific and faster, allowing products to be tested in real time. Because gold nanoparticles, carbon nanotubes and quantum dots have special optical, electrical and chemical qualities, they are often used in biosensors to detect the presence of biomolecules at very early stages in disease (Ramesh et al., 2022). Figure 3 depicts the working principle of a biosensor, which involves several stages: first, the analytes (inorganic or organic substances) interact with a bioreceptor (such as antibodies, enzymes, or microorganisms), triggering a biochemical conversion. This biorecognition event generates a signal, which is then detected and converted by a transducer (e.g., optical, magnetic, electrochemical). The transducer's signal is amplified and processed to ensure clarity and accuracy. A reference component stabilizes the signal, and the final processed data is displayed on an instrument or computer for analysis, providing a measurable response related to the presence of the analytes.

Technology based on nanotechnology has greatly supported improvements in point-of-care diagnostics. Sensors made with nanomaterials can rapidly recognize signals of cancer, cardiovascular diseases and infectious diseases. Nanotechnology enabled immunosensors and biosensors locate tumor markers and manage glucose levels in diabetics better than previous options (Jalalvand & Karami, 2025).

The COVID-19 crisis saw nanotechnology help create new rapid diagnostic technologies. Pregnancy test-like lateral flow assays that use nanoparticles worked well to test for SARS-CoV-2 antigens. Through these tests, it was found that nanotechnology could offer global solutions for combating health crises by developing affordable, accurate and useful diagnostic tools, with ongoing research working on adding AI and data analysis to nanobiosensors for better personal diagnostics (Kakkar et al., 2024).

As well as being used in medicine, biosensors based on nanotechnology are being used to monitor the environment and food. As an example, nanosensors can reliably spot harmful materials in water, air and food, helping to keep public health safe and the environment clean (Sharma et al., 2024).

4. Innovations in Nano-Bio Interfaces for Tissue Engineering

Repairing, replacing or regenerating damaged tissues and organs is the goal of tissue engineering which uses cells, scaffolds and bioactive molecules. Now nano-bio interfaces can be used to let biological systems and made materials connect at a molecular level. Such interfaces copy the ECM of living tissues, so cells can easily attach, divide and specialize (Han et al., 2020). For tissue engineering, nanofibers, hydrogels and nanoporous materials are important types of nanoscale scaffolds. With scaffolds, cells have a way to organize and produce working tissues. Both electrospinning and nanofibers are methods of production that can reproduce the ECM's structure, making nanofiber scaffolds suitable for cell proliferation in tissue regeneration. It is also possible to program the release of growth factors from bioactive nanoparticles when they are added to the scaffolds (Matić et al., 2023).

Three-dimensional (3D) bioprinting is possible because of nanotechnology and enables the printing of complex tissues using bioinks and nanomaterials. This technology has worked for making skin, cartilage and simple organ test models. Introducing nanomaterials in the bioinks improves the mechanical and biological activities, linking printed tissues with native tissues (Kannayiram & Sendilvelan, 2023). Because of nanotechnology, engineers can now make nanocomposites that have the same composition and structure as regular bone. Tissues engineered with hydroxyapatite nanoparticles and polymers have demonstrated good integration into bones due to their great strength and osteoconductivity and when used in implants have led to faster bone growth and solution of infection risks (Zhang et al., 2024).

The use of nano-bio interfaces is also found in neural interfaces in addition to tissue engineering. Biomaterials such as carbon nanotubes and graphene have been included in neural scaffolds to support the regrowth of nerves and set up electrical links between neurons. The potential in using these interfaces for treating spine and brain damage, alongside other severe neurological conditions, highlights how much they can change regenerative medicine (Hammam et al., 2024).

5. Nanotechnology in Agriculture and Food Biotechnology

The field of nanotechnology has become a strong influence on agriculture and food biotech by supplying innovative ideas for solving big global issues around food security, sustainable growing and keeping food safe. Working with materials at the nanoscale has made it possible to invent technologies that increase harvest yields, are better for the environment and improve the quality and safety of foods. Because the world's population is growing and climate change harms farmland, nanotechnology is an important way to support sustainable and stable food supplies (Rana et al., 2024).

Among its greatest contributions, nanotechnology has helped treat fertilizers and pesticides. Many conventional fertilizers do not make effective use of their nutrients because much of them is wasted by runoff, leaching and volatilization, resulting in pollution and more expenses. Because they are so small and have high surface areas, nanofertilizers supply nutrients as needed to different parts of the plant. They improve how much nutrition is taken in, prevent many losses and help the environment by causing less pollution. In fact, using nano-encapsulated fertilizers for nitrogen and phosphorus helps nutrients be released over time, satisfying plant needs better and cutting back on the need for extra fertilizer (Pramanik et al., 2020). Otherwise, phytochemicals in nanopesticides have better control over pests as they are more soluble, bioactive and less likely to degrade too soon. Investigations into using chitosan and silica nanoparticles have demonstrated that they enhance the distribution of agrochemicals and reduce the amount needed (Abdollahdokht et al., 2022).

Plant protection and stress management are greatly helped by advances in nanotechnology. Nanoparticles such as zinc oxide (ZnO), titanium dioxide (TiO₂) and silver (Ag), have been examined because of their ability to reduce plant pathogens. They break through bacterial membranes, reduce several enzyme actions and disturb cells within the body, interrupting disease development without added synthetic chemicals (Sehsahb et al., 2023). In addition, plant stress resistance to dryness, saltiness and heavy metal toxins has been enhanced through the use of nanomaterials. Exposure of plants to silicon nanoparticles leads to better tolerance of drought by helping improve water uptake and trigger antioxidant activity (Faizan et al., 2023).

Apart from helping farming, nanotechnology is making major contributions to food biotechnology and food safety. New methods using nano-based technology can help identify pathogens, allergens, toxins and contaminants in food very efficiently. By using gold nanoparticles, carbon nanotubes and quantum dots, these biosensors become more precise, so they can be used to monitor food quality at any time and on-site. Using gold-based colorimetric sensors to find Salmonella in poultry in a fast manner, confirming their value in fighting food poisoning (Özcan et al., 2020).

Intelligent and active food packaging made possible by nanotechnology helps food stay fresh longer and ensures the product is safe. Depending on their properties, nanomaterials in active packaging help to release antimicrobial agents or remove oxygen and moisture which preserves products better. It has been discovered that polymer films containing zinc oxide and silver nanoparticles can stop growth of *E. coli*, *Listeria monocytogenes* and *Staphylococcus aureus*. Unlike regular packaging, intelligent packaging has nanosensors capable of sensing ammonia, changes in pH and temperature. Smart systems not only make things safer but also help cut down on food waste by telling consumers and retailers when food is fresh (Babu, 2022).

In the future, nanotechnology efforts in agriculture and food biotechnology aim at creating new solutions that are sustainable, protective of the environment and less costly. More attention is being given to green nanotechnology, the field that makes nanoparticles from natural or biodegradable sources. Nanobionics which combines nanotechnology with plant biology, is aiming to boost the photosynthetic, nutrient-sensing and signaling functions in agricultural crops. In addition, scientists are using AI and machine learning to make special nano-delivery systems that suit the needs of each crop and region (El-Khateeb et al., 2025).

6. Nano-Based Solutions for Crop Enhancement and Protection

There is strong potential for nanotechnology to help enhance and protect crops. Traditional farming can cause the environment to suffer, reduce soil nutrients and harm people because it depends on too many chemicals. Nano-based solutions answer these challenges by ensuring agricultural chemicals are applied more precisely and economically, leading to low wastage and also a better environmental profile

for farming (Shang et al., 2019). Nanofertilizers are considered a very promising new way to improve crops. With nanofertilizers, the nutrients are safely given to plants over a long period, unlike with many chemical fertilizers which can be lost before reaching the plants' roots. Nanoscale carriers in these fertilizers let nutrients be absorbed more easily by plants, resulting in bigger harvests with less fertilizer. As a result, using nano-encapsulated fertilizers rich in essential elements such as nitrogen, phosphorus and potassium often leads to better crop yields, according to Gade et al. (2023).

7. Food Safety through Nano-Sensors and Packaging Technologies

Everywhere, food is considered very important due to the serious risks of contamination and food spoilage for both health and economies. With nanosensors and improved packaging, nanotechnology now addresses food safety problems by spotting contaminants, protecting food for longer and maintaining its quality. They give an effective solution to solving food safety challenges at any point in the supply chain (Zhou et al., 2023).

Nanosensors have the ability to notice biological, chemical and physical contaminants in our food. With conventional detection methods, one has to spend a lot of time in a laboratory, but the same work can be done with a nanosensor much faster and more accurately outside the lab. Gold nanoparticles and quantum dots are used to construct nanosensors for Salmonella, Listeria and E. coli in food samples. When these sensors bind to their specific markers, they emit detectable signals to show if food has been contaminated. With real-time monitoring, problems in the plant can be addressed quickly, so that contamination cannot spread (Awilqadr et al., 2024). Nanotechnology is useful in food safety because it helps build smart packaging systems. Traditional packing only helps block outside factors from affecting the product, while nano-packing also works to help the product in more active and smart ways. Some active packaging includes nanotechnology with microbial capabilities, for example, silver and zinc oxide nanoparticles, to control bacterial and fungal growth on food surfaces. Active packaging means less food waste and ensures better quality for consumers (Otlés & Yalcin, 2015).

Intelligent packaging, on the other hand, lets you know at any moment about the condition of your packaged food. Nanosensors in different systems are used to check the temperature, level of humidity and types of gas in packaging. Tracking these qualities can let both consumers and suppliers know if food is no longer safe. When food is contaminated and has unsafe temperatures, it may change color and warn users not to consume it. Nanotechnology has improved the ways food products can be checked and verified (Chelliah et al., 2021). Combining nanomaterials with labels and tags can help you follow food from the source to the store. Because nano barcodes are made of tiny patterns or markers, they can hold detailed information on the source, components and quality of food products. This helps the food industry become fairer, reduces fraud and helps customers feel more secure (Aggarwal & Idrishi, 2023).

Nanotechnology helps to make food packaging more sustainable. Packaging made from nanocellulose and chitosan which are biodegradable, is an environmentally friendly alternative to regular plastic packaging. Such materials are strong, flexible and can act as barriers and they also help reduce waste and support environmental efforts worldwide (Gupta et al., 2024).

8. Nanotechnology in Environmental Biotechnology

Nanotechnology has transformed environmental biotechnology by introducing fresh answers for major global issues like pollution, harm to ecosystems and climate change. Work with nanoscale materials and processes has allowed scientists and engineers to design better ways to find pollution, clean up the environment and oversee the sustainable use of natural resources. The field of nanotechnology has made important contributions to both detecting and cleaning up pollution as well as to developing green bioremediation approaches. Apart from solving today's environmental issues, these innovations will support healthy environmental conditions in the future (Laxmi et al., 2023).

9. Applications in Pollution Detection and Remediation

A key part of environmental management is identifying pollution quickly, precisely and economically, by detecting contaminants in the air, water and soil. Most traditional methods for detection require complex tools and high effort, making them difficult to use for real-time surveillance. With nanosensors and nanomaterials, nanotechnology has greatly improved our ability to detect pollution by identifying tiny amounts of heavy metals, different compounds and pathogens (Zulkifli et al., 2018).

Although nanotechnology shows great potential in dealing with pollution, there are worries about how safe it is to use nanomaterials for these purposes. Because nanomaterials may be hazardous, stay in the environment and accumulate, we must assess risks and develop practices that reduce environmental damage (Xuan et al., 2023).

10. Nano-Bioremediation for Sustainable Environmental Solutions

Nano-bioremediation mixes the technology of nanoparticles with the idea of bioremediation to improve the cleaning of polluted sites. Until now, bioremediation has typically count. Adopting nanotechnology allows these methods to handle environmental issues with higher efficiency, greater control and scalability (Shahi et al., 2021).

Nanoparticles help increase the number of pollutants that microorganisms can deal with. Iron oxide nanoparticles and graphene offer a simple way to nurture microorganisms at contaminated locations, helping to speed up waste removal processes. Moreover, nanomaterials also provide enzymes or other biocatalysts with protection which helps these processes run much more smoothly (Dhanapal et al., 2024).

Nano-bioremediation is of great value when cleaning up sites affected by oil. Oil has been dispersed by adding nano-silica and nano-iron which both also maximize the surface area and encourage microbes to break it down. As a result, cleanup efforts for oil spills are sped up by enhancing interaction between nano-bioremediation and hydrocarbon materials. Nanoparticles that are functionalized can trap heavy metals which reduces their risk to humans and helps convert them to safe forms using microbes (N. Gupta et al., 2024).

Wastewater treatment has shown that nano-bioremediation can be very effective at getting rid of both types of pollutants. When wastewater is treated with both microbes and nanoparticles, the process is effective, saves on energy and lowers the cost, all making the system more sustainable (Hidangmayum et al., 2023).

Nano-bioremediation approaches are being considered to manage emerging pollution from pharmaceuticals, personal care products and microplastics which endanger ecosystems and humans. Nanomaterials, including some that have surface area, changeable porosity and functional surfaces, are capable of adsorbing or removing contaminants like microplastics from rivers and lakes (Johnson for example, working to prevent them from building up in water bodies (Shrivastava et al., 2024).

Adopting nano-bioremediation is limited by several difficult challenges, despite its good points. There is particular concern that nanomaterials could be dangerous to non-target organisms and the whole ecosystem. If nanomaterials are not safe and compatible with nature, nano-bioremediation won't succeed, so this is very important. Scalability and affordability are also important for using these technologies in large-scale projects (Liu et al., 2024).

11. Future Innovations in Nanobiotechnology

As nanobiotechnology grows, it leads to new advancements that solve medical, industrial and wider issues around the world. As advanced tools and nanotechnology are used together, they will help to reform how science and technology progress and what we are able to accomplish. Growing interest includes the use of AI and machine learning with nanotechnology and the chance to use nanorobots in many medical and industrial sectors (Elzein, 2024).

12. Role of AI and Machine Learning in Nanotechnology

Artificial intelligence (AI) and machine learning (ML) are bringing major changes to nanotechnology by helping researchers work faster, improve material design and improve process efficiency. Using these tools, we can review large data, spot regularities and predict outcomes which saves time and expense in doing experiments. Currently, AI and ML are helping to create nanoparticles, predict their outcomes in biological systems and get them ready for specific functions (as shown in Tripathy et al., 2024).

13. Potential for Nanorobots in Medical and Industrial Applications

Nanorobots, working on tasks too small for the human eye, are a high point in nanobiotechnology. Created from tiny sensors, actuators and molecular motors at the nano-scale, these devices offer the chance to change both medicine and industry because of their exactness and flexibility (Giri et al., 2021).

Nanorobots provide exciting opportunities in medicine for conducting tests, applying treatment and bringing drugs to their targets. They are most useful in drug delivery, especially where nanorobots move inside the body to deliver medication right to the sick tissues or cells. As an illustration, nanorobots that have molecular recognition skills can detect cancer by checking for specific biomarkers and then safely release drugs exactly where they are needed, making treatment effective and causing fewer side effects (Haleem et al., 2023).

Nanorobots may one day be used for easy diagnostics. Through the bloodstream, these devices can measure body functions, discover warning signs of disease early and send detailed data to outside devices. As a result, patients can be closely monitored and treated quickly, raising the success of treatment. Besides this, nanorobots help with delicate surgeries such as cleaning blocked arteries and fixing damaged tissues, improving recovery time and reducing risks (Kong et al., 2023).

Industries will see manufacturing, quality control and the way they manage the environment transformed by the arrival of nanorobots. Because they allow exact control at the atomic level, nanostructures are best fabricated with them in electronics to improve component compactness and efficiency. Besides, nanorobots are essential for monitoring and protecting the environment by finding and removing different kinds of pollutants from air, water and soil. With the help of magnetic nanorobots, heavy metals can be efficiently purified from contaminated water and the process is economically and environmentally friendly (Li et al., 2023).

The use of nanorobots is restricted by many serious challenges during both development and release. The development of functional nanorobots is challenging, as is ensuring they are biocompatible, innovative and stable at the nanoscale. There are also ethical and regulatory challenges such as ensuring their safe and private use and these challenges must be solved (Giri et al., 2021).

Conclusion

In conclusion, nanotechnology in biotechnology is expected to achieve great results, boosted by permanent innovation and connections among experts. Smart nanoparticles, AI-based design and nanorobots are opening up new applications in medicine, farming, the environment and industrial work. As a result, sectors are becoming more precise, energetic and eco-friendly. But achieving the highest potential of nanotechnology calls for dealing with safety, legal, scaling and ethical questions. When scientists, policymakers and industry work together on these developments and when technologies are shared equally, nanotechnology can make a big difference in biotechnology and help improve global health, nutrition and sustainably.

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Nanoparticles in Genetic Engineering: A New Era of Precision Editing

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Abstract

Nanoparticles are changing genetic engineering by acting as well-defined, effective and safe methods for bringing advanced gene-editing technologies such as CRISPR-Cas9 into cells. Their adjustable physicochemical qualities, these particles can boost how medications are delivered, prevent them from affecting the wrong cells and prevent a strong immune response. Such features suggest that nanoparticles can be a reliable method for targeting genes, useful in treating inherited disease as well as making genetically altered food materials. Focus has also been placed on innovative ways to deliver drugs and on making use of nanoparticles in unusual biological communities such as those of extremophiles, plants and people with rare diseases. The use of nanoparticles improves the potential benefits of gene editing in many new fields of science. Also, ethical questions and clear rules are taking on greater relevance to support responsible use of this technology. Because research advances, this technology should completely reshape medicine, sustain agriculture and biotechnology by giving extremely precise, safe and flexible solutions for genome engineering. The use of nanoparticles in gene editing will soon open the way for precise and organized genetic alterations.

Keywords: Nanoparticles, Gene Editing, CRISPR-Cas9 Delivery, Genetic Engineering, Agriculture, Biotechnology, Genome Engineering

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Introduction

Enabled by nanoparticles, genetic engineering can work better, faster and more safely than before. Due to their tiny size, from 1 to 100 nanometers, these materials show properties that make them different from larger-scale samples (Chehelgerdi et al., 2023). Their capacity to interact at the molecular level, together with their adjustable shape and thin size, means nanoparticles are especially suited for biomedical uses such as delivering gene-editing agents. By adding these materials to the latest gene-editing techniques, scientists have introduced better precision into genetic engineering with major effects on medicine, agriculture and biotechnology (Rahimi et al., 2020). Performed with nanoparticles, placing DNA, RNA or CRISPR-Cas9 gene-editing tools into target cells is specific and very little is lost (Sharma et al., 2024). Often, viral vectors, as a classical way to deliver genome-editing, run into problems such as immune reactions, not enough room for the release and integrating randomly around the genome which can result in unexpected effects and health threats (Aljabali et al., 2024). Alternatively, nanoparticles offer an efficient way to protect against these problems, as they offer superior guidance for delivering drugs. Using ligands, antibodies or peptides on the surface of nanoparticles improves their ability to reach target tissues, protecting cells near the treatment area. For instance, lipid nanoparticles are commonly used to deliver mRNA and are found to be highly successful in reaching liver cells which supports new methods in treating specific diseases (Tao et al., 2019). Precise control over nanoparticle characteristics improves the ways they are used in genetic engineering. Nanoparticles produced in the lab can react to changes in pH, temperature or enzymes, permitting the release of genetic material at the proper target site (Janjua et al., 2023). Specifically, this feature is important in in vivo applications since it greatly lowers chances of harmful impacts outside the target area and in other parts of the body. Selective release of CRISPR-Cas9 allows polymeric nanoparticles to target just the cancer cells in tumors, thus harming fewer healthy tissues. These small inventions prove that nanoparticles may help make gene-editing safer and more precise (Goldberg et al., 2007).

Precision is necessary in genetic engineering, because tiny mistakes might produce unwanted changes and unpleasant results. By adding nanoparticles to gene-editing, gene treatment can be done more efficiently and safely. To make new medicines with CRISPR-Cas9, guide RNA and Cas9 proteins must be added with precision to specific cells (Li et al., 2023). When nanoparticles are used, damage to the elements is

avoided and their transfer inside the cell makes genome editing more effective. Gold nanoparticles are commonly used to ensure that the CRISPR-Cas9 cargoes reach the right sites and are not likely to have side effects (Lei et al., 2024).

It is also valuable in these fields to treat people who have various conditions. Using nanoparticles to deliver genome-editing tools in plants alters their genes to produce bigger harvests, increase illness resistance and improve their reactions to their environment. Using silica nanoparticles, the CRISPR-Cas9 system has been applied to plant cells, resulting in precise gene changes required for increased crop productivity. This technology helps sustainable agriculture and provides a valuable solution to worldwide hunger (Hamdana & Tana, 2024).

New biological systems for synthetic biology can be accurately created with the help of nanoparticles. Because nanoparticles accurately end up DNA elements, they are needed to create bio factories that make biofuels, pharmaceuticals and industrial enzymes. Ensuring synthetic biological processes are both reliable and can be repeated many times helps to make them useful in various areas (Burgos-Morales et al., 2021).

Nanoparticles could be useful in genetic engineering, but they also lead to certain problems. Researchers are putting great effort into discovering the possible risks of nanoparticles, as we do not know how they may harm humans and the environment in the future (Xuan et al., 2023). Scaling up nanoparticle-based delivery is often expensive and challenging, mainly in places that are short of resources. Solving these difficulties will be possible if people from diverse areas team up and make tough regulations for using nanotechnology in genetic engineering, as suggested by PJ et al. (2021).

2. Nanoparticles as Delivery Vehicles for Gene Editing Tools

These new technologies in gene editing have radically changed molecular biology by supplying precise ways to alter an organism's genome. How well these tools function mainly depends on safe and efficient systems. Nanoparticles, rather than viral vectors, now present a better way to deal with challenges in gene-editing methods. Such surfaces, adjustability and overall compatibility mean that using these particles with CRISPR-Cas9 and similar tools is safer (Liu et al., 2021).

3. Role of Nanoparticles in Delivering CRISPR-Cas9 and Other Gene-Editing Tools

Nanoparticles are made by humans to aid in transporting biomaterials into living cells. They have been adjusted to perform the task of inserting essential elements from CRISPR-Cas9, guide RNA (gRNA) and Cas9 protein, into the chosen cells. Genome editing requires these molecules to be sent accurately to the nucleus, so they do not become inactive or break down (Smith et al., 2020). Nanoparticles allow delicate proteins to be protected from unwanted activity by enzymes and recognition by the immune system (Hejabi et al., 2022). RNPs of CRISPR-Cas9 are delivered by nanoparticles, offering an important advantage. Because plasmid-based delivery needs the cell to produce messenger RNA, it may be time-consuming, while RNP delivery does not, so editing the genome works quickly and precisely. To introduce the CRISPR-Cas9 RNPs into some mammalian cells, they are frequently coated in lipid nanoparticles. Once the nanoparticles link to cell walls, their content is moved into the cytoplasm inside the cell, making editing possible (Givens et al., 2018). Figure 3 shows the schematic illustration of the use of smart nanoparticles (NPs) with stimulus-responsive properties for the efficient delivery of CRISPR/Cas9 systems. These nanoparticles are designed to respond to specific stimuli, such as pH changes, temperature variations, redox conditions, or enzyme activity, enabling controlled release of the CRISPR/Cas9 components at the target site. Upon encountering the appropriate stimulus within the cellular microenvironment, the nanoparticles undergo structural or compositional transformations, releasing the Cas9 protein and guiding RNA complex into the cytoplasm. The complex then translocates to the nucleus to facilitate precise gene editing with minimal off-target effects. This approach improves the stability, specificity, and therapeutic efficacy of CRISPR/Cas9 in gene editing applications.

CRISPR-Cas9 can be successfully delivered using AuNPs. DNA- or RNA-labeled AuNPs improve the access of CRISPR components to the nuclear region of cells. Gene editing experiments have found that AuNP systems are highly effective in both test tubes and in the body, so they are a perfect option for using this technology. In addition, nanoparticles made with poly (lactic-co-glycolic acid) (PLGA) are applied to deliver Cas9 mRNA and gRNA, increasing the time of treatment and yielding better effects (Ferreira et al. 2020). Delivering genes using magnetic nanoparticles is now an option. The introduction of magnetic fields to the system gives these particles greater accuracy as they are delivered. Once inside the cell, the nanoparticles transfer their cargo, making genome editing much simpler. It concludes that selective antibodies can be used for cancer treatment as well as for other types of diseases (Rarokar et al., 2024).

4. Advantages over Traditional Delivery Methods (e.g., Viral Vectors)

Viral vectors are efficient and make it easy to introduce genetic data into a cell; they do well for gene editing. Yet, these approaches present a few big issues: immunogenicity, few cells they can carry and the risk of accidental genomic insertion. As they are non-viral, nanoparticles help meet all these requirements and offer strong efficiency, high flexibility and safety too (El Karoui et al., 2019).

1. Reduced Immunogenicity and Toxicity

Viral vectors, for example, adenoviruses and lentiviruses, frequently cause a negative immune reaction and can even be dangerous when being used for treatments. On the other hand, nanoparticle-based drugs are made to be friendly to cells and immune systems, making many adverse side effects much less likely. In fact, lipid nanoparticles were tested in human clinical trials and worked effectively and safely for delivering RNA-based drugs (Shirley et al., 2020).

2. Higher Payload Capacity

The restriction on large gene-editing components with viral vectors is caused by their small capsid size. By comparison, multiple payloads can be fitted into nanoparticles, for example RNP complexes, mRNA and other functional molecules. As a result, editing tools and the needed donor DNA can be co-delivered using this approach (Asmamaw Mengstie, 2022).

3. Targeted Delivery and Cellular Uptake

Targeting abilities with nanoparticles are better than those possible with viral vectors. Tissue-targeting precision can be achieved by modifying the surface of NPs with molecules that recognize the target cell receptors. As an example, nanoparticles with folate receptors can accurately deliver CRISPR-Cas9 to cancerous cells, reducing the errors and boosting its usefulness (Figueroa et al., 2021).

4. Avoidance of Genomic Integration

There is a big risk with viral vectors because they might drop their DNA at a random place in the genome, raising the chances of causing insertional mutagenesis and oncogenesis (Jones et al., 2019). With nanoparticles, the CRISPR-Cas9 materials are removed from the cell as soon as their task is done, minimizing the chance of unintended changes. As a result of this short expression, off-target effects and future problems become less likely (Butt et al., 2022).

5. Scalability and Versatility

The creation of viral vectors is both complicated, lengthy and costly, so they are not easily scaled up leading to limited use (Y. Zhang et al., 2024). In fact, nanoparticles are typically produced using easy chemical and physical approaches which means they are both less expensive and easier to use for clinical or industrial purposes. These nanoparticles are also adjustable depending on the desired route, including into veins, into muscles and on the skin (Gutiérrez-Granados et al., 2018).

6. Environmental and Regulatory Considerations

Nanoparticles are accepted as safer for the environment and regulators, because they are unable to replicate and are synthetic in nature. Viral vectors, unlike lentivirus vectors, must go through tough regulatory tests because they raise concerns about safety and their environment effects. Due to their synthetic construction, nanoparticles can be approved efficiently and added to therapeutic pipelines (Wang et al., 2022). Applying nanoparticles to deliver CRISPR-Cas9 and similar editing tools has already seen helpful results in therapeutics, agriculture and synthetic biology. Using nanoparticles as carriers, researchers are trying gene therapies for genetic diseases, including Duchenne muscular dystrophy and sickle cell anemia, where correcting the genome can bring back the missing or mutated genes. Scientists use nanoparticles in the agricultural industry to help crops gain better qualities such as being resistant to drought and nutritious (Li et al., 2023).

Integrating nanoparticles with the latest technologies, for example, artificial intelligence and machine learning will likely produce important results going forward. These algorithms can help improve nanoparticles by foreseeing their effects on the body which makes them safer and easier to use. Improvements in nanorobotics may open the way for smart nanoparticles to find their own routes in difficult biological locations, possibly expanding where they can be used. Although they are helpful, many are still hesitant about using nanoparticle-based delivery systems because of safety, how well they work on a large scale and their cost. To handle these problems, we will need help from experts in various fields and will need to keep funding research and development. Conquering these obstacles could allow nanoparticles to influence gene editing by improving its accessibility, accuracy and overall safety in many uses (Nandipati et al., 2024).

5. Applications in Therapeutics and Agriculture

Nanoparticle-assisted genetic editing is making an important difference in medicine and agriculture because it provides improved precision and efficiency. Researchers are using the various properties of nanoparticles to advance how genetic disorders are treated and how robust crops are grown. These advancements are set to improve medicine and agriculture, solving tough problems and allowing for new ways to support the environment and improve human health (Wu et al., 2023).

6. Treating Genetic Disorders Using Nanoparticle-Facilitated Editing

Much progress has been made in treating genetic disorders using gene editing by adding nanoparticles to deliver the CRISPR-Cas9 tool. Genetic disorders usually result from changes in genes that interrupt their functions. Because nanoparticles are precise and able to protect payloads, they can take delivery components to the proper cells in different tissues and help with correcting these mutations (Kolanu, 2024). When compared to viruses, nanoparticles give us a safe way to transfer DNA that avoids the issues of responses by the immune system and genetic changes in cells. LNPs such as lipid nanoparticles, are now considered the top way to deliver CRISPR-Cas9 materials. By allowing RNP complexes to be carried in their structure, AAVs can support the delivery and function of the editing tools needed for in vivo editing (Taghdiri & Mussolino, 2024). LNPs are used in experiments with animals to treat alterations that cause Duchenne muscular dystrophy, allowing affected proteins to work and strengthen muscles (Ibba et al., 2021).

Gold nanoparticles (AuNPs) represent another successful technology in therapeutic gene editing. When DNA or RNA is bound to them, nanoparticles can remove genetic errors precisely at a certain location. AuNPs have been found to help treat monogenic diseases like sickle cell anemia by delivering important gene editing materials to hematopoietic stem cells (Mitchell et al., 2020). Because of this method, therapies are less likely to harm the wrong cells or cause immune problems (Kanu et al., 2022). Now, using nanoparticles, it is also possible to edit genes in hard-to-access tissues. Medicines can rarely cross into the brain from the blood, so treatment for Huntington's and Alzheimer's diseases is challenging. When engineering nanoparticles, researchers are able to transfer gene-editing equipment directly into neurons in the brain. The availability of this technique creates space for addressing conditions we currently lack treatments for (Ereej et al., 2024). Besides studying monogenic diseases, nanoparticles are currently used to look into polygenic diseases and cancer. The use of nanoparticles can help change the genes that control tumor development and drug responsiveness in oncology. With this strategy, scientists have been able to take CRISPR-Cas9 into cancer cells to try to control how cancer spreads (Shchaslyviy et al., 2023).

7. Enhancing Crop Traits and Resilience through Targeted Genetic Modifications

Nanoparticles improve how genetic editing is done in agriculture, providing options for better crops and meeting problems regarding food and climate. Frequently, genetic and breeding methods are slow and can run into problems with regulations. People agree that nanoparticle delivery is an effective and accurate method for changing genes in plants (Ahmar et al., 2021). Delivering the CRISPR-Cas9 system to plant cells using nanoparticles has become much simpler than with older ways. To illustrate, scientists are using silica nanoparticles to help maize and wheat cell. Relying on this strategy means researchers avoid using *Agrobacterium* or biolistic delivery and this makes the whole process simpler and less risky (Babaeianjelodar et al., 2025).

Nanoparticles improve a plant's resistance to both living and non-living pressures. Researchers have successfully placed CRISPR-Cas9 into rice using nanoparticles which protected the rice from bacterial blight. Scientists have now updated soybean genes using nanoparticles, so they can resist drought and boost water usage and crop yields in hard conditions (Naik et al., 2022). Precision in farm work is improved by letting growers fine-tune the traits of crops with nanoparticles. If genes controlling when fruits ripen or their nutrients are changed, crops can be produced with a larger shelf life and healthier nutrients. By using nanoparticles to modify ripening genes, tomato growers now enjoy more time to store their produce before it spoils and less waste (Jiang et al., 2021). As well as altering individual crop features, nanoparticles make it possible to change several genes at once. The ability to explain these traits by considering pathways is especially important since they use several genes. In one study, using silica nanoparticles in a multiplexed system increased how wheat utilized nitrogen and cut back on the need for synthetic fertilizers (Ahmad, 2023).

Gene editing presents special problems for plant scientists and nanoparticles offer ways to deliver editing tools into difficult-to-edit plant species. Optimized size, charge and number of surface proteins on nanoparticles have allowed researchers to penetrate plant cell membranes and reach the nucleus with DNA editing tools. By making gene editing possible in more crops such innovations help enable these technologies to support different agriculture sectors (Demirer et al., 2021).

7. Ethical and Regulatory Considerations in Nanoparticle-Enabled Genetic Engineering

Adding nanoparticles to genetic engineering has triggered major developments in medicine, agriculture and biotechnology. Using these tiny vehicles helps to improve delivery of CRISPR-Cas9, increasing accuracy, minimizing effects on unintended cells and reducing immune responses. Even though nanoparticles hold great promise for genetic technologies, several challenging ethical and regulatory issues should be taken care of to make sure these technologies are safe, fair and acceptable for society (Iavicoli et al., 2017).

A main issue is ensuring that nanoparticles used in genetic applications do not pose biosafety and risk problems. People often view nanoparticles as safer than viral vectors, but there are concerns that they could gather in organs and interact strangely with living tissue. It's especially worrying that germline editing can cause genetic changes to be passed on to future generations. These uses are separated by ethics because enriching human traits may bring about social inequality and possible discrimination (Hayenhjelm & Nordlund, 2025).

There is also a concern about how nanoparticles affect the environment in genetically modified agriculture. Gene flow from genetically changed crops to wild plants may cause invasive weeds or upset existing natural plant communities. The main goal of regulatory frameworks should be to do environmental risk assessments and implement measures to stop accidents where they are needed. Usually, just to be sure, the precautionary principle is brought up; requiring regulatory bodies to hold off on approval until the possible consequences are better understood (Labrioglio et al., 2025).

Trust from the public and getting permission should both be prioritized. Before joining tests, patients must be fully aware of the risks, whether they are identified or not, linked with gene editing. Although they show improved accuracy, nanoparticles remain concerned about their spread throughout the body, their ability to break down and what impact they might have in the long run. The process of getting informed consent should always change when new information is discovered and the situation evolves (Delhove et al., 2020). Similarly, these technologies are approved by society when public views are positively influenced by cultural and ethical beliefs. According to studies, most concerns among the public about nanotechnology and genetic engineering revolve around "playing God," unusual interventions and the chance of wrongful uses (Benjamin & Familusi, 2020).

Work is being done to resolve these issues. Both the World Health Organization (WHO) and the Organization for Economic Co-operation and Development (OECD) see that a global framework is needed to manage nanotechnology. Any frameworks used should cover safety standards, correct labeling, designs for long-term monitoring and observing what happens after the products reach the market. Furthermore, making sure ethical advisory boards and stakeholders are part of policy creation helps a committee to be properly accountable and recognized (Khatoun & Velidandi, 2025).

9. Advancing Non-Invasive Gene Editing Techniques

The field of genetic editing aims to create methods that minimize problems, help patients recover better and make treatments more accessible. Injections and surgeries, traditional delivery methods, sometimes cause infection, inflammation and pain to the patient. Using modern technology and safe ways, scientists now try to fix these issues without affecting the patient too much (Huang et al., 2022). Non-invasive gene editing is advanced largely through the use of nanotechnology. Nanoparticles meant for inhalation, ingestion or applied directly to the skin may replace unpleasant invasive options. Researchers are investigating the use of lipid nanoparticles (LNPs) for the pulmonary delivery of CRISPR-Cas9 goods which avoids the need for injections in lung tissue. Therapies designed this way could be promising for cystic fibrosis and pulmonary arterial hypertension, as they do not cause much discomfort to those being treated (Lei et al., 2024).

Using nanoparticles made from hydrogels is an additional way to achieve non-invasive gene editing. Such materials may be put on top of the skin or into mucous membranes to control the local delivery of gene-editing agents. Because of these systems, doctors can deliver corrective gene therapies straight to areas affected by genetic skin disorders such as epidermolysis bullosa. Continued progress in hydrogel development is believed to improve how effective they are and increase their usefulness (Su et al., 2024). These nanoparticles provide new non-invasive possibilities for gene editing. Both magnetic and ultrasound-responsive nanoparticles can target tissues by guiding themselves

with external technologies and only releasing their content at the desired sites. It demonstrates that physics methods can join forces with molecular biology to produce innovative non-invasive ways (Qian et al., 2020).

Many forms of extracellular vehicles (EVs) are now being employed as safe and effective carriers for gene-editing reagents. Because EVs are not recognized by our bodies, they can clear the blood-brain barrier. Using CRISPR-Cas9 components, we are able to introduce gene-editing medicines to specific tissues by means of engineered EVs which target the brain and the central nervous system. Alzheimer's disease and Huntington's disease may respond well to treatment since scientist struggle to find suitable treatments for these conditions (Payandeh et al., 2024).

Conclusion

Genetic engineering now benefits from safer, more powerful and precisely focused tools made possible by adding nanoparticles. They give cell-friendly alternatives to viral carriers for carrying CRISPR-Cas9, so off-target events and cell toxicity are markedly reduced. Because nanoparticles can be modified in size, charge and function, they find use in areas such as treating genetic diseases, increasing crop resistance to diseases and learning about complex biological systems. What's more, new types of intelligent nanoparticles and improved non-invasive methods are helping researchers use gene editing in places that were previously not possible. Although there is a lot of hope, important obstacles stand in the way, including biosafety, immunogenicity, controversies over ethics and well-defined regulations. Yet, new developments in nanoparticle delivery are ready to transform genetic engineering through increased precision, safety and accuracy. As technology develops, it could bring new changes to personalized medicine, eco-friendly farming and make biotechnological innovation more successful, allowing for sweeping genetic interventions worldwide.

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Nanotechnology in Drug Delivery: Revolutionizing Medicine

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Abstract

Nanotechnology is changing modern medicine by making it possible for drugs to be safer, more effective and delivered more specifically. Using this strategy, many problems faced by traditional drug delivery systems, including low absorption rate, side effects and little targeting, can be minimized. Delivering drugs like nanocarriers, including liposomes, dendrimers, polymeric nanoparticles and metallic nanostructures, makes it possible to enhance their solubility, control their release and target the drug precisely to a chosen area. Crossing over into cells and shielding cargoes from breakup have allowed these carriers to improve how diseases like cancer, neurological diseases and infections are treated. A focus on multitasking nanocarriers is now helping the theranostics field advance. Moreover, when bioinspired materials and biodegradables are used, the implant becomes safer and less likely to cause lasting toxicity. Invention of cost-effective manufacturing and the use of innovative ingredients are expanding healthcare services around the world. Even if there are difficulties related to scale, approval and safety, it is obvious that nanotechnology can greatly change how drugs are delivered. Because nanomedicine is always improving to meet doctors' demands, it is ready to revolutionize drug treatments and begin a new chapter in personalized and precision medicine.

Keywords: Nano-drug Delivery, Multifunctional Nanocarriers, Biodegradable Materials, Global Healthcare Accessibility

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Introduction

Nanotechnology has brought new ways to deliver drugs, solving the issues faced with old systems. Precise, efficient and targeted drug delivery is possible in modern medicine because of the way nanotechnology makes use of the special properties of small materials (Hsu et al., 2023). Typical drug delivery methods, including oral and intravenous administration, often have issues with poor solubility, low bioavailability, quick degradation and general distribution, causing treatment results that are not ideal and a rise in unwanted effects. Nanotechnology has tackled these problems by introducing nanocarriers that boost drug performance and at the same time reduce negative side effects (Ganta et al., 2014).

Nanotechnology deals with working with materials at a nanoscale—this means between 1 and 100 nanometers. When the materials are at this scale, they display different physical, chemical and biological aspects than they do in bulk forms. Because nanomaterials have all of these properties—high surface area to volume, responsive chemical properties and adjustable ways to function—they form excellent candidates for delivering medicine to patients (Khan et al., 2022). There are several nanocarriers such as liposomes, polymeric nanoparticles, dendrimers and inorganic nanoparticles, created to keep drugs secured and safe from enzymes as they reach their target tissues (Chamundeeswari et al., 2019). Nanotechnology is mostly used in drug delivery to improve how easily and how long drugs remain stable in the body (Liu et al., 2024). Since hydrophobic substances are not easily combined with water, a lot of drugs are not well absorbed in the body. The addition of nanoparticles to drugs helps them dissolve better and transport through biological liquids. Lipid nanoparticles can deliver poorly soluble anticancer drugs and increase their effectiveness at lower doses. The use of polymeric nanoparticles is also effective at maintaining proteins in their natural form and extending drug treatment (Waheed et al., 2024). It represents a complete change in the way drugs are given and how treatment is carried out. These systems commonly use passive or systemic ways which results in both broad coverage and impact on healthy tissues. On the other hand, with nanotechnology, it is possible to use both active and passive targeting which enhances drug precision delivery (Egwu et al., 2024).

Nanotechnology is important for therapeutic delivery, but also for imaging and diagnosis. Such nanocarriers are called theranostics because they bring together therapy and testing in just one system. By combining drug delivery and continuous real-time monitoring, these methods reveal useful information on how well a treatment is working (Hosseini et al., 2023). Gold nanoparticles tagged together with

imaging dyes and cancer drugs have been employed to view how tumors respond to treatment and to deliver chemotherapy more precisely (Ghazal et al., 2024). Yet, there are many obstacles to moving from traditional to nanotechnology-based delivery methods for drugs. The fact that nanotechnology can't be scaled easily and is expensive is hindering its widespread use in healthcare. The specialized steps required for making and customizing nanoparticles typically make them too expensive for most to purchase (Malik et al., 2023). Acceptance of nanotechnology by the public is very important for its use. Small-molecule drug delivery is promising, so making sure safety, ethical points and distribution are fair is key to earn users and doctors' trust (Đorđević et al., 2022).

2. Nanocarriers

Nanocarriers bring an important upgrade to nanotechnology by fixing limitations in traditional drug delivery methods. The flexibility, security and efficiency of nanoparticles make them essential for moving therapeutic drugs to their needed locations. Among the best-known nanocarriers are lipid-based systems, polymeric nanoparticles and dendrimers, as well as inorganic nanocarriers. Each type has its own benefits which support unique medical uses and help create strong and modern treatment plans (Din et al., 2017). Nanocarriers formed using lipids are old subjects of research, as they work safely in living tissue, resemble fluid membranes and can contain drugs that are either polar or nonpolar. Liposomes and solid lipid nanoparticles (SLNs) are the primary types among lipid-based nanoparticles. Liposomes are tiny spheres made when one or several lipid layers encircle a water core. As they are modeled on biological membranes such liposomes can store water-soluble drugs inside their core and water-insoluble drugs in their outer layers (Smith et al., 2020). Liposomes are used by oncology because they help cancer drugs attack cancer cells quickly and with less risk of harming other cells. Stimulation nanotechnology has led to both better results and less harmful reactions in patients treated for breast or ovarian cancer (Zhang et al., 2023). Giving liposomes ligands, antibodies or peptides allows you to deliver cargo specifically to certain body tissues. Because of PEGylation, nanoparticles stay in the body longer, as the immune system does not spot them and they accumulate in tumors via the EPR effect (Brown et al., 2021). Tumors are naturally quite acidic, so nano-medicines have been made to focus on them by reacting to both pH and temperature changes (Suk et al., 2016). Table 1 elaborates applications of nanotechnology in drug delivery.

Table 1: Applications of Nanotechnology in Drug Delivery

Nanotechnology System	Key Features	Applications	Advantages	Challenges
Liposomes	Phospholipid bilayer, biocompatible	Cancer therapy, antifungal drugs, vaccine delivery	Reduced toxicity, enhanced drug solubility	Stability issues, high production costs
Dendrimers	Branched structure	Gene delivery, anticancer therapy	Precise drug loading, multivalency	Toxicity at high generations, complex synthesis
Polymeric Nanoparticles	Biodegradable and tunable polymers	Sustained drug release, vaccine adjuvants	Controlled drug release, biodegradability	Scalability, potential immune response
Gold Nanoparticles	Unique optical properties	Imaging, photothermal therapy, targeted drug delivery	High stability, multifunctional capabilities	Cost of synthesis, potential toxicity
Carbon Nanotubes	Hollow cylindrical carbon structures	Delivery of small molecules, siRNA, and proteins	High surface area, ease of functionalization	Cytotoxicity, poor biodegradability
Silica Nanoparticles	Mesoporous structures	Delivery of anticancer drugs, imaging agents	High loading capacity, biocompatibility	Long-term safety concerns
Quantum Dots	Semiconductor nanocrystals	Imaging and diagnostics, drug tracking	Bright fluorescence, stability	Potential toxicity, environmental impact
Nanogels	Hydrophilic networks	Delivery of hydrophilic drugs, protein therapeutics	High water content, responsive behavior	Limited stability, complex manufacturing
Micelles	Amphiphilic copolymers	Delivery of poorly soluble drugs	Enhanced solubility, selective drug delivery	Limited stability in vivo
Exosomes	Natural extracellular vesicles	Gene therapy, drug delivery for cancer, neurodegenerative diseases	Natural origin, immune evasion	Scalability, variability in isolation

SLNs are next-generation lipid-based nanocarriers that adopt features of liposomes and make them stronger for use. An SLN consists of a combination of solid lipids surrounded by surfactants as its solid form for drugs. Although liposomes take time to release their drug, SLNs provide better safety by safeguarding them against fast degradation (Mitchell et al., 2020). They find use in helping poorly-water soluble drugs and in shielding sensitive substances such as proteins and nucleic acids from harm (Viegas et al., 2023). One important example of SLN use is found in developing vaccines for cancer as well as vaccines against COVID-19 infection. Polymeric nanocarriers are made from biocompatible and biodegradable polymers and include poly (lactic-co-glycolic acid) (PLGA), chitosan and polyethyleneimine (PEI) as examples. There are numerous ways these carriers can be used, allowing release to be controlled, high loads of drugs placed and targeting to specific areas (Wu et al., 2024).

Hydrophilic, hydrophobic and biological medications are easily contained in Polymeric Nanoparticles. Clinical use of PLGA-based nanoparticles is allowed because they are safe, biocompatible and break apart into non-harmful materials. This controlled and steady release

means patients don't have to take as many doses which improve both compliance and their health. PLGA nanoparticles have been used in this way to deliver medicines that help people with inflammatory illnesses such as rheumatoid arthritis (Danhier et al., 2012).

Polymeric nanoparticles are valuable for use in genetic medicine. Gene modification was enabled in target cells by transporting both siRNA and plasmid DNA using PEI nanoparticles (Piotrowski-Daspi et al., 2020). Surface coating with PEG makes them more stable and safer since the body will not react to them (Padín-González et al., 2022).

Dendrimers are special nanocarriers since they are built with branches and end in a central core. Such an architecture offers maximum options for controlling size, shape and structure on their surfaces (Soliman et al., 2024). Chemists usually favor dendrimers because they can be filled with drugs in their center or can have drugs attached to their outside. Nanoparticles give the chance to introduce different drugs, genetic material and imaging compounds at the same time (Abbasi et al., 2014). Dendrimers can deliver drugs through the blood-brain barrier and reach the central nervous system, as shown by Zhu et al. (2019). People are developing this technique to treat Alzheimer's and Parkinson's disease. Designed dendrimers are able to deliver their cargo to particular cells, making it easier to target cells precisely and lowering the risk of problems. Because of these features, inorganic nanocarriers can support imaging, diagnostics and theranostic applications. Among all these materials, the most studies have been conducted on gold nanoparticles (AuNPs) and quantum dots (QDs) (Ashique et al., 2023).

Gold Nanoparticles (AuNPs) are valuable nanocarriers appreciated for being friendly to living organisms, simple to make and having tunable surfaces. Adding therapeutic compounds, targeting substances and imaging materials to AuNPs creates possibilities for their drug delivery and diagnostic use. Their ability to penetrate small areas makes these particles good for carrying drugs and CRISPR-Cas9-based gene-editing tools (Jadhav & Mandlik, 2024). Using photothermal therapy, AuNPs in cancer treatment absorb light and change it into heat that destroys cancer cells in the tumor area. Being both a delivery system and a therapeutic agent is evidence of their place in theranostics (Jadhav & Mandlik, 2024). AuNPs are being investigated as vaccine ingredients, as their immunosupportive properties advance antigen uptake and boost the immune system (Ferrando et al., 2020).

QDs are tiny semiconductors with optical properties that allow them to give off high light, not fade quickly and their brightness can be adjusted by their size. The first use for QDs is usually imaging and diagnostics, yet they are growing in use for drug delivery by nanocarriers (Mitchell et al., 2020). Through their fluorescence, experts can see how the drug moves and where it has an effect, helping to measure treatment success (Hamidu et al., 2023). Still, people are concerned about QDs that have toxic metals which has caused scientists to research biodegradable and safer types of fluorescent materials. Carbon quantum dots have recently been made in a way that provides biocompatibility and light emission that matches their optical equivalents. Such improvements broaden the range of QDs used in drug delivery and various biomedical tasks (Sahu & Sahoo, 2024).

3. Comparative Advantages and Challenges

The different kinds of nanocarriers have advantages of their own and also face particular challenges. Lipid-based systems are very safe for use in the body, but their poor stability and lack of drug-loading space limit their use. The use of polymeric nanoparticles and dendrimers is useful because they provide precise release and many properties, yet they are usually difficult to make (Alshawwa et al., 2022). Even though nanocarriers such as AuNPs and QDs have outstanding optical and therapy-related properties, they still raise some doubts about safety and environmental impact (Prasad and Selvaraj, 2024). Meeting these obstacles involves exploring various areas of science to prototype better nanocarriers, produce them in large amounts and obey rules. Improvements in how materials are coated, responsiveness to stimuli and biodegradable products are likely to help nanocarriers achieve even more in modern medicine (Aswini et al., 2024). Nanotechnology has helped improve drug delivery by getting around the challenges of previous methods and making therapies easier for people. Compared to other delivery methods, nano-based approaches give the best results in making drugs more soluble, giving more control and helping to deliver drugs to their targets. This allows them to support the success of treatments while reducing the risks of side effects which is why nano-based systems play a key role in current medical research (Sim & Wong, 2021).

4. Enhanced Drug Solubility and Bioavailability

Drug delivery is a major challenge since a lot of therapeutic agents do not dissolve easily or cannot be absorbed properly into the blood. Such drugs are less effective because water does not dissolve them well enough for our bodies to make use of them. These systems solve the problem by placing hydrophobic drugs in carriers that improve their solution and their stability (Xie et al., 2024). These nanoparticles are designed to solve the issue of water insoluble medicines by turning them into soluble forms. Their structure traps water-fearing molecules within, helping the drugs to be mixed with water. Packaging paclitaxel which breaks down in lipids, within liposomes vastly enhances its solubility and provides better outcomes for certain patients (Mehta et al., 2023).

When used, polymeric nanoparticles boost how well drugs are soluble and can be used by the body. PLGA and similar biodegradable polymers shield the drug, avoiding its breakdown in the gut or in the blood while it is in the body. The drug level in the body remains even which improves how well it is absorbed. Nanocrystals are an example of nano-nanotechnology because they shrink drugs to the nanoscale which boosts surface area and allows faster drug dissolution (Herdiana et al., 2022). A better solubility level in the body provides better chances for drugs to achieve desired effects at the target tissues. Due to this advantage, people can take smaller amounts of myelinated oral and intravenous drugs which cuts the danger of possible toxicity and side effects. With nano-based systems, optimal drug action is obtained while also reducing the chance of side effects (Bhalani et al., 2022).

5. Controlled and Sustained Release Profiles

One more advantage of using nano-based drug delivery methods is that they allow controlled and regular drug release. Adhering to older dosing schedules can result in you having both low and high levels of medication which may make patients less willing to take the drugs

as required. Because of nano-based systems, medications are slowly released, so patients always get the therapeutic effects they need (Cheng et al., 2023). Polymeric nanoparticles make it highly possible to control drug release. Because these carriers break down inside the body slowly, they can release their substances at the right time. Using PLGA nanoparticles, a single dose of anti-inflammatory medicine for arthritis can work for up to several weeks which helps patients take medication regularly and live better (Begines et al., 2020).

Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) are highly effective for controlled release applications. Using SLNs to give antiviral drugs for chronic infection treatment helps keep a regular amount of medicine in the body and diminishes the chance of resistance (Ghasemiyeh & Mohammadi-Samani, 2018). A different path to controlled release involves using nanoparticles made from hydrogels. Because these systems respond to changes in pH, temperature and enzymes, drugs can be released only at the desired location in the body. For example, pH-sensitive nanoparticles are designed to release their lethal anticancer cargo only when the microenvironment in the tumor becomes acidic. This minimizes the drug's effect on other parts of the body and guarantees enough drug is present for the therapy to work. These types of medicines make dosing less regular, lower the threat of loss of balance and result in better care outcomes (Adepu & Ramakrishna, 2021).

6. Improved Targeting and Reduced Side Effects

Nano-based systems focus on targeted drug delivery which is an important advantage over older systems. Most of the time, transporting medicine this way means the drugs reach all over the body, impacting both sick and healthy cells. Because drugs are not precise enough, they are less effective and can cause major side effects. Nano-based systems achieve this by offering both passive and active targeting, so drugs are delivered to the right places with little disturbance to other tissues (Li et al., 2023).

Turbulent vasculature and an insufficient draining system in tumor tissue cause passive targeting using the enhanced permeability and retention (EPR) effect, where nanoparticles congregate. In oncology, this feature has made it possible for nanoparticles to treat cancer by bringing chemotherapeutics only to the tumor, not to nearby healthy tissues. A liposomal formulation of doxorubicin was found to improve results in treatment and decrease the risk of heart side effects, compared to traditional doxorubicin (Bazak et al., 2014).

Active targeting counts on adding ligands, antibodies or peptides that bind to receptors found on the wanted cells to the nanoparticles. Using such a method improves how medicines are sent which ensures the drugs are only sent to the site where they work. Nanoparticles that bind to folate are drawn to cancer cells with lots of folate receptors which helps deliver drugs directly to the cancer, improving their capability (Davis et al., 2020). Inflamed parts of autoimmune diseases are also being treated by using antibody-covered nanoparticles, avoiding many adverse effects according to (Al-Thani et al. 2024).

Targeted delivery helps personalized medicine by making treatments specific to each patient's gene and body composition. Designing systems at the nano level means they can interact with particular biomarkers, leading to safer and more specific therapies for cancer, genetic disorders and infections. With such specific doses, the risk of harmful reactions is decreased and treatment works better. Besides making drugs more suitable for a target, nano-systems cut down on systemic exposure and the resulting side effects. By confining drug activity to specific sites, these systems protect healthy tissues from off-target effects, lowering the risk of toxicity and complications. For example, nanoparticle-mediated delivery of chemotherapy drugs has significantly reduced common side effects such as nausea, hair loss, and immune suppression, improving the quality of life for cancer patients (Dash et al., 2024).

7. Targeted Drug Delivery with Nanotechnology

Targeted drug delivery represents one of the main effects nanotechnology provides in medicine. It makes it possible to send medicines accurately, efficiently and securely to chosen body parts or cells. Authentication of standard drug delivery often results in the medication affecting healthy as well as diseased tissues. Not being specific in doses means drugs don't work as well and can cause more side effects. Through its use of active and passive methods, nanotechnology aims the delivery of drugs precisely at the intended location. Using the special biological and physical traits of nanomaterials, scientists can make medicines more effective with less risk of side effects (Ma et al., 2024).

8. Active Targeting Using Ligands and Antibodies

Active targeting means adding molecules to nanoparticles that bind selectively to receptors displayed by specific cells. When medicines are delivered with this approach, they precisely reach the treatment site, avoiding problems with other parts and making drugs, work more efficiently (Elumalai et al., 2024).

9. Ligand-Functionalized Nanoparticles

Many treatments for diseases use small molecules, peptides or vitamins to bind to a specific receptor found in distressed cells. In one example, using nanoparticles that bind to folate has allowed targeting of many cancers that commonly overproduce these receptors. Chemotherapeutics delivered through these nanoparticles are directed to cancer cells and enter these cells without harming normal healthy tissue. It helps the treatment become safer in many respects because it reaches the target location more precisely (Ebrahimnejad et al., 2022). An additional class of ligands that plays a role in active targeting are peptides. Using RGD peptides that connect to extra integrins in tumor blood vessels, nanoparticles are now being used to bring the drugs directly to the cancer. These functional nanoparticles have superior tumor accumulation and greater effectiveness for treating tumors than non-targeted systems (Hosseinihah et al., 2024).

10. Antibody-Functionalized Nanoparticles

Antibodies have a much greater ability to bind to precise parts of the cell because they can tell antigens apart. The monoclonal antibody trastuzumab (Herceptin) has been attached to nanoparticles for use in targeting HER2-positive breast cancer cells. Together, this method provides higher sensitivity, better delivery and superior results for therapy When antibodies recognizing CD44, common in tumor cells, are

joined with nanoparticles, chemotherapy can be delivered, increasing tumor-selectivity and decreasing damage to healthy tissues (Montaseri et al., 2020; Sitia et al., 2022).

11. Dual-Functionalized Nanoparticles

Nanotechnology advances now allow for designing dual-functionalized nanoparticles packed with several types of ligands or antibodies to help them target the right cells. They simultaneously interact with several targets, helping to address the differences between cells in the tumor and improve treatment results. In particular, combining folate and transferrin ligands on nanoparticles can improve the delivery of drugs to cancer cells that express these receptors (Fan et al., 2023).

Helping personalized medicine, active targeting aims treatments for diseases based on a patient's own unique biomarkers. Choosing ligands or antibodies that match the biomarkers seen in a patient's disease makes the therapy both tailored and accurate (Al-Thani et al., 2024).

12. Passive Targeting Through Enhanced Permeability and Retention (EPR) Effect

Passive targeting exploits the distinct traits of tumors so that more nanoparticles are found nearby. Passive targeting relies mainly on the enhanced permeability and retention (EPR) effect. The large holes in tumor blood vessels and few lymphatic channels cause nanoparticles to be attracted into the tumor (Bazak et al., 2014).

13. Advantages of Passive Targeting

Cancer therapy which relies on the EPR effect, means that nanoparticles will move to the tumor on their own, without requiring a device to guide them. For these reasons, creating nanoparticles is simpler, so medication delivery becomes much more affordable and convenient. Furthermore, integrating passive targeting with active targeting gives many advanced systems stronger and more accurate results (Rosenblum et al., 2018).

Conclusion

In short, nanotechnology has transformed the field of drug delivery by giving us thorough, precise and focused drug treatments that handle the challenges inherent in traditional methods. A variety of nanocarriers, including liposomes, dendrimers, polymeric nanoparticles and inorganic systems, have made drug solubility, bioavailability, controlled release and targeted delivery possible through nanotechnology. As a result, therapy is more effective and patients suffer fewer systemic side effects which is a big step forward for custom and safe treatments. By blending diagnostic and treatment features into multifunctional nanocarriers, it is now possible to see the progress of treatments in real time. Although these new findings show great promise, difficult challenges in scaling, high costs of production, strict regulations and possible long-term side effects must be managed so that clinical translation is safe. The rise of biodegradables, the use of AI in drug design and new methods in green synthesis are opening doors to improved nano-drug systems. The growth of interdisciplinary work is helping nanotechnology become the backbone of future medicine, providing the world with more secure, better performing and accessible healthcare.

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Applications of Spermatogonial Stem Cell Technology in Wildlife Conservation

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Abstract

Spermatogonial stem cells (SSCs) technology is the most popular and effective technique used in wildlife conservation to provide future strategies for conserving genetic variation and to rescue threatened species. SSCs, which are the primary sperm producing stem cells, can both, self-renew as well as differentiate into mature spermatozoa. The transplantation, cryopreservation, and its in-vitro manipulation offer the chance to mitigate the effects resulting from habitat destruction, climate change and anthropogenic pressures. This particular chapter explores the various uses of SSC technology in the preservation of genetic resources, rehabilitation of species, interspecies germ cell transplantation, and developments in SSCs isolation, culture systems, and molecular characterization to improve utilization of these approaches. Moreover, philosophical and/or ethical factors and implications and/or possible adverse effects, for instance, the danger in genetic modification are outlined. Applying SSCs technology together with other biotechnological potentialities including somatic cell nuclear transfer, induced Pluripotent Stem cells could transform the prospects of ex-situ and in-situ conservation. Using SSCs technological applications, wildlife conservationists can protect biodiversity and help with sustainable ecosystem management.

Keywords: Stem Cell Technology, Wildlife Conservation, Genetic Modification, Ecosystem Protection

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Introduction

The constant reduction of numbers of animal species because of habitat loss, overexploitation and climate change has led to a need to create more effective technologies for conserving the animals (Hagedorn et al., 2018). For these difficulties Spermatogonial stem cells (SSCs) technology proved to be a breakthrough tool since it allows preserving genetic stock and performing species reclamations. SSCs are found in testes and play a crucial role in the ever replenishment process of sperm cells throughout the organism reproductive stage. Their capacity to self-multiply and to transform themselves into spermatozoa put them in a good position in wildlife conservation (Lara et al., 2018).

Wildlife in the world is under immense pressure as has never been witnessed before. Habitat degradation mainly due to communal grazing, conversion of land to agriculture, expansion of human settlement and wetland destruction has led to isolation of breeding sites and reduced availability of natural resource. At the same time, excessive killing by hunting and poaching and destructive fishing methods have pushed many different species to the edge of extinction (Guo et al., 2020). Even more, climate change fuels these difficulties worsening the conditions of ecosystems and making some kinds of habitats almost impossible. Such factors have the combined effect of causing a very fast rate of biome degradation, hence high extinction rates, which destabilize the ecosystems and their functions. Therefore, such calls for development of more effective strategies in the conservation and successful management of threatened species (Abofoul-Azab et al., 2019).

Of the diverse set of new biotechnological techniques, SSC technology has received considerable interest due to its possible application in conservation biology. SSCs are immature and morphologically non-specific gonocytes anchored in the seminiferous tubules of the testes (Irie et al., 2014). They are unlike most tissues in that they are bipotential for stem cell regeneration, thus providing an inexhaustible source of stem cells for the organism, and differentiation in order to generate mature spermatozoa. These characteristics make SSCs very important for male fertility and extremely useful for reproductive technologies (DeFalco et al., 2015). Current chapter explores the SSC technology in wildlife conservation and protection focusing on its potentials of genetic preservation, species restoration and reproductive biotechnology. Additionally, the advancements in SSC-based technologies are discussed. Furthermore, there are some ethical concerns and potential risks. Ultimately SSC discussed as valuable tool in biodiversity conservation and ecosystem as well as sustainable resource management.

The application of SSC technology in wildlife conservation can be broadly categorized into three domains.

Conservation of genetic resources under the techniques of isolation and culture of SSCs from pre-imaginal stages of endangered or threatened species (Cicarelli et al., 2020). This method affords an opportunity to store SSCs in a manner that benefits the genetic variety of these species regardless of the fact that the natural population may reduce significantly to perilous levels. This approach augments ordinary gamete banking by offering possibility to check male germline cells that may be used to regain fertility and breeding in the future (Zhang et al., 2016).

In vitro fertilization has the potential to revitalize populations of many species with dwindling numbers. For example, SSC transplantation

requires implantation of the donor SSCs directly into the testes of another male where it has the capacity to home in on the seminiferous tubules and differentiate to functional spermatozoa (Lord et al., 2022). This technique has been shown in several model organisms which includes mice and primates and has capabilities on interspecies. Hoping that SSCs of closely related surrogates could work for artificial insemination or in vitro fertilization, conservationists translocate SSCs from endangered species' testicular tissue into males belonging to the same species' group (Vazquez et al., 2016).

Specie conservation projects provides direction to genetic rescue of the species. This in fact means to revive the genetic variation in diminished small isolated subpopulations by trans-plant y genetic material preserved in SSCs (Hagedorn et al., 2018). Such interventions are necessary in order to prevent the consequences of inbreeding depression that worsen reproductive fitness and cause high levels of diseases. Through revitalizing the genetic variance, SSC-based approaches are indeed useful for increasing population recovery ability and overall adaptive capacity, both of which are important aspects of successful long-term population and species conservation (Jan et al., 2017).

Biology and Function of SSCs

SSCs are the undifferentiated male germ cells that sit in the base of the seminiferous tubule of the testis. These cells are important for male fertility because they provide the foundation for ongoing seminal tubing. SSCs up on initiation can only remain as stem cells through mitotic divisions, but at the same time actively produce progenitor cells that enter the pathway of spermatogenesis. This equilibrium, between self-renewal and differentiation, is maintained with a high precision so that the spermatogenic capacity is lifelong (Abofoul-Azab et al., 2019). The understanding of SSC regulation entails the use of both the intrinsic and extrinsic factors.

Intrinsic factors are main categories, which involve transcription factors that control self-renewal and differentiation of SSCs including PLZF, NANOS2, and FOXO1. These factors either activate or repress the genes which possess importance to retain stem cell identity or to start the differentiation program (Jan et al., 2017).

Extrinsic factors play the same role and are also important, SSC niche offers conduits that determine their destiny. Special groupings include Sertoli cells, peritubular myoid cells or any other supporting cell found in the seminiferous tubules (Hermann et al., 2018). Chemical factors expressed by the niche encompass GDNF, FGF, and CSF1 among others for the neuronal, growth factor and cytokine families respectively. Sertoli cells synthesize GDNF, which is critical for SSC (utilized throughout the textual passage) self-renewal and FGF and CSF1 are involved in SSC proliferation and survival. Moreover, basal lamina and collagen present nearby Sertoli cells with structural support as well as biochemical signals that help them to be anchored and signaled (Costa et al., 2012).

Thus, constant reciprocal interplay between the intrinsic cell properties and the extrinsic signals guarantees the homeostasis of SSCs and the ability of adult males to produce several millions of sperm per day. Aberrations in these mechanisms may result in infertility or other related pathologies meaning that advances in SSC biology were necessary for the development of related therapies (Figure 1) (Martinez et al., 2020).

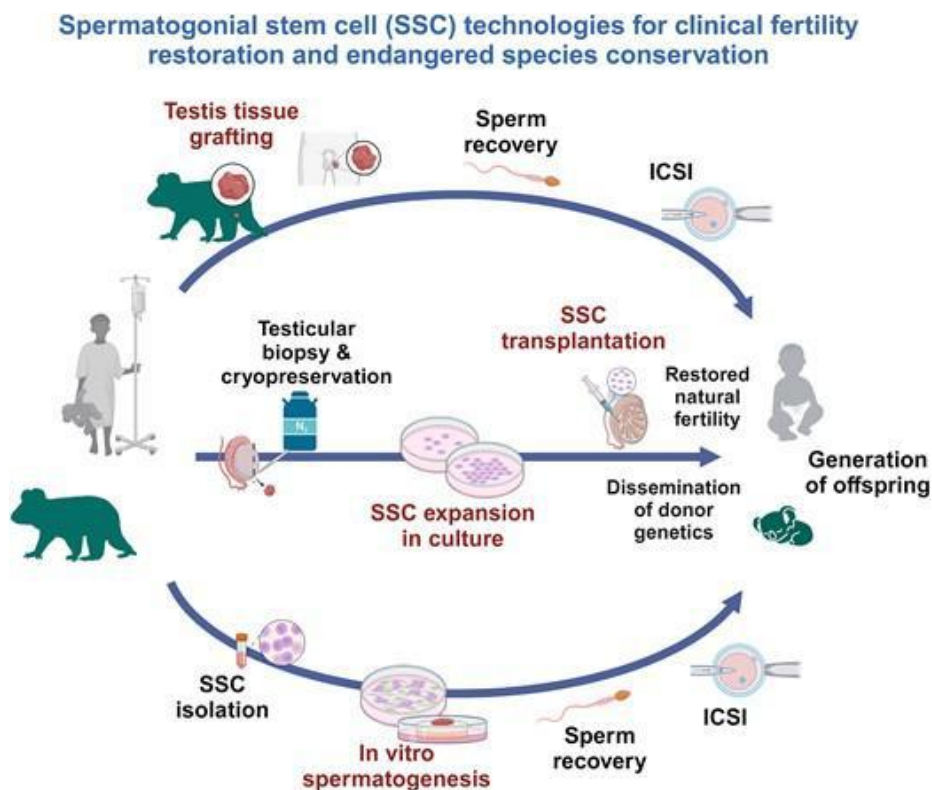


Fig. 1: SSC technology for treating infertility in endangered species (Damyanova et al., 2024)

Applications of SSC Technology in Wildlife Conservation

Genetic Resource Banking

SSCs based genetic resource banking is a revolutionary concept in conservation biology that can potentially provide unique solutions for effective conservation of genetic stocks of endangered species. Despite the fact while SSC cryopreservation is distinct from sperm banking,

through which sperms are pre-designed for make use of at any later date, but there are possibility of creating sperms in an unlimited fashion given proper in vitro or in vivo conditions (Mall et al., 2020). This feature is especially beneficial for the species that have specific problems connected with their reproduction, for example, these having the seasonal character in their reproduce duties and in which the sperm supply is present only during the certain periods of the year. Furthermore, SSC banking can eliminate problems concerning the cryopreservation of mature sperm since in some species their sperm is easily damaged; or in other cases, the effectiveness of the sperm is low (Devi et al., 2014).

A distinct strength to SSC banking is that it is suitable for prepubertal people. When young males of endangered species die before reproducing, the remains with their SSCs collected and preserved, useful for future generations or populations. Likewise, SSCs can be obtained at postmortem of individuals depending on the tissue samples collected and preserved shortly after the death. This capability greatly extends the original concept of genetic resource banking because it provides a means of genetic material storage even in emergent situations (Andrae et al., 2021).

Moreover, SSC cryopreservation facilitates the creation of biobanks, where only all sorts of genetic materials of various individuals, within a particular species, can be stored. Such biobanks proved to be useful for researches and conservation, as they can act as the source of genetic material for the following experiments or the breeding stock for the species (Binsila et al., 2018). Recent improvements in vitrification or other methods of mammalian gamete freezing have given increased post-thaw survival and function to SSCs, thus consolidating this technology for conservation purposes (Zehmal et al., 2020).

Assisted Reproductive Technologies (ARTs)

As for SSC technology, although it has not been widely used in ARTs, its incorporation has broadened the enlarged the application and effectiveness of ARTs in wildlife conservation. Ectopic transplantation of SSCs into recipient testes is a novel procedure that allows for the generation of sperm from donor derived SSCs. This approach allows those with low fertility or skewed sex ratios to pass on their genes, solving two major biological problems in endangered species (Oatley et al., 2016).

Owing to the inability to perform some traditional ARTs such as artificial insemination or in vitro fertilization because sperm is lacking or difficult to obtain in good quality, SSC transplantation is most useful for species that require assisted reproduction techniques. Therefore, by transplanting SSCs into the testes of a recipient male sperm can be produced naturally without a need for repeated interventions. This technique has been successfully used in a number of mammal models and this work sets the stage for using these techniques for improved conservation of wildlife (Mall et al., 2020).

Another advancement in the arena of SSC research is the cross-species SSC transplantation. In this case, SSCs from a donor species are transplanted in the testes of a phylogenetically close related species which then serves as surrogate for spermatogenesis (Johnston, 2019). This strategy has been advantageous for those poorly represented species which closely related species are common but easily accessible. For example, SSCs have been taken from endangered felids and then transplanted into surrogate domestic cats, in which viable sperm was developed. Such cross-application also offers heightened probabilities of improving the reproductive performance of threatened species, besides easing the invasive ways of collection (Pothana et al., 2016).

However, ARTs that embraces SSC technology can solve reproductive difficulties in such species with many social structure or behavioral restrictions. For instance, in a species where dominant male genitors control all the breeding opportunities then SSC transplantation can increase the genetic representation of subordinate genitors and improve genetic subpopulation within founding stock (Yang et al., 2018).

Species Restoration

SSC technology appliqué in species restoration and what can be deemed as the de-extinction is living evidence of this reality. Through utilizing preserved SSCs, lost heritable characters may be brought into breeding populations or even create new species other such advanced means of breeding are employed. This approach provides a special chance to solve the problems of genetic erosion and population depletion which endanger the variety of life on the earth (Devi et al., 2014).

Among all the promising uses of SSC technology in species restoration, the use of surrogate species has been of significant importance. In the method, the preserved SSCs from an endangered or an extinct species are then implanted in to the testes of a closely related species (Sahare et al., 2014). Thereafter, the surrogate also provides sperm that contains genetic characteristics of the donor species to be used in fertilization and breeding. This technique has been implemented in several species, for example, felids, SSCs from endangered cats have been put in domestic cats surrogate where they gave birth alive and healthy offspring (Lee et al., 2014).

The application of SSC technology in de-extinction has attracted much attention according to various techniques in reestablishing the species that were eradicated by various human interventions (Paul et al., 2017). The successful transplantation of SSCs' genetic material into current populations provides the opportunity to restore lost genes that provided specimens with durability and flexibility they otherwise would not possess helping species overall survival against their diminishing environments. For example, there is intentionally breeds some SSCs from the former population to the present population of an endangered species, thus following the loss of genetic variation and inbreeding depression (Kim et al., 2015). The survival and successful reintroduction of SSC-based species is therefore a function of improvements in cryopreservation, transplantation, and in-vitro culture. Present studies focus on fine-tuning of these techniques to enhance the immediate and durable functionality of SSCs after transplantation. Moreover, concerns on the ethic of the project and relevance to the overall environmental objectives and impact to the ecology of the area must also be given thorough consideration to confirm that the results of the species rehabilitation are in with modern conservation vision (Kong et al., 2018).

Genetic Diversity Enhancement

Genetic management is one of the most fundamental concerns for wildlife conservation and SSC technology is developed to serve that purpose. Although, it is good practice to be extra cautious when transplanting animals and plants from one place to another, genetic variability

plays an important role in the survival and the wellbeing of endangered populations because species need it in order to counter changes in the environment; to fend off diseases; and to improve the general health of the population without which, many species are likely to go extinct. SSCs are useful tools for bringing new alleles into a population and reducing such problems of small isolated populations as inbreeding and genetic drifts (Patra et al., 2021).

In many endangered species, loss of genetic variation due to small population size, gene flow and habitat fragmentation, increases the accumulation of bad genes. The fundamentals of SSCs can also help solve such obstacles to the extent that SSCs can act as a way of transferring genetic material derived from genetically differentiated individual or populations. Through grafting of SSCs into recipient males, sperms harboring different gene characteristics can be generated for artificial insemination or natural mating. It may take a positive turn and perhaps counter the ill effects of inbreeding and increase the general well-being of endangered species (Suyatno et al., 2018).

SSC application for genetic improvement is most appropriate for species whose breeding patterns are not so straightforward or do not have knowable social systems. In species where dominant males control mating, subordinate males will rarely or never assist in gene pool creation. Through the SSC transplantation, the genetic material of these individuals is well represented hence equality in distribution of the same amongst the population (Pramod et al., 2023).

Advances in SSC Technology

- Some changes have though been achieved on the scope of cryopreservation in SSCs such as vitrification and use of cryoprotectant. Such techniques guarantee that the genetic material stays viable and will be helpful for further uses in preservation (Kim et al., 2015).
- The SSCs has also been greatly witnessed by RNA-seq and ChIP-seq Next-generation sequencing technologies to unravel and better understand the SSC transcriptome and epigenome that has in turn informed culture and transplantation strategies (Yang et al., 2018).
- Attempts to reproduce spermatogenesis have yielded positive results in mice through production of testicular elongated cells from SSCs. This could eliminate the need for the use of animals and their characteristics would not be reproduced through transplantation between species as it has been a huge concern (Suyatno et al., 2018).

Ethical and Ecological Concerns

Ethical and ecological concerns are important for those of us who are living now they constitute the germination of tough questions that should be posed to society and result from understanding the importance of human life and the environment (Shah et al., 2018). SSC technology can make a significant difference, yet, their application is questionable both from ethical and ecological aspect. Genetic engineering could also bring insertional mutagenesis, or lead to population disruption. Furthermore, the case with the selection of target species for SSC based interventions may distort other conservation objectives in the ecosystem. Prominent decision making patterns should be transparent along with tough risk analysis to combat these potential issues (Lee et al., 2014).

Future Directions

1. Relation with Other Biotechnologies

The use of SSC technology integrated with somatic cell nuclear transfer (SCNT), jointly with gene editing tools such as CRISPR-Cas9, could improve significance and range of its application. For example, one may modify genes in SSCs to get rid of detrimental changes that can harm the animal before their utilization in conservation (Kong et al., 2018).

2. Towards Wider Cross Species Compatibility

Studies exploring how to increase the cross species SSC transplantation success may expand the list of suitable surrogates making this technology more useful in preserving the critically endangered species (Pramod et al., 2023).

3. Participation and Policy-making

Mainly due to the distinct potential impacts of the SSC technology in conservation, there is a strong call for public awareness and stakeholder engagement in the ethical application of the technology. It will thereby be possible to adopt policies that respond to technological progress while at the same time preserving the ecological and cultural environments (Mall et al., 2020).

Conclusion

SSC technology has great potential to counterpart continuing biodiversity threat like conservation of genetic assets, recovery of endangered species and improvement of genetic stock. Being part of the conservation sector, integration of those emerging biotechnologies like gene editing, reproducing spermatogenesis and cryopreservation together with strict compliance to ethical issues will be the decisive factors for its success in wildlife conservation. Utilizing these viewpoints that were developed through the improved SSC-based interventions, we can establish a less volatile environment in the existence of world's wildlife and the ecosystems they call home, in essence the strengthen the stability of our earth's biodiversity.

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Revolutionizing Prostate Cancer Treatment: Gold and selenium Nanoparticles in Precision Photothermal Therapy

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Abstract

Nanotheranostics, a single modality that combines therapeutic monitoring and optically multiplexed disease detection, has the potential to advance nanomedicine toward truly personalized medicine such as Abirateron. Due to its numerous potential and ability to bridge the gaps in the existing treatment modalities' limitations, nanoparticle technology has gained acceptance in the fight against cancer. Prostate cancer tumor ablation can also benefit from the synergistic effects of photodynamic therapy reactive oxygen species (ROS) are used in Photodynamic therapy (PDT) and photothermal therapy (PTT), which offers insights into the potential for even more from this technology. This review explores the use of gold (Au) and selenium (Se) nanoparticles in photothermal therapy (PTT) and photodynamic therapy (PDT) drug delivery for prostate cancer treatment. It covers key subtopics, including the complex biology and chemistry of pharmacologically active Se- and Au-containing compounds, their mechanisms of action, and their synergistic effects. By investigating their therapeutic potential, this review aims to establish a comprehensive understanding of their role as a targeted and effective approach for prostate cancer therapy. Additionally, this chapter presents a comprehensive review of the current state of research, challenges, and future prospects in the ongoing fight against prostate cancer.

Keywords: Cancer nanotechnology, Photothermal therapy, Gold nanoparticles, Selenium nanoparticles

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Introduction

Recently, 1900, novel nanoparticle (NP) technology has become a major creative force behind the integration of medical diagnosis and therapy into a "unified" single-step platform called "nanotechnology." Although still in its early stages, this approach shows great promise as advanced optical technologies and treatment modalities gain importance in cancer management. However, many of the mechanisms underlying its use in medicine still need to be clarified (Siegel et al., 2019). Globally, prostate cancer is a common condition that significantly contributes to the mortality rates linked to cancer in men. Prostate cells are usually the source of the disease which frequently presents as a localized or metastatic tumor (Karavitaikis et al., 2017). Prostate cancer has a significant death and disability rate, which makes the investigation and application of innovative therapeutic strategies imperative. Using gold and selenium in delivery systems is one potentially beneficial for treating prostate cancer. The capacity of selenium to alter redox signaling pathways and promote oxidative stress-induced apoptosis has demonstrated its anticancer effects.

1.1. Why Selenium is Important for Research on Prostate Cancer

1.1.1. Properties of Antioxidants

Selenium, an essential trace mineral, plays a crucial role in antioxidant enzymes like glutathione peroxidase. These enzymes help reduce oxidative stress by neutralizing free radicals, which can damage DNA and contribute to cancer development. A variety of cellular processes,

such as governing the cell cycle and apoptosis (programmed cell death), have been demonstrated to be impacted by selenium. This is especially important since one of the characteristics of cancer is the ability of cancer cells to evade apoptosis. By encouraging apoptosis in cancer cells, selenium can stop the growth and multiplication of these cells (Hirsch et al., 2003). Selenium is necessary for the immune system, which is crucial for identifying and getting rid of abnormal or cancerous cells. According to research findings, selenium could hinder the process of angiogenesis, which creates new blood vessels and supplies nutrients to cancers (Grzelczak et al., 2020). Gold nanoparticles have distinct photoactive properties that enable specific hyperthermia and precise tumor adaptation. One promising application of gold nanoparticles is photothermal therapy (PTT), which uses them to specifically target and kill cancer cells.

1.2. Gold's Importance in the Study of Prostate Cancer

Research suggests that selenium may prevent angiogenesis, the process that creates new blood vessels and gives tumours nourishment. The growth as well as spread of cancer may be hindered by the element selenium through the restriction of angiogenesis (Hu et al., 2024). The unique photoactive properties of gold nanoparticles enable precise tumor adaptation and targeted hyperthermia. One ensuring use is photothermal therapy (PTT), which uses particles of gold to focus on and kill cancer cells specifically. The gold nanoparticles which have been provided to the cancerous cells are irradiated using near-infrared (NIR) light in photothermal therapy (Lal et al., 2008). The gold nanoparticles absorb light and convert it to heat. This localized heating causes thermal damage to the cancer cells, killing them without causing damage to the surrounding healthy tissue.

The following ways are used to treat prostate cancer

1.3.1. Targeting

Gold nanoparticles are functionalized using specific ligands, peptides, or antibodies that can attach to prostate cancer cells (Cheng et al., 2021).

1.3.2. Accumulation

After being injected into the bloodstream, nanoparticles acquire in the tumor site because of the improved and permeability effect of retention (EPR) because they are more likely to do so in tumor tissues than in normal tissues (Bastús et al., 2011).

1.3.3. Tumor Destruction

By inducing necrosis, coagulation, programmed cell death, or apoptosis, the heat generated can effectively destroy cancer cells. Numerous techniques, including sound waves, microwave stimulation, laser-assisted photothermal therapy (PTT) () and photodynamic therapy (PDT) (), are being investigated for their potential to treat cancer by inducing hyperthermia (Valerio et al., 2014). Like traditional cancer treatments, these alternative therapies may not be tumor-specific and may have unintended side effects. Therefore, it is necessary to produce new therapeutic strategies which may improve tumor control by means of mutually beneficial effects, fewer side effects, and greater practical applicability. However, the infectious and lytic nature of Oncolytic Viruses OVs also comes with a number of drawbacks: pathogenicity is of great concern for OVs due to the risk of uncontrollable viral replication, even when attenuated through genetic modifications, safety issues are not completely eliminated, and there is a potential that the OVs might return back to their infectious wild type through the recombination with wild type viral strains. The immune system produces an anti-OV immune response within 1-2 weeks that eliminates the OV infection, which is another drawback of OVs. Finally, it is more difficult to impart new functionalities to OVs than to VLPs or VMNs. As viruses evolved to have an optimized structure as well as genome that carries out their entire lives, surface alteration and genetic fusions may adversely impact viral fitness. Our body uses blood clots as a natural defense against blood loss. These thick blood clots seal wounds, scrapes, and blood vessels that are leaking. Your body may bleed excessively if it takes too long to form them. Your blood clotting time is measured by a partial thromboplastin time (PTT) test. The activated partial thromboplastin time (aPTT) test is another name for this test that doctors use (Leite et al., 2011). Due to their high surface-to-volume ratio, they can also more easily penetrate tumor sites through a phenomenon called enhanced permeation and retention (EPR). The production of reactive oxygen species by selenium nanoparticles (Se NPs) may be an additional way to prevent tumor growth (Omiyale et al., 2023). The combined effect of these elements increases the efficiency of thermal energy evaporation in the designed capsule, so the combined effect of Se NPs and Au NPs leads to dual pharmacological effects.

1.4. Principles of Photothermal Therapy (PTT)

Photothermal therapy is the application of heat that is photoinduced to treat cancer. This therapeutic strategy has been seen as a promising anti-cancer treatment because it can be spatially controlled, avoiding harm to non-targeted areas. Photothermal therapy is a subset of nanomedicine since most materials that cause photothermal heating are nano scaled. For photothermal therapy to be effective, a few basic prerequisites must be met. First and foremost, template nanomaterials intended for therapeutic use must have high photothermal conversion efficiency—that is, the ability to transform light energy into heat energy. Second, to guarantee deep tissue penetration, the photothermal effects ought to be triggered by near-infrared (NIR) light. Finally, for photothermal treatment to be effective, the surface of the nanomaterials should be easily modified. According to earlier studies, these conditions can be met by using nanoparticles with targeting ligands, which enable selective internalization and laser irradiation to create photothermal effects inside the target cell (Figure 1).

1.5. Gold Nanoparticles for PTT

AgNPs used in photothermal applications must meet several design specifications, such as plasmon resonance tunability and high photothermal conversion efficiency (Hirsch et al., 2003). These parameters indicate that nanoshells, nanostars, nanorods, and nanocages are the most used photothermal transducers (Jing et al., 2014). Using these formulations as examples, the desirable properties of AuNPs for PTT are discussed here. AuNPs used in PTT must first be made using light from the first NIR window because AuNPs embedded in tumors can be safely and deeply penetrated through healthy tissue by these light wavelengths (Bastús et al., 2011).

The ability to adjust the structural dimensions of AuNPs to achieve maximum absorption in one of these two light regions is a significant characteristic. Most AuNPs are made to absorb as much as possible within the first NIR window, which is safe to enter between two and three centimeters of tissue (Prodan et al., 2003). For instance, by varying the ratio of core diameter to shell thickness, NSs—which are made up of thin gold shells surrounding spherical silica cores—can have their peak plasmon resonance tuned. Because they can maximally absorb light at 800 nm, NSs with cores that are 120nm in diameter and shells that are 15nm thick are commonly used for PTT. The longitudinal surface plasmon resonance (SPR) ($\lambda \approx 650\text{--}850\text{nm}$) and transverse ($\lambda \approx 500\text{--}550\text{nm}$) are represented by two absorption peaks that are provided by NRs' short and long axes. To attain the highest longitudinal SPR in the NIR region, the rod length can be either elongated or shortened. NRs that are around $10\text{nm} \times 40\text{nm}$ are the most common for PTT due to their ability to absorb light up to 800nm. New AuNP designs for PTT in the second NIR window has recently surfaced, whereas the majority of AuNPs were created to absorb as much as possible within the first NIR window. The reason for this is that these wavelengths can safely reach deeply embedded tumors by penetrating up to 10cm of tissue. Nanotubes of carbon with a single wall coated with AuNP as a multipurpose platform for PTT and imaging in the second NIR window (Pelaz et al., 2017).

1.6. Applications in Prostate Cancer Treatment

Prostate cancer (PCa) treatment now heavily relies on genetics, genomics, and biomarker applications. Nowadays, risk assessment, treatment course determination, prognosis, and monitoring all frequently use germline Tumor genomics, genetic testing, and additional biomarkers. When it comes to PCa diagnosis and treatment response tracking, molecular imaging is essential (Riley et al., 2017). The following are some noteworthy uses in the treatment of prostate cancer:

1.6.1. Surgery

A radical prostatectomy, which is frequently done in cases of early-stage cancer, entails excising the prostate gland entirely along with some surrounding tissue. Techniques that are not too invasive are Precision, a quicker recovery, and fewer complications are all benefits of robotic-assisted laparoscopic surgery, such as that provided by the da Vinci surgical system (Zhou et al., 1994).

1.6.2. Radiation Treatment

High-energy radiation is used to destroy cancer cells, external beam radiation therapy (EBRT) is focused on the prostate. By directly implanting radioactive seeds into the prostate, brachytherapy offers targeted treatment with the least amount of tissue damage possible.

1.6.3. Androgen Deprivation Therapy (ADT)

ADT is a type of hormone therapy. The goal is to lessen or stop the synthesis of androgens, or male hormones, which can promote the growth of cancer (Ashikbayeva et al., 2019).

1.6.4. Techniques

1.6.4.1. Drugs: The production of testosterone is decreased by LHRH agonists and antagonists.

- 1.6.4.2. Anti-Androgens: Prevent cancer cells from being affected by androgens. An orchiectomy lowers testosterone levels by surgically removing the testicles.
- 1.6.4.3. Chemotherapy Use: Frequently for hormone-resistant or advanced prostate cancer.
- 1.6.4.4. Common Medications: Prednisone is frequently used in conjunction with docetaxel and cabazitaxel to help reduce symptoms and slow the progression of cancer.

1.6.5. Immunotherapy

One kind of cancer vaccine called Sipuleucel-T (Provenge) is intended to boost the patient's capacity of the immune system to combat prostate cells of cancer. Castration-resistant prostate cancer that has spread is its main application. Checkpoint inhibitors are medications that strengthen the defenses of the body against cancer by blocking particular proteins found on cancerous or immune cells (Songca et al., 2023).

Targeted Therapy

PARP Inhibitors: Medications such as olaparib can prevent cancer cells from repairing their DNA, which can result in cell death in patients with specific genetic mutations (e.g., BRCA₁/BRCA₂) (Grzelczak et al., 2020).

- Radionuclide Therapy: Radium-223 (Xofigo), which targets cancer cells in the bone while preserving nearby healthy tissue, is used to treat advanced cancer with bone metastases.
- Active Monitoring and Vigilant Waiting

Monitoring without prompt treatment is an option for slow-growing, low-risk prostate cancer. To monitor progress, this routine PSA testing, digital rectal exams, and biopsies (Hu et al., 2024).

Focal Therapy

Methods that target and eliminate cancerous tissue while preserving healthy prostate tissue incorporate HIFU, or high-intensity focused ultrasound and cryotherapy. Using laser light and photosensitizing agents, photodynamic therapy (PDT) kills cancer cells. Its effectiveness in treating prostate cancer is still being studied. Gene therapy is the process of altering a patient's genes to boost immunity or introducing therapeutic genes to stop or eradicate cancer cells (Lou et al., 2023).

Lifestyle Modifications

Stress reduction, exercise, and a healthy diet can enhance general health and support treatment. Counseling, support groups, and palliative care all aid in symptom management and enhance quality of life. The following are some thorough case studies and clinical situations pertaining to the treatment of prostate cancer:

• 1.6.6. Case Study 1: Prostate Cancer in its Early Stages

Gleason score 6 (3+3) and T1c prostate cancer are the diagnoses for the patient, a 55-year-old man with PSA 4.5ng/mL. Active surveillance, including yearly biopsy and routine PSA monitoring, is the treatment. Result: After five years, PSA levels remained stable with no indications of improvement. A fifty-year-old man with a history of prostate cancer in his family is the patient. A BRCA2 mutation was found during genetic testing.

Treatment: ADT plus olaparib, a PARP inhibitor. Improved PSA control and the possibility of increased overall survival are the results (Thapa et al., 2018). Prostate cancer patient with high-risk characteristics: a 60-year-old man with a Gleason index of 9 (5+4) and PSA of 20 ng/mL is treated with EBRT + ADT + docetaxel chemotherapy, which improves local control and reduces the risk of distant metastases (Ramamoorthy et al., 2020).

A 65-year-old man with PSA recurrence after prostatectomy was treated with ADT and SBRT. This approach improved his PSA control and reduced the risk of further recurrence.

1.7. Gold Nanostructure Synthesis for Theranostics

Notwithstanding the widespread use of nanostructures, there are two methods: top-down and bottom-up. The bottom-up strategy of producing gold salt reduction produces nanostructures of gold from atoms of gold techniques has been well-liked for many years. Ultra-thin NRs, which with the AR of roughly 10–20 that show the mid-IR (MIR) region's LSPR have recently been reported. Even though the transparency window and their LSPR overlap, this should NRs' typical polydispersity (in a synthesized batch) is greater than that of the NPs of spherical, which effectively lowers their total absorption and translates into higher photothermal efficiency (Yu et al., 1997). Another factor to take into account is that heating causes the NRs to melt and change shape, producing NRs that have lower LSPR and AR than the initial. This could make the NRs unsuitable for therapeutic use because it would alter the effectiveness of their transduction light-heat over the course of a treatment cycle. This effect has been thoroughly examined and reported by Jana et al. (2001). Because their peaks of LSPR can be in the region of NIR, gold nano shells and gold nanostars are other nanostructures that have gained popularity (Jana et al., 2001). For nano shells of gold, adjusting the shell thickness between nm1 and 30nm and for gold nano stars, adjusting the number of branches, length of tip, and tip sharpness gives control over the λ LSPR tunability. Initial synthesis of nano shells onto dielectric silica cores involved the formation of seeds of gold that eventually formed a sphere of silica with nano roughness, ultimately resulting in covering the silica core with a smooth gold shell. The LSPR blueshifts as the shell thickness increases.

1.8. Impact of Shape and Size of Particles

The primary factor influencing the physiochemical characteristics of the size of AgNPs has a significant impact on the theranostic platform's behavior both *in vitro* and *in vivo*. Crucial factors that regulate their cellular absorptions, biodistribution, and the geometric effects of their size and clusters order are endocytosis efficiency, clearance places, and clearance rates (Chhatrec et al., 2018). According to reports, although pristine NPs with a diameter of less than 100nm might be able to enter cells, those smaller than 40nm might approach the cellular nuclei. NPs less than 100nm in diameter might likewise have access to cells. However, the renal filter removes NPs from the body that have a diameter of less than 10nm. As a result, size and surface functionalization/coating are crucial for Gold nanostructures' targeted delivery in tumors (Shields et al., 2010).

These factors can help to achieve the best therapeutic activity while minimizing toxicity and adverse effects on healthy cells and tissues. By employing functionalizing or coating agents that impact NPs' ability to enter or be transported to the cell membrane, as well as the degree of potential entry and clearance pathways. The transfer and growth of gold nanostructures, as well as their associated toxicological impacts on various using both *in vitro* and *in living cells test models*, extensively studied in relation to particle shape and surface functionalization (Cheng et al., 2018).

1.9. Conclusions and Future Perspectives

An increasing number of innovative AuNPs are being developed to combine photothermal therapy and optical diagnostics in a single process. Enhancing raman nanotheranostics based on gold nanostructures could be essential for moving towards treatments and detection to more complicated biological processes *in vivo* within clinic. Additionally, SESORS has made significant strides recently in providing damage and optical imaging localization in conjunction using direct optical feedback and PTT to deliver precise *in vivo* pH and temperature monitoring. We have examined the data supporting this expanding consensus and have emphasized the integration of two approaches (treatment and evaluation) into a single, effective, economical, and focused procedure. By addressing the difficulties in developing novel methods for functionalizing AuNPs containing molecules capable of promoting efficient binding, corona formation, clarity, biocompatibility, biodistribution, and toxicity, this review also offers noteworthy advancements. Additionally, it has addressed the translational barrier and unmet clinical need for quick, efficient nonsurgical cancer diagnosis and detection with high sensitivity and specificity using raman spectroscopy. Additionally, it has tackled the translational barrier and lacking medical need of employing gold nanostructures in one, efficient nonsurgical procedure to detect and diagnose cancer with great sensitivity and specificity. Nanostructures of gold have been extensively investigated for potential medical uses, but commercialization of these (NPs) for standard in options for *in vivo* light-triggered therapy has been delayed for a long time.

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Enhanced Photo-Catalytic Degradation of RhB Dyes under UV/Visible Irradiation using Sm Doped ZnFe₂O₄ with g-C₃N₄ Nanocomposites

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Abstract

Industrial dye pollution poses a threat to ecosystems, but semiconductor photocatalysis offers a sustainable solution. In this study, Sm doped ZnFe₂O₄ with g-C₃N₄ composites were produced with co-precipitation for the environmental degradation of RhB dye. The composites were characterized using different methods. The synthesised samples' crystal structure was clearly visible through X-ray diffraction, with an average crystallite size of 20–30 nm and a cubic structure. The basic composition of the materials, as determined by EDX, indicates that the composite was prepared correctly. The micrographs of SEM indicate average grain sizes of 10 nm for SGZ1, 14 nm for SGZ2, and 23.14 nm for SGZ3 nanocomposites. FT-IR measurements in the 4000–400 cm⁻¹ range showed the O-H, C-N, and C=N functional groups are present. Analysis of UV-Vis spectrums showed the optical band gap value from 1.24 to 1.41 eV. The ideal conditions for photocatalytic At a pH of 8, degradation was seen, and the dosage of the photocatalyst of 60mg/50mL, and an dosage of H₂O₂ 10 mM, used a SZG3 composite. In these conditions, efficient RhB dye degradation was accomplished at 98.3% using this SZG3 composite within 70 min. Over five cycles, the reusability of the nanocomposite was also assessed.

Keywords: Co-precipitation, Composite, Heterogeneous photocatalysis, Wastewater treatment

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Introduction

The textile industry's massive expansion has caused a notable rise in water contamination, primarily because of the release of industrial wastes like various inorganic and organic dyes into water sources. According to Konstantinou and Albanis, between 1 and 20% of the globally produced dyes are disappearing during the dyeing process and end up in textile effluents. The waste products from the dyeing process in these industries are highly toxic, impacting the metabolism of living organisms. They also present serious risks to human health, the environment, and natural processes such as eutrophication. The textile industry, which mainly uses synthetic dyes, is one of the major sources of these persistent organic compounds (Ebrahimi et al., 2021). Many of these dyes are dangerous to humanity and aquatic life because they are not biodegradable (Bera et al., 2018). Therefore, it is essential to break down non-biocompatible organic compounds and purify the water to preserve the ecosystem (Faheem et al., 2022). The RhB is recognised as among the most toxic dyes found in textile wastewater. It holds significant value in the textile industry as a colourant due to its exceptional stability and non-biodegradability. When RhB is used extensively, it can be toxic to the thyroid, eyes, and skin. It can also be harmful to the throat and liver (Mousavi et al., 2024). In this present work, the focus is on the degradation of RhB. Conventional wastewater treatment techniques like sedimentation, coagulation, chemical flocculation, ozonation, filtration, and so on are used in removing dyes from textile effluent (Abdulhamid & Muzamil, 2023). But these methods have a number of drawbacks, including energy consumption and toxic by-products.

Among them, photocatalysis has generated a great deal of interest because of the expense effectiveness, high efficiency, and simplicity of use. Since the 1970s, hydroxyl radicals have been used an efficient technique in oxidation processes purifying water, to reduce organic pollutants that are not biodegradable. In photocatalysis, reusable photocatalysis, along with an active source of light like sunlight and an oxidising agent like air or oxygen, are employed to degradation the organic pollutants such as dyes. Particle size reduction in this process increases the quantity of active sites and their surface area, which improves reactivity. With an increase in the number of active sites, the adsorption of pollutants on surface of the catalyst also increases (Mamba & Mishra, 2016). During the previous 20 years, research has focused on using semiconductors as photocatalysts.

Among various semiconductors, ZnFe₂O₄ is considered particularly important due to their ability to remove organic dye contaminants, thanks to their physical and chemical properties, environmental friendliness, and stability (Shahraki et al., 2023). However, their

photocatalytic activity is only activated by UV-visible irradiation. Rare earth elements are also used in photocatalysis process due to their unique electronic properties, which boost the performance of photocatalytic materials (Rabiee et al., 2021).

The polymeric without metal photocatalyst graphite carbon nitride ($g\text{-C}_3\text{N}_4$) has drawn more interest because of its non-toxicity, appropriate electron band gap (about 2.7 eV), and consistent stability. But the restricted absorption of visible light and the quick efficiency of photogenerated electron-hole pair complexation greatly limit the applications of $g\text{-C}_3\text{N}_4$ (Rawal et al., 2013).

For the first time in this process, $g\text{-C}_3\text{N}_4$ heterojunction with Sm-doped ZnFe_2O_4 according to reports, as a supported electron mediator. In this work, a photocatalyst Sm-doped ZnFe_2O_4 with different amounts of $g\text{-C}_3\text{N}_4$ (2%, 3%, and 4%) was created and utilised to break down rhodamine B (RhB) dye in the presence of regular sunlight. The analysis of prepared material using FTIR, XRD, UV-Vis spectroscopy SEM/EDX, was used to define the functional group, crystalline structure, morphology, optical characteristics, chemical composition and purity of the created samples. The results indicate that Sm-supported ZnFe_2O_4 with $g\text{-C}_3\text{N}_4$ increases surface area and that photo-induced charge carrier separation significantly improves the photocatalyst's response to visible light.

Experimental Work

Synthesis of $g\text{-C}_3\text{N}_4$

The process of to create $g\text{-C}_3\text{N}_4$, thermal polymerisation was employed. After adding ten grams of melamine to the crucible, it was heated to 550 °C for three hours. The melamine was burned out in the furnace to produce the yellow-colored $g\text{-C}_3\text{N}_4$ (Fu et al., 2018).

Synthesis of $\text{Dy-ZnFe}_2\text{O}_4$

A stoichiometric ratio of $\text{Zn}_{1-x}\text{Sm}_x\text{Fe}_2\text{O}_4$, $x = 0.03$, was used to dissolve nickel nitrate $(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, Samarium nitrate (SM $(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$), and ferric nitrate $(\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O})$ in 50 ml of distilled water. Throughout the process of synthesis, solutions were constantly stirred to attain homogeneity, and drops of the precipitating agent (NaOH) were added to reach and maintain pH 8. After that, the solution was elevated to 80 °C for one hour. The brown color precipitate that formed due to these processes was centrifuged two times, initially with double-distilled water and then with ethanol, to eliminate the impurities and nitrate ions. After being dried for 12 hours at 70 °C, the resultant byproduct was examined. The final product was converting into tiny nanoparticles using a mortar, and the muffle furnace was used to calcine the powder at 500 °C for three hours. Several characterization techniques were used to analyze the properties of prepared material (Ullah, 2023).

Synthesis of $\text{Sm-ZnFe}_2\text{O}_4/g\text{-C}_3\text{N}_4$

The $\text{Sm-ZnFe}_2\text{O}_4/g\text{-C}_3\text{N}_4$ binary composite was synthesized by a simple co-precipitation method. First, 0.2g of $\text{Sm-ZnFe}_2\text{O}_4$ and 0.2g of $g\text{-C}_3\text{N}_4$ were individually dissolved in 50 mL of water to obtain homogeneous solutions, which were then combined, stirred on stirrer for 15 minutes, and subsequently sonicated for 15 minutes to form a well-dispersed suspension. Then $g\text{-C}_3\text{N}_4$ solution was added dropwise in $\text{Sm-ZnFe}_2\text{O}_4$ solution with burette and stirred for 30 minutes at room temperature. The resulting solution was sonicated for 15 minutes. This mixture was then heated in an electric oven, collected by centrifugation, and dried at 70°C in an oven. The conclusion by-product was crushed into fine nanoparticles using a mortar, and the resulting nanopowder was then burned at 500 °C within furnace for 3 hours, and collected in brown color shown in Figure 1 made in canva. By changing the $g\text{-C}_3\text{N}_4$ content to be 20, 30 and 40 mg, the samples were named as SZF/GCN-X (X = 20, 30 and 40 mg) and their properties were analyzed by different characterization (Karthik et al., 2017).

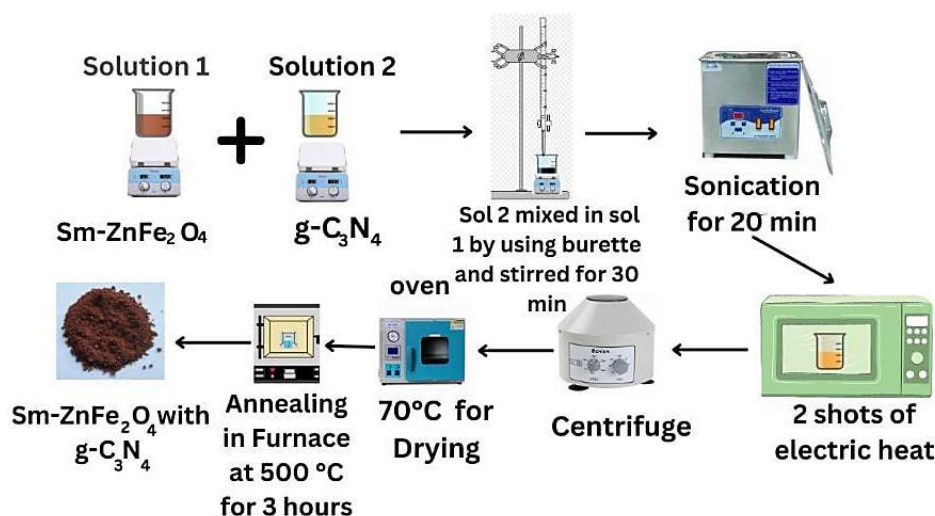


Fig. 1: illustration of the synthesis of $\text{Sm-ZnFe}_2\text{O}_4/g\text{-C}_3\text{N}_4$

Activity of Photocatalytic

For the purpose of evaluating the activity of photocatalytic, 50 ml of the RhB solution was added to a 250 mL beaker flask and it was mixed at 180 rpm. To find the equilibrium of desorption and adsorption between the photocatalyst and dye solution, 20 mg/50 ml and 30 mg/50 ml were distributed in the 50 ml RhB solution and exposed to darkness for 30 minutes. After 30 minutes in the dark, an oxidant

(H₂O₂) solution was added. After that the whole setup was exposed in sunlight. By using a LUX meter, the intensity of sunlight which was 1080 Wm² was measured. After centrifuging for 15 minutes the solution of 5mL volume was taken out from beakers and using of UV-Vis spectroscopy absorbance was determined (Sudha & Sivakumar, 2015). The efficiency was determined by using the following Eq. (1) (Jouyandeh et al., 2021):

$$\text{Photocatalytic efficiency } (\eta) = (1 - \frac{C_t}{C_0}) \times 100 \quad 1)$$

The dye concentration is indicating by C_t after time 't.' C₀ indicate the dye's initial concentration, and "t" indicate for time.

Characterization

The structural features of ZnFe₂O₄ and ZnFe₂O₄ samples doped with Sm were analyzed through X-Ray Diffraction employing CuKα (λ = 1.54056 Å). The scanning angle ranged 20° to 80° (2θ), and the scanning rate was set at 2°/min. The structure of the creating samples was examined using a scanning electron microscope to analyze their morphology. The absorption bands were identified and checked using a FTIR spectrometer. Optical measurements in the wavelength (λ) range of 200-800 nm were conducted using a UV-Visible spectrometer (Singh et al., 2020).

Results and Discussion

XRD Analysis

XRD analysis was used to estimate the phase and fundamenta information of synthesized Sm doped ZnFe₂O₄ with g-C₃N₄ nanocomposites. XRD widely used method to investigate structural properties as well as crystal solid sample's lattice parameters in powder form. The XRD results were taken with CuKα radiations with a 1.54056 wavelength at room temperature and angles ranging from 20° to 80°. Fig. shows the pattern of XRD of Sm -doped ZnFe₂O₄ with g-C₃N₄ with different concentrations of g-C₃N₄. In XRD spectra the Diffraction peaks were seen at 2θ = 29.69°, 35.88°, 43.19°, 53.3°, 57.25°, 62.91° where were indexed to (220), (311), (400), (422), (511), (440) crystal planes of Sm doped ZnFe₂O₄ with g-C₃N₄ with the JCPDS card data 89-1012, which showed the cubic structure respectively shown in Figure 2. The Sm doped ZnFe₂O₄ with g-C₃N₄ structure was successfully obtained, as demonstrated by the strong interaction between g-C₃N₄ and ZnFe₂O₄. As the mass percentage of g-C₃N₄ increased, g-C₃N₄ diffraction peaks gradually increased (Bai et al., 2018). Doping with Sm ions indicate in a decrease of the crystallite size. The large surface area will be enhanced by the reduction in size. The crystallite size was calculated 30 nm, 26 nm and 24 nm. The crystallite size of a Sm doped ZnFe₂O₄ with g-C₃N₄ composite was estimated using the Debye-Scherrer equation (Karthik et al., 2017).

$$D = \frac{k\lambda}{\beta \cos \theta} \quad 2)$$

The variables in this equation are the average size of crystallites (D), (FWHM) in radians (β), the angle of diffraction (θ), or Bragg's angle (measured from the 2θ scale), and a constant of proportionality called Scherer's constant that is shape-dependent and size distribution of the crystallite structure. In most cases, this constant is taken to be k = 0.9.

SEM-EDX Analysis

The SEM images show Sm³⁺ morphology for zinc ferrite with g-C₃N₄ having some agglomeration with uniform distribution of particles; nonmetal (samarium) doping in the zinc ferrite lattice resulted in The SEM images demonstrate Sm³⁺ morphology for zinc ferrite with g-C₃N₄ having some clustering with uniform particle distribution; nonmetal (samarium) doping in the zinc ferrite lattice led to enhanced particle aggregation, possibly because of a decrease in surface area caused by the formation of interstitial spaces from samarium doping and with varying amounts of g-C₃N₄ enhanced aggregation of particles, which may be owing to an reduced in surface area as a result of formation of interstitial spaces due to doping of samarium and with different amount of g-C₃N₄. The average grain size of manufactured SZG1, SZG2, SZG3 nanocomposites was stimate to be 0.08 nm, 0.13 nm, 24.15 nm, as demonstrated by using Image j software. Using energy-dispersive spectroscopy, the element contained in the prepared Sm³⁺ doped ZnFe₂O₄ with g-C₃N₄ was examined. Zn, Fe, and O elements show that the composite was prepared. Certain impurities in the sample are revealed by a small amount of other elements (Karthik et al., 2017; Kannan et al., 2020).

FT-IR Analysis

For identifying functional groups in prepared nanomaterials FTIR is the most effective and dynamic method available. FTIR can be used to determine the bonding that is present in the material. The FTIR characteristic peaks of Samarium-doped zinc ferrite with g-C₃N₄ in the range of 400-5000 cm⁻¹ (Yang et al., 2014). The Fe-O and Zn-O vibrations in the Sm- ZnFe₂O₄ appear in the 400-600 cm⁻¹ range, confirming the ferrite structure, with potential peak shifts because of Sm doping. The triazine ring appears around 812 cm⁻¹ for the g-C₃N₄ component, while C-N and C=N stretching vibrations are detected between 1200-1600 cm⁻¹. Chemical bonding can be indicated by shifts in the C=N or Fe-O peaks caused by interactions between the two components.

4.5.2 UV-Visible Spectroscopy Analysis

The optical properties of semiconducting nanomaterials are investigated using UV-visible spectra. The optical bandgap (E_g) of a material can be computed using a Tauc plot. The band gap, absorption spectrum, and absorption edge for the synthesized Sm doped ZnFe₂O₄ with g-C₃N₄ (Manohar et al., 2021). It can be seen that the The absorption peak typically shifts towards a longer wavelength as the g-C₃N₄ concentration in the Sm doped ZnFe₂O₄ increase. The equation mentioned as was utilized to determine the optical band gap (Wang et al., 2019).

$$chv = A (hv - E_g)^n \quad 3)$$

The (α) absorption coefficient is estimated in cm^{-1} , while characteristic parameter represents (A). Planck's constant denotes (h), show frequency (ν), optical band gap energy represents (E_g) and A variable unique to the transition process is (n). The respective band gap values at different contents of $g\text{-C}_3\text{N}_4$ nanocomposites are determined as 1.41 eV, 1.32 eV and 1.24 eV respectively. It confirms that the hybrid ferrites nano-composite has superior visible light absorption capacity.

4.3 Dielectric Properties

Determining how the dielectric parameters of nanocomposites, specifically the tangent loss ($\tan \delta$) and dielectric constant (ϵ'), affect their electrical properties. The tangent loss evaluates the amount of energy lost as heat throughout an electric field's cycle, whereas the dielectric constant shows a material's ability to hold electric field-containing electrical energy. These parameters play a vital role in the field of nanocomposites (Koops, 1951). The increased capacity of nanocomposites with a higher dielectric constant to store electrical energy makes them advantageous for energy storage devices like capacitors. On the other hand, tangent loss values represent the amount of energy dissipated as well as the possibility of effective dielectric properties of heating. Increased $\tan \delta$ values indicate potential uses in fields such as microwave heating and flexible electronics development.

The ability of the material to retain electric polarization is indicated by the real part of dielectric permittivity (ϵ'), whereas the imaginary part (ϵ'') indicates its ability to dissipate power through electric loss. The formula is used to calculate ϵ (Ansari et al., 2018):

$$\epsilon' = \frac{ct}{A\epsilon_0} \quad 4)$$

Here, " c " and " t " indicates for the samples' capacitance and thickness, respectively, and " A " indicate for the pellet's surface area and the permittivity of free space, which has a value of $8.85 \times 10^{-12} \text{ m}^{-3} \text{ kg}^{-1} \text{ s}^4 \text{ A}^2$. The loss factor of a dielectric material, ϵ'' , is calculated by the equation: (Muhammad & Iqbal, 2016)

$$\epsilon'' = \tan \delta \times \epsilon' \quad 5)$$

Here, ϵ'' denotes the loss factor, while δ indicate the loss angle. The dielectric constant (ϵ') throughout all samples varies with applied frequency, Compared to the substituted samples, the pure sample ($x = 0.0$) notably shows a lower frequencies and a lower dielectric constant. Impact of various parameters on the degradation of RhB

Effect of pH

The ability of the photocatalyst to degrade RhB under sunlight is depends upon the pH level of the solution. The research was conducted to examine the impact of pH on the degradation of RhB. For this purpose at various pH ranges 2-10 the ability of the photocatalyst degradation of RhB checked. Diluted HCl or NaOH was used to change the pH of the solution. The highest photo degradation of RhB using of Sm doped ZnFe_2O_4 with $g\text{-C}_3\text{N}_4$ at different concentrations were attained at pH 9 and 8. It was found that more degradation was seen at a particular dye solution pH. Using of Sm doped ZnFe_2O_4 with $g\text{-C}_3\text{N}_4$ at different concentration composites the effectiveness of degradation of RhB was 98.3% at pH 8 in 70 minutes. At this pH, positive holes are important oxidising species, and the nanocomposite also functions as a photosensitizer. Hydroxyl radicals ($\text{OH}^\bullet$) can be produced by the photogenerated hole in the valence band of the nanocomposite due to its sufficient positive redox potential (Pattnaik et al., 2018).

Effect of Catalyst Concentration

The photocatalyst's quantity in the dye solution determines how effective it is for the degradation process. As the dosage of the catalyst was enhanced from 10 to 80 mg for 50ml dye solution at pH 8 and irradiated for 70 min, the percentage degradation of the Rh B dye was analyzed to enhance for all the catalysts. Maximum degradation of Sm doped ZnFe_2O_4 with $g\text{-C}_3\text{N}_4$ at different concentration was observed at 60 mg was enhanced from 72 to 98.3%. Increased active sites on the catalyst's surface are considered to be the cause of the increased degradation because they increase the formation of hydroxyl radicals, which further accelerates the degradation process. Additionally, it was noted that a continued rise in photocatalst dosage led to a decrease in degradation efficiency in all samples (Abdellah et al., 2018). The cause of this is that as the catalyst dose increases, the number of active sites enhanced so penetration of light slow due to shielding effect.

Effect of H_2O_2 Dose

Oxidants (H_2O_2) are essential in photo-degradation as they prevent the recombination of ($e^- - h^+$) pairs by capturing electrons. When a catalyst and an oxidant (H_2O_2) are present, Rhodamine B dye undergoes complete oxidation. To optimize the oxidant dose, the concentration of H_2O_2 was varied from 2 to 14 mM. The graph indicates that increasing the oxidant dose causes degradation to increase, but only to a certain point, after which it begins to decrease (Soleimani & Rahmani, 2022). In order to optimise H_2O_2 , the following experimental parameters were used: pH = 8 = 60 mg for Sm doped ZnFe_2O_4 with $g\text{-C}_3\text{N}_4$ at different concentration 10 ppm RhB dye concentration, and 70min irradiation time maximum degradation occurs which is 98.3%. The effects of varying H_2O_2 concentrations from 2 to 14 mM on RhB photo degradation (Kumar et al., 2009)

Effect of Irradiation Time

The effect of irradiation time on removal (%) at optimum conditions was analyzed and represented. In the early stages of irradiation, a pronounced rise was noted in the RhB degradation. With time, the rate of degradation slows down. The catalyst's active site needs a certain amount of time to completely degrade RhB. This is because $\text{OH}^\bullet$ radicals are produced influenced by the solution's pH, the degradation rate in removal processes gradually slows down. The catalyst's active site is inhibited by the reaction of hydroxyl ions with ferrous, which suppresses the Fenton-like reaction (Singh et al., 2020).

Reusability

It is vital to look into a photocatalyst's stability and reusability from an environmental and economic point of view. When the completion of the degradation reaction, the magnet was used to restore the composites, which were then cleaned three times in distilled water and oven-dried at 80 °C before being used again for a later cycle. Every composite undergoes a reusability study under the same ideal circumstances, i.e., pH 8, oxidant dose 10 mM, composite dosage 60 mg/50 mL for different concentration of Sm doped ZnFe₂O₄ with g-C₃N₄. With little loss in product yield, the photocatalyst can be reused up to five times while maintaining 85% photocatalytic activity (Kannan et al., 2020).

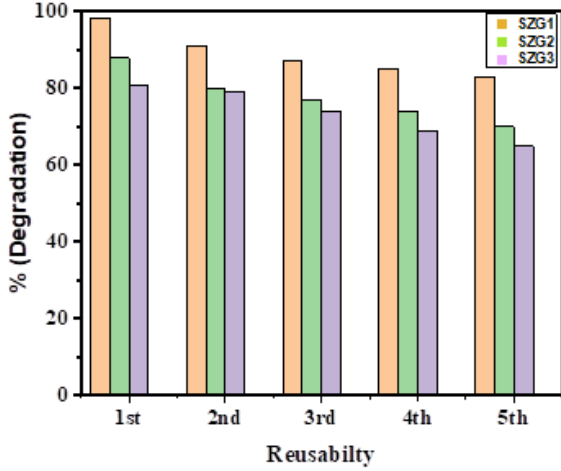
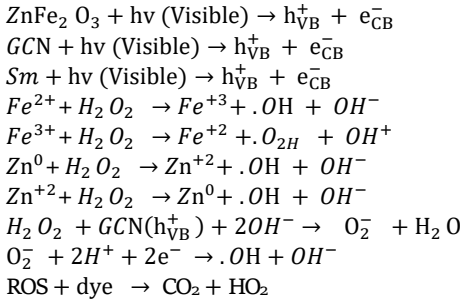


Fig. 2: Effects of Sm-ZnFe₂O₄/g-C₃N₄-X (X=0.2, 0.3, 0.4) Reusability on degradation efficiency



Photodegradation Mechanism

A photocatalytic mechanism is illustrated in Figure 3. Both Sm-ZnFe₂O₄ and g-C₃N₄ can be excited and generate light-induced e⁻ and h⁺ when exposed to visible light. The Sm-ZnFe₂O₄ valence band (VB) readily absorbs photo induced e⁻ in the g-C₃N₄ conduction band (CB). Consequently the O₂ anion reacts with H₂O₂ to generate the hydroxyl radical, which efficiently degrade the RhB dye. RhB degrades into CO₂, H₂O. Hence, it proposes the Sm doped ZnFe₂O₄ with g-C₃N₄ composite as a photocatalyst, possessing effective photocatalytic activity, prolonged charge carrier lifetime, and increased charge separation efficiency (Raza et al., 2020). Specifically, Sm can encourage the flow of electrons from ZnFe₂O₄ to g-C₃N₄ and suppress movement in reverse of electrons to ZnFe₂O₄. Consequently, photoactivity of Sm doped ZnFe₂O₄ with g-C₃N₄ was significantly improved. Some steps are involved in this process from eq (6-15) (Fatima, et al., 2024). In photocatalysis, materials absorb photons denoted as hν, where h is Planck's constant and ν is the frequency of light with energy equal to or greater than their bandgap. This absorption excites electrons from the valence band to the conduction band, generating electron-hole pairs. These pairs can migrate to the material's surface, where they participate in oxidation and reduction reactions, leading to the degradation of pollutants or other chemical transformations.

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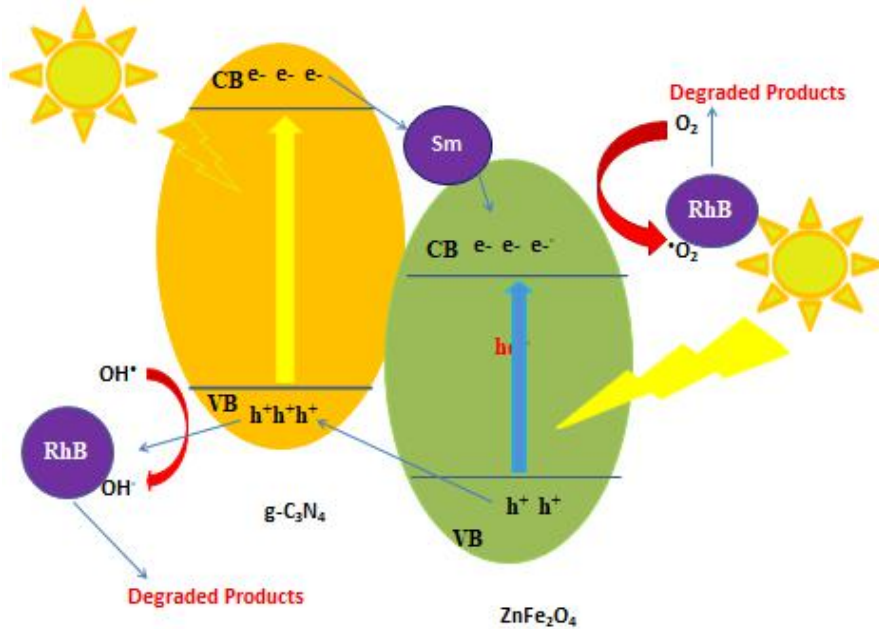


Fig. 3: Schematic diagram of photocatalytic activity

Conclusion

This study introduces the novel application of Sm doped ZnFe₂O₄ supported by g-C₃N₄ as an electron mediator for the first time. Sm doped ZnFe₂O₄ with g-C₃N₄ was found to be an effective photocatalyst. For the environmental degradation of dyes in solar light irradiation Sm doped ZnFe₂O₄ with g-C₃N₄ composite was fabricated successfully using a simple co-Precipitation strategy and was clearly defined by comprehensive analyses using UV-Vis spectroscopy, SEM-EDX, XRD, DIELECTRIC and FTIR techniques. Sm doped ZnFe₂O₄ with g-C₃N₄ (SZG3) composite exhibited 98.3% improved photodegradation of RhB in 70 min at ideal conditions such as pH (8), composite dosage (60 mg/50 mL) and H₂O₂ dosage (10 mM). Compared to SZG1, SZG2, the SZG3 composite demonstrated enhanced photocatalytic activity. Key attributes of the Sm doped ZnFe₂O₄ with g-C₃N₄ composite include its straightforward synthesis process, excellent photocatalytic capabilities, magnetic recoverability, and notable durability. This work proposes a novel approach to improving the photo efficiency and recyclability of g-C₃N₄ based photocatalysts through the Sm doped ZnFe₂O₄ with g-C₃N₄ composite.

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Nanobiotechnology: Revolutionizing Drug Delivery and Therapeutics

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Abstract

Drug Development and the transport of medicines have been drastically altered by the innovative field of nanobiotechnology. By merging biological disciplines with the fields of nanotechnology the investigators have invented new approaches to boost the potency and accuracy of medicinal properties medications. The fundamental issues related to standard drug distribution systems, like target less effects, accelerated metabolism, and inadequate solubility are studied by this technique. Miniaturized carriers, consisting of nano-sized particles, cascade molecules, and liposomes, can be used to accurately transport medicines to particular regions, decreasing harmful effects and optimizing the clinical results. The distinctive features of nanoparticles that allow for monitored discharge procedures and persistent medicinal effects are presented as well in this chapter. New discoveries have also contributed to the emergence of modified treatments, which improve therapeutic efficacy by boosting absorption by certain cells, particularly tumor cells by changing the outermost layers of nanocarriers. In general, the fields of nanotechnology possess the capacity to improve drug administration and rehabilitation, leading pathways for more productive and tailored therapy treatments in a number of medical disciplines.

Keywords: Drugs, Nanotechnology, Liposomes, Dendrimers, Nanocarriers, Nanoparticles

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Introduction

Nature is a constant source of inspiration for scientists. The vast bulk of Earth's biological processes operate at the nanoscale. A scientist can produce, characterize, and formulate nanoscale biological molecules and devices using biological systems by combining all of the biological principles with chemistry, physics, nanotechnology, and engineering concepts. Utilizing these findings, nanobiotechnology a new technology was created (Khan et al., 2015). Nanobiotechnology is the fusion of nanotechnology with biotechnology. It integrates molecular biology techniques with conventional microtechnology. It is expected that nanobiotechnology will lead to breakthroughs and be a key component of many biomedical applications, including medication delivery, gene therapy, biomarkers, molecular imaging, and biosensors. The primary focus of study where this technology may be crucial is targeted medication therapy and early pathology diagnosis techniques (Raju et al., 2023).

Pharmaceutical development will undoubtedly be the most important area in which clinical nanotechnology is used. Research on drug delivery is currently moving from the micro to the nanoscale. Applications of nanoparticle (NP) technology as medications or therapeutic ingredients include innovative methods for targeted delivery, controlled release, and improved bioavailability (Raju et al., 2023). Nanoscale-formulated polymer capsules offer the following benefits: high absorption, controlled drug release, degradation, and targeted site. Today, researchers worldwide are concentrating on creating novel polymers and analyzing certain polymer-drug combos. For example, straightforward nanodeposition of a completed polymer or the use of monomers have been used to create nanocapsules. Nowadays, liposomes and albumin are used to create nanocapsules. Nanospores will be used in the implantable drug delivery system to control the release profile of the medicament. Additionally, nanomaterials have several uses in the medical sciences, including nanomedicine, which modifies their physical traits and adds new ones (Umaphathi et al., 2021).

1. Historical Background

Another member of the fullerene family, hollow graphitic tubes or carbon nanotubes, were discovered by Iijima in 1991 using Transmission Electron Microscopy (TEM). When Xu et al., were purifying single-walled carbon nanotubes in 2004, they unintentionally found a new category of carbon based nanomaterials known as carbon dots (C-dots), which have a dimension of less than 10nm. Carbon-based materials formed the foundation of practically every scientific and technical discipline after the discovery of "graphene" in 2004 (Bayda et al., 2019). Meanwhile, nanoscience made strides in other scientific domains, such as computer science, biology, and engineering. In computer science, nanoscience and technology have advanced to reduce the dimension of a conventional computer from a room-sized device to incredibly effective portable

laptops. The fields of nanoscience and nanotechnology saw a surge in attention around the start of the twenty-first century. Feynman's idea that matter may be manipulated at the atomic level was crucial in determining national research goals in the US. The "scaffolded DNA origami" was developed in 2006 by Paul Rothemund, who used a "one-pot" process to make self-assembled DNA nanostructures larger and more intricate. In order to address upcoming nanotechnology difficulties, scientists from physics, chemistry, materials science, computer science, and medicine are already collaborating in the field of DNA nanotechnology (Kinnear et al., 2017).

The design and production of nanostructured materials with regulated forms and properties, such as gold and silver nanostructures for drug administration and biomedical imaging, was Younan Xia's area of expertise in 2010. Carbon nanotubes and graphene derivatives were the focus of Hongjie Dai's (2020) research on enhanced bioimaging and photothermal cancer treatments. For their work on quantum dots, Mouni G. Bawendi, Louis E. Brus, and Aleksey Yekimov were awarded the 2023 Nobel Prize in Chemistry. These nanoparticles, whose size determines their optical characteristics, are now essential in a variety of applications, from medical imaging, where they help illuminate biological tissues during surgery, to display technology (such as QLED screens). Utilizing nanotechnology has improved the environment and produced more economical and efficient energy (Sharma et al., 2020).

2. Importance in Modern Medicine

One of the most fascinating fields of scientific study is probably nanomedicine. Recent years have seen the completion of thousands of clinical trials and the filing of over 1500 patents pertaining to nanomedicine. Many research have shown the use of nanomedicine in the detection and treatment of cancer, some of which have not involved the use of medical devices. In this study, non-medical technologies have also been employed. Furthermore, the targeted delivery of medications to damaged cells, including cancer and tumor cells, is made possible by the use of a wide variety of nanoparticle forms without impairing cell function. The use of metal nanoparticles for diagnostic purposes has also advanced significantly. The wider usage of nanomedicine may potentially result from the use of other metals, such as gold and silver, in diagnostics and treatments. Although nanomedicine has a lot of potential advantages, its possible risks to people and the environment also need careful consideration. Therefore, it is necessary to conduct a thorough investigation into the acute and long-term harmful consequences of new nanomaterials on human populations and ecosystems. If the cost of nanomedicine dropped as its availability rose, significant scientific advancements would be made (Mout et al., 2012).

3. Fundamentals of Nanomaterials in Drug Delivery

Nanomaterials' unique composition, size, and shape define their physical and chemical characteristics. The size, structure, and other characteristics of nanomaterials also affect how they affect the environment and human health. The scientific community is presently discussing a rigorous definition of nanomaterials, and it is challenging to come up with a single, widely recognized definition for nanoparticles. "A synthetic or natural material containing loosely bound, assembled or dispersed particles with an external diameter between 1 and 100nm" is how the EU Commission defines a nanomaterial. The produced nanoparticles' optoelectronic and magnetic characteristics. For instance, color changes in the suspensions can be used to track the size of the particles and the addition of different synthetic materials to the cells. Different types of nanomaterials used in drug delivery shown in Figure 1 (Lv et al., 2022).

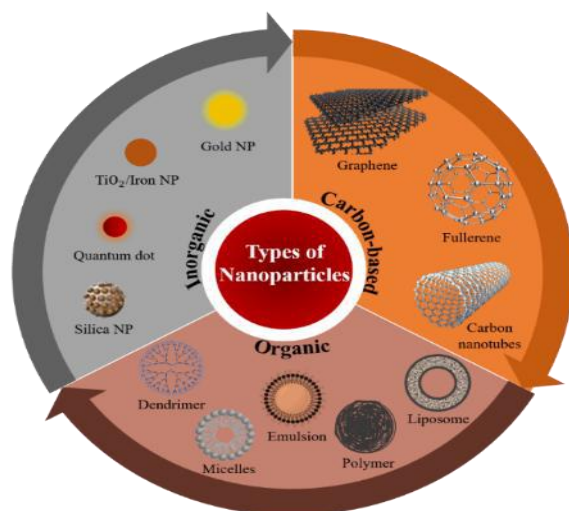


Fig. 1: Types of Nanoparticles.

4. Nanoparticles as Drug Carriers

i. Liposomes

The pharmaceutical industry makes extensive use of liposomes as medication carriers because of their remarkable biological flexibility and biocompatibility. Liposomes are spherical vesicles with an aqueous core encased in a lipid bilayer. These synthetic membranes work similarly to biological cell membranes and can be created from natural substances like phospholipids. Liposomes can incorporate lipophilic and amphiphilic medications into their phospholipid membrane or encapsulate hydrophilic chemicals in their watery core. Consequently, the safety and effectiveness of medication administration at the site of action can be enhanced by liposome compositions. Liposomes and nanomaterials have been employed for producing a number of chemotherapy drugs. They produce droplets in water that, after being integrated into their framework, permit chemotherapy drugs to degrade and remain steady. A couple of specific methods can be employed to efficiently generate liposomes. These approaches entail the removal of surfactants from phospholipid/detergent-micellar amalgams, the application of synthetic solvents, and physical methods (Chandrasekaran & King, 2014).

ii. Polymeric Nanoparticles

The bloodstream has to consume nanoparticles composed of polymers prior to their arrival at the desired level, which may be either normal or tumor tissue. The physical attributes and external characteristics of nanomaterials often impact their motion. The nanomaterials interfaces are covered with polymer compounds, particularly polymers with hydrophilic properties, to avoid phagocytosis. Such polymers often serve to encapsulate, covalently connect, and physically dissociate pharmaceuticals necessary for therapy of certain disorders or damages (Ai et al., 2022).

iii. Gold Nanoparticles

The intracellular devouring capacity of tiny gold atoms (GNPs) is at maximum in particles that are 20–50 nm in dimensions, with a size ranging from 2–100 nm. A distinct cellular damage has been observed for nanoparticles that are 40–50 nm in dimensions. GNPs are defined by their survival and simplicity of vascular transportation to the designated region, their adaptability in fabrication, capability to improve medicinal effectiveness, and their potential to be packed with medications. Additionally, they are harmless to cells that are viable. The utilization of modified GNPs has grown as a consequence of their advantages, which includes everything from the production of photonic devices to the detection of organic and biomolecules to charge storage systems (Sztandera et al., 2018).

iv. Synthesis of GNPs

Many technologies, such as chemical and physical approaches, can be used to manufacture GNPs as presented in Figure 2.

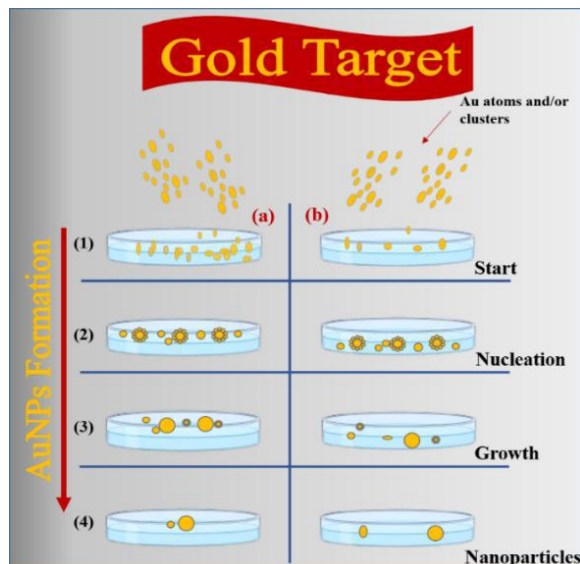


Fig. 2: Steps Showing the Synthesis of GNPs. (1) Self-assembly or a bottom-up strategy (2) The period of nucleation to create a new structure through self-assembly (3) The growth phase, during which surface development takes place (4) GNP Synthesis.

v. Silver NPs

Prior to the advent of nanotechnology, silver was considered merely a metal. It was later discovered that nanoscale production was possible. Modern engineering methods for metallic silver produced ultrafine particles in the nanometer (nm) range with unique shapes and characteristics. SNPs' antifungal, antibacterial, anti-inflammatory, antiviral, and osteoinductive qualities make them useful in the medical field. They have visual qualities, can be produced using a range of methods, and hasten the healing process of wounds. SNPs have a lot of promise for treating cancer. The anti-cancer effects of SNPs have been investigated on a variety of human cancer cell types, including breast cancer cells (Huy et al., 2020).

vi. Dendrimers

Inner and outer covering along with symmetric layer make up the precise structure of dendrimers, which are hyperbranched macromolecules with radial symmetry (Figure 5). These are the polyvalent, self-assembling nanoparticles that can change in size and shape, which makes them appropriate for use as agents for the delivery of drugs. A manganese-based polyester dendrimer nanoparticle (MHD) loaded with hypericin was recently developed to enhance hypericin-based photodynamic treatment (PDT) and MRI cancer detection (Porterfield et al., 2023).

5. Targeted Drug Delivery Using Nanotechnology

Therapeutic medications have become more successful as a result of recent advancements in the biomedical sciences. Among the issues with

conventional medications are non-selectivity, unfavorable side effects, inadequate efficacy, and unsuitable biodistribution. Thus, scientists are working to create highly regulated systems that can perform a variety of tasks. "Targeted delivery" is the term used when a medication is successfully delivered to a certain location and primarily accumulates there (Figure 3) (Yetisgin et al., 2020).

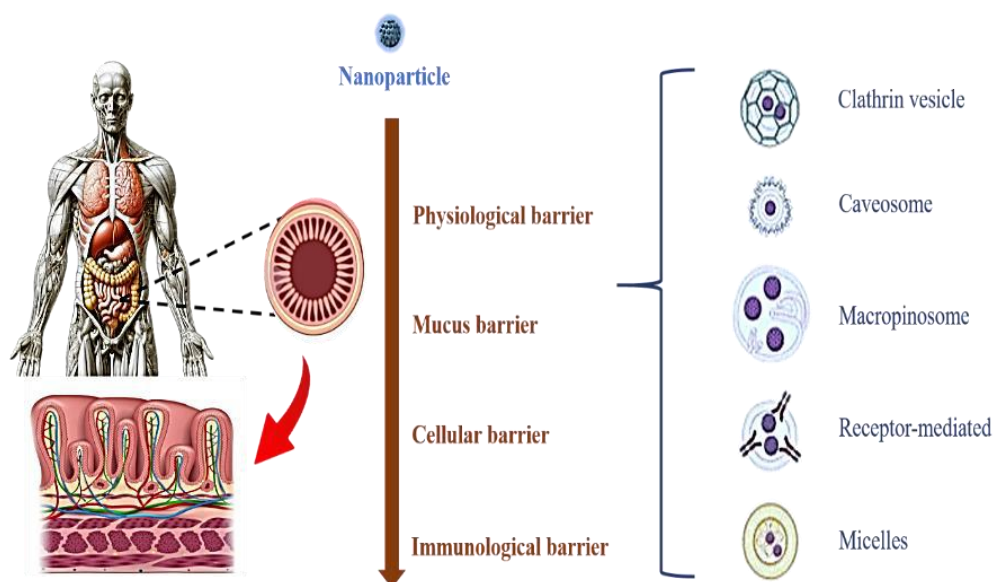


Fig. 3: Targeted Drug Delivery System.

6. Functionalization

The potential of drug distribution systems that use nanoparticle to precisely target cancerous cells while decreasing harmful impacts on normal tissue is an essential indicator of the potency of these treatments for intestinal cancer (CRC). A critical phase in attaining this specificity is the integration of nanomaterials with specific ligands. To enhance the curative effect and minimize systemic effects, investigators may boost the detection and attachment of nanoparticles to certain sensors overstated on CRC cells by conjugating different compounds, including immunoglobulins, amino acids, microbes, and aptamers to the microscopic particles covering (Krasteva & Georgieva, 2022).

a. Active Targeting

The intricate method known as "active targeting" includes embedding ligands onto nanostructures that preferentially bind to targets on colorectal cancer cell membranes. This tailoring technique promotes the intracellular administration of the medicinal product by improving receptor-driven endocytosis and augmenting amount of nanoparticle at the malignancy area (Hong et al., 2023).

b. Passive Targeting

Passive targeting is a further vital technique that utilizes the increased flexibility and absorption (EPR) effect. This process happens when solid tumors exhibit permeable capillaries and insufficient flow of lymph, resulting in the favored gathering of nanoparticles within cancer cells. This passive approach provides the optimum amount of tiny particles in the malignant the micro setting, enhancing the regional amount of the medicine and its therapeutic effect, despite the absence of certain ligand-receptor associations. Passive targeting is essential for delivering nanoparticles to solid tumors, such as colorectal cancer, despite being intrinsically less selective than active targeting (Jiang et al., 2023).

7. Nanoparticle-Mediated Overcoming Drug Resistance

A frequent occurrence in clinical cancer treatment is the emergence of medication resistance. For instance, MDR protein levels tend to rise in patients receiving traditional chemotherapeutic treatment, which lowers intracellular drug concentrations or inhibits drug activity before the medicines reach their intracellular targets (Figure 4) (Singh et al., 2017).

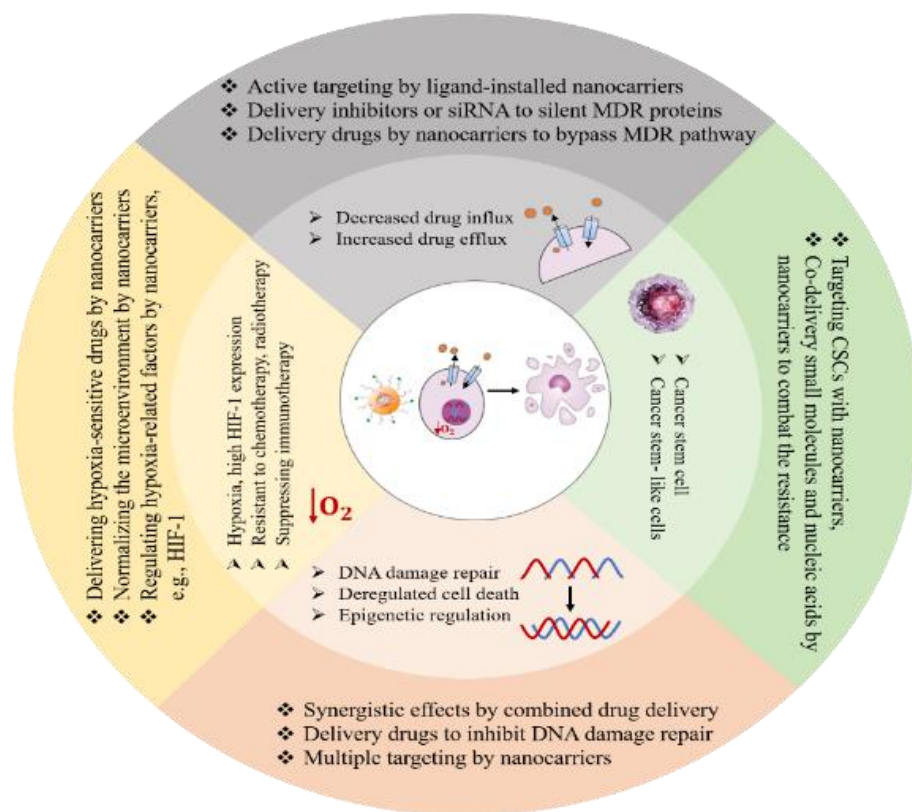


Fig. 4: Strategies of Applying Nanocarriers to Overcome Drug Resistance.

8. Photothermal and Photodynamic Therapy using Nps

The five main geometries of AuNPs at the preclinical or clinical research stage gold nanospheres, gold nanoshells (AuNSs), gold nanorods (AuNRs), gold nanostars, and gold nanocages (AuNCs) each have a unique red-shifted absorption peak. Usually produced within a certain size range, each individual shape of AuNPs exhibits distinctive features. Since AuNPs were first used as a straightforward carrier of the photosensitizer for PDT, the field has made significant progress, including the following: the development of nanorods and nanostars to enable combined PDT and photothermal therapies; the use of PEGylated modification to provide aqueous compatibility and stealth properties for in vivo use; the enhancement of singlet oxygen generation by gold metal surfaces; and the functionalization of the AuNP surface with biological ligands to specifically target over-expressed receptors on the surface of cancer cells (Liu et al., 2019).

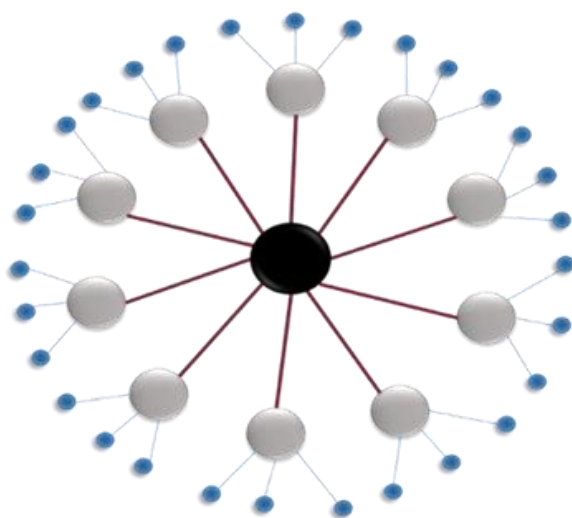


Fig. 5: Typical Structure of Dendrimer Nanomaterial Used for Cancer Immunotherapy.

9. Nanotechnology for Gene Therapy and Immunotherapy

Nanotechnology, a discipline of science and technology that revolves around small scales activities, has gained major international fascination in health care. Many investigations suggest that tiny particles can be relied on in addition to typical medical procedures for example radiotherapy and diagnostic techniques like magnetic resonance imaging (MRI) for diagnosing illnesses (e.g., photoacoustic imaging) and cure (e.g., photothermal radiation therapy [PTT] and magnetic hyperthermia) (Bai et al., 2023). Multiple networks, that involve microbes, dendrimers, nanostructures, micelles, polymeric combinations, and liposomes, have been widely studied for pharmaceutical and DNA delivery purposes. The beneficial effect of encased pharmaceuticals is considerably affected by the surface behavior of small systems, which are viewed as vital to their association with tissues and intracellular delivery mechanisms. The conjugation of paclitaxel-loaded nanoparticles to the transferrin (Tf) ligand, for instance, demonstrated increased efficacy in vitro in breast and prostate cancer cell lines (MCF-7 and PC 3), as well as in a mouse model of prostate cancer (Yan et al., 2019).

10. Nanotechnology in Cancer Immunotherapy

Traditional surgery, chemotherapy, and radiation therapy will no longer be the only options for treating cancer thanks to the emergence of immunotherapy. Immunotherapy for cancer has progressively shown therapeutic benefits with wide-ranging potential and useful applications. By boosting the host immune system or preventing tumor immune evasion, cancer immunotherapy generates a systemic, targeted, and long-lasting anticancer response (Matsueda & Garaham, 2014). Biodistribution and targeted medication delivery have benefited greatly from the use of nanoparticles (NPs) with high biocompatibility. Crucially, NPs coated with medications can increase their bioavailability and stability, shield them against deterioration, and extend their half-life (Manjili et al., 2018).

11. Nanoparticles in Gene Therapy

The prevention, detection, and treatment of deadly disease conditions, including genetic anomalies, have all advanced in the medical sector in the current era of biomedical technology. Nevertheless, not all medical diseases can be treated with pharmaceuticals, biologics, or peptide-based therapies (Poongavanam et al., 2024). The perfect platform for combining all the desired features into a single gene delivery device is provided by nanoparticles (NPs). NPs can carry genes to specific cells or tissues, maintain the effects of genes in the target tissue, and increase the stability of therapeutic medicines against enzymatic breakdown (nucleases). One of the most often researched materials for medication and gene delivery via nanocarriers is polymers. This is because of a variety of intrinsic qualities that have been advantageous for PNP design, including the adaptability of structural conformations, biodegradability, and simplicity of synthesis. Optimal gene administration in the definite tissues and low hindrance of the transporting carrier in the body to reduce harmful effects are the two main aspects that are concurrently sought by the majority of emerging methods in polymeric gene delivery. This function is effectively carried out by natural or synthetic biodegradable polymers with a variety of functionalization patterns (Rai et al., 2019).

12. Chitosan Based Nanoparticles

Because of their ability to regulate the release of proteins, peptide drugs, antibiotics, DNA, and vaccines, polysaccharides and other cationic polymers have recently found widespread use in pharmaceutical research and industry as illustrated in Figure 6. They have also been thoroughly investigated as nonviral DNA carriers for gene delivery and therapy. Since it can encourage the long-term release of integrated medications, chitosan is the most often used of them (Jayakumar et al., 2010).

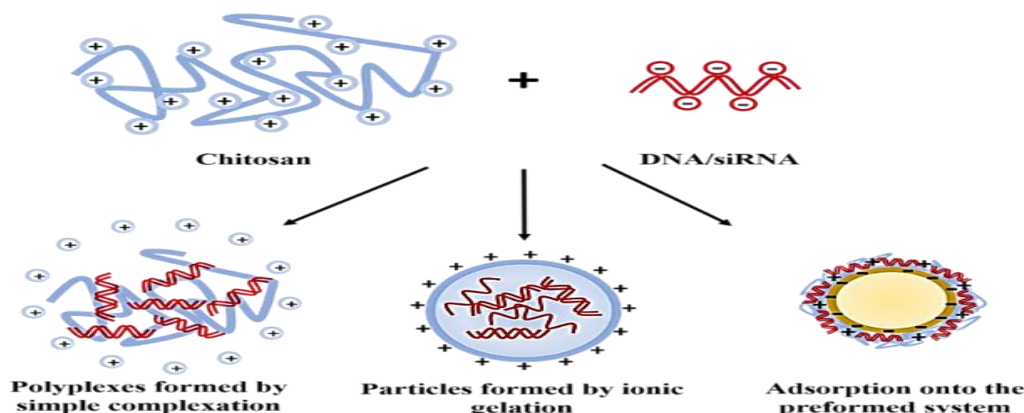


Fig. 6: Synthesis of Chitosan-Based Nanoparticles (DNA/siRNA) By Adapting Various Approaches.

13. Nanovaccines and Immunomodulation

Over the past ten years, the application of nanotechnology in particular to vaccination has grown rapidly, giving rise to the field known as "nanovaccinology." (Mamo & Poland, 2012). Nanoparticles are employed as an immunostimulant adjuvant to activate or improve immunity or as a delivery route to improve antigen processing in both preventative and therapeutic approaches. The primary use of therapeutic nanovaccinology is in the treatment of cancer (Bolhassani et al., 2011). It is being investigated more and more to cure various illnesses or ailments, such as nicotine addiction, hypertension, and Alzheimer's. Conversely, prophylactic nanovaccinology has been used to prevent a variety of illnesses. Numerous preventative nanovaccines have received approval for use in humans, and further ones are undergoing preclinical or clinical testing (Roldao et al., 2010).

It has been demonstrated that immunomodulators alter the immune system's reaction to a danger. Your immune system is kept in a highly prepared state for whatever threat it may face by their modulation and potentiation of its weaponry. All ensuing immunological reactions get better as a result of this balancing effect. The invading organisms do not have time to gather power and force when your immune system is in this highly prepared state; instead, the immune system assaults, eliminates, and/or weakens the invader. Immunomodulation is the process of either favorably or adversely modifying an immune response by giving a drug or chemical. Proteins, amino acids, and natural chemicals including hormones, DMG, and interferon- γ (IFN- γ) have all shown a great ability to regulate immune responses. Both the adaptive and innate arms of the immune response can be stimulated, suppressed, or modulated by these biological or synthetic agents (Kushwaha, 2012).

14. Self-Assembly and Self-Healing Nanocarriers

The use of different nanocarriers, such as dendrimers, carbon tubes, lipid-based carriers, polymeric nanoparticles, and gold nanoparticles, can increase the treatment's efficacy. Employing such carrier systems depends on the bioactive substances' characteristics (charge, size, solubility, etc.), the bioactive-carrier complex's effectiveness and safety, as well as how the complexes are applied and administered to the systemic circulation (Paul et al., 2022). Therapeutic medications can be encapsulated, surface adsorbent, surface attached, or entrapped into nanoparticles to be transported and supplied to specific locations, creating nanocarriers. Depending on the kind of nanoparticle, these medications could then be released in response to internal or external stimuli. High surface area-to-volume ratios and nanoscale dimensions promise quicker medication release and more effective drug uptake by tumor cells (Liao et al., 2020).

15. Applications of Nanobiotechnology in Drug Delivery

Nanotechnology has greatly impacted drug distribution, supplying cutting-edge remedies for numerous difficulties related to typical drug distribution. A variety of nanocarriers, like cascade molecule, liposomes, microscopic particles, and micro gels, have proved substantial potential for boosting the potency, security, and accuracy of medications. To decrease adverse effects and boost medical results, these small carriers promote directed administration to certain tissues or cells, controlled dissolution of drugs, and securing medicinal products from deterioration as presented in Figure 7. Nanobiotechnology has permitted effective administration of medicinal products, including medications, growth regulators, and genetic material, to facilitate the cure of malignancy, bacterial infections, or wound healing through the application of tiny particles, micro topological frameworks, crystalline frameworks, tiny carriers, or an array of such techniques (Fauzian et al., 2023).

A nanobiotechnology-based microscopic modifying method has revealed that the physical and chemical features of transporting substances can be regulated at the microscopic level. This facilitates the transportation and differentiation of carrier molecules, along with the regulated, stimulated, and efficient distribution of bioactive compounds. By topping, encasing, or modifying nanocarriers, their attributes and features can be changed, modified, customized, and improved, hence multiplying their ability and performance. The primary emphasis must be on the investigation and creation of revolutionary techniques, tactics, nano-biomaterials, and technology. Modern polymer-based nanomaterials and tiny carrier particles, along with a limited array of inorganic nanotechnology, offer structural diversity, biodegradable properties, accessibility, and biological suitability. These smaller structures can be extensively developed and manufactured using multiple nanobiotechnological procedures and practices (Dutt et al., 2023).

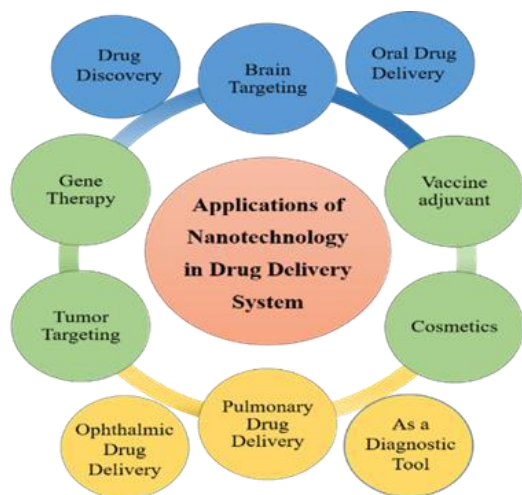


Fig. 7: Different Applications of Nanotechnology.

Conclusion

In summary, nanotechnology is changing the administration of drugs and remedies by offering determined, productive, and legally protected treatment possibilities. To provide pharmaceuticals immediately to cells with infections while minimizing unwanted effects and maximizing performance, researchers have developed novel pharmaceutical carriers employing nanoscale compounds. The combined use of nanotechnology and medical equipment for diagnosis has resulted in improvements in individual healthcare. Consequently, therapies can be adapted to specific patient histories according to the distinctive features of the ailments, significantly enhancing their efficacy. The course of therapy of malignancy, long-term illnesses, and alternative therapies has substantial implications. Administrative challenges and in actual toxicity problems are significant impediments; yet, multidisciplinary teamwork and creativity tend to generate innovative study prospects. Finally, nanotechnology is at the cutting edge of a biomedical transformation that could significantly influence healthcare for patients and enhance global quality of life. Realizing its complete ability necessitates additional investigations and financial support.

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Nanobiotechnology in Regenerative Medicine and Stem Cell Therapy

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Abstract

Nanobiotechnology has transformed regenerative medicine and stem cell therapy by applying nanotechnology to biological systems to improve tissue repair and organ regeneration alongside targeted therapeutic delivery. The unique physicochemical properties of nanomaterials enable effective scaffold creation while facilitating both cell adherence and proliferation which proves essential for tissue engineering. PLGA and PEG represent examples of biodegradable polymeric scaffolds that offer both structural and biochemical support that emulates natural tissue environments. Nanoparticles such as AuNPs and AgNPs deliver controlled drug delivery and function as bioactive cue modulators with antimicrobial protection to produce superior regenerative results. Nanobiotechnology improves stem cell therapy by creating superior cell viability and targeted differentiation while enabling in vivo tracking through SPIONs advanced imaging agents. Nanomaterials contribute to genetic engineering approaches led by CRISPR/Cas9 to maximize effectiveness in stem cell treatments. Current obstacles still exist because they include regulatory challenges and both cytotoxicity concerns and difficulties with scaling up processes for medical applications. Upcoming studies will concentrate on developing better biomaterial surfaces while designing nanomedicines and improving stem cell interaction performance with nanoparticles to enhance therapeutic results.

Keywords: Nanobiotechnology, Nanoparticle, Tissue engineering, Stem cell therapy

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Introduction

Nanotechnology allows the manipulation of materials on the nanoscale, which ranges from 1 to 100 nm, and gives nanomaterials enhanced mechanical, chemical, and biological properties, making them a choice for the regenerative field (Nurbaeva et al., 2024)). Researchers controlled the assembly and functionalization of these materials to produce biomaterials that mimic the natural structure of tissue, essential in tissue engineering (Asghari et al., 2017). Nanobiotechnology is a central aspect of regenerative medicine; it can aid in the development of scaffolding, support tissues, and promote cell adhesion, differentiation, and proliferation (Babu et al., 2024).

The objective of this chapter is to evaluate how tiny technological tools, particularly nano-sized particles, contribute to the improvement of tissue healing and stem cell treatments. It aims to explore the mechanisms through which these nanoparticles aid in repairing damaged tissues and facilitating targeted drug delivery. Furthermore, the chapter investigates how these nano-tools interact with stem cells to enhance therapeutic outcomes and supports advancements in diagnostic and therapeutic approaches for conditions like skin cancer, especially melanoma. Additionally, in this chapter we will address the existing challenges within this emerging field and propose future directions to translate these scientific advancements into practical clinical applications.

Nano Scaffolds and Nanoparticle

The scaffolds, constructed from biodegradable polymers such as PLGA and PEG, can provide a framework for tissue regeneration by allowing cells to grow and function in a microenvironment that closely mimics natural tissues (Chowdhury et al., 2021). These materials could be designed to adjust following the specific needs of the target tissue, providing both the needed physical structure as well as the biochemical signals in regeneration (Becker et al., 2024). Besides this, nanoparticles have greatly contributed to the drug delivery system for regenerative medicine, serving as a mechanism for controlled release that improves the outcomes of therapy (Veronica, Agrawal, Gopenath, Basalingappa, & Gobianand, 2025). For example, metallic nanoparticles such as gold (AuNPs) and silver (AgNPs) have been proven to exhibit antimicrobial activity and, therefore, are very efficient in preventing infection during tissue regeneration and wound

healing (Babu et al., 2024; Chittipolu, 2025).

Additionally, nanoparticles can be engineered to boost the biological functionalities of stem cells, which is the central component of regenerative medicine (Trayford, 2025). Such cells have the extraordinary capability of transforming into different cell types that are essential for tissue regeneration (Herawati, 2025). Nanobiotechnology enhances stem cell therapies by promoting the survival of cells, enhancing the process of differentiation, and promoting the movement of stem cells to the appropriate injury site (Chowdhury et al., 2021). This is achieved by using nanoparticle-based drug delivery systems that offer bioactive cues leading stem cells to the damaged tissue, which induce them to proliferate (Asghari et al., 2017). Furthermore, SPIONs are also on their way to being used in regenerative medicine, where stem cells can be tracked in real time. By attaching these nanoparticles to stem cells, researchers can monitor the behavior, migration, and survival of the cells after transplantation, thereby providing valuable data to optimize therapies (Becker et al., 2024). This in-vivo tracking allows for the precise assessment of stem cell function and ensures that stem cells are performing as expected during tissue repair (Glover et al., 2020; Zhang et al., 2018). As shown in figure 1, there are various applications of nanobiotechnology in regenerative medicine ((Haleem et al., 2023).

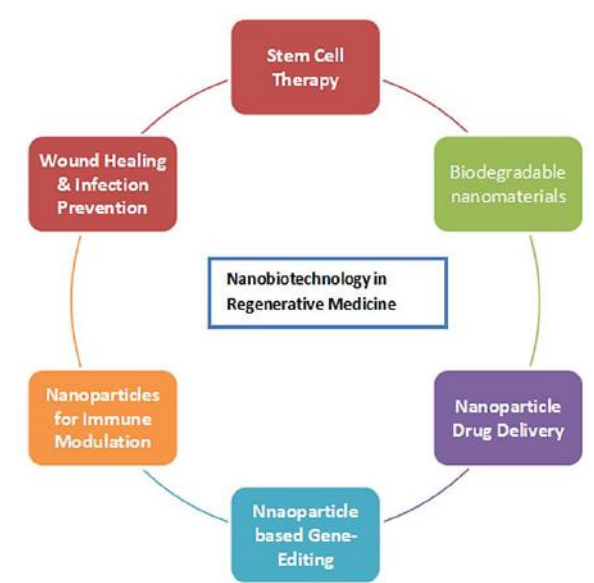


Fig. 1: Overview of nanobiotechnology applications in regenerative medicine, including stem cell therapy, wound healing, immune modulation, biodegradable nanomaterials, nanoparticle drug delivery, and gene editing (Haleem et al., 2023).

to play an increasingly important role in regenerative medicine. Improved properties of biomaterials, better stem cell therapies, and effective drug delivery systems will bring a great revolution in tissue regeneration. Although toxicity, regulatory approval, and clinical translation remain to be accomplished, much success with the future of regenerative medicine is still in sight with further advances in personalized nanomedicines and genetic engineering (Asghari et al., 2017; Rajkumar et al., 2024).

Role of Nanoparticles in Stem Cell Therapy

Nanoparticles (NPs) play crucial roles in the regulation of stem cell behavior because of their unique features, including size, shape, surface area, and surface charge. NPs facilitate stem cell therapy through gene delivery. The survival rate of patients suffering from different diseases has improved through surgical procedures and pharmacological treatments but these methods have limited efficacy (Sun et al., 2020). Hence, there is a dire need for regenerative medicine involving stem cells. For therapeutic purposes, stem cell therapy has unprecedented advantages over gene therapy.

Delivery Systems for Therapeutic Agents

Nanoparticle-based delivery systems change the distribution of therapeutic agents such as drugs via target-oriented, site-specific delivery and controlled release of drugs (Table 1) (Yang et al., 2022).

Table 1: Nano delivery systems and their features (Aswini et al., 2024)

Nano delivery systems	Features
Liposomes	Spherical structures, made of the lipid bilayer, carry both hydrophilic and hydrophobic molecules, and target delivery for therapeutic outcomes.
Mesoporous silica nanoparticles (MSNPs)	Silica-based particles, with porous structures, hold an enormous number of therapeutic agents, and prolonged therapeutic effects.
Gold nanoparticles (AuNPs)	Capabilities of surface modification, unmatched precision, and efficacy, and accurate prognosis.
Magnetic nanoparticles (MNP)	Precise control over stem cell localization, monitoring stem cell responses in real-time, least toxicity, and immune reactions.
Carbon nanotubes (CNTs)	Cylindrical nanostructures offer tailored treatment strategies and enhanced regenerative potential.

Challenges and Future Directions in Nanobiotechnology for Regenerative Medicine

Besides the therapeutic role of nanoparticles, these also decrease risks associated with stem cell therapy like oxidative stress and immune rejection (Aswini et al., 2024). Nanoparticles protect the cells from damaging environmental conditions as they provide a coating that guards the cells against harmful action that might lead to damage to them, hence increasing their efficacy as therapeutic agents. Another very important issue is the regulatory approval of nanobiotechnology-based therapeutics (Bruun et al., 2018). The regulatory agencies, including the FDA, are advancing further with the establishment of clear guidelines on the application of nanoparticles in hospitals. Therefore, it is important that nanobiotechnology therapeutics need to be active and nontoxic to apply to humans (Jain et al., 2025). Growing nanobiotechnology calls for well-defined and standardized testing and approval protocols for these innovative therapeutic approaches (Chaudhury et al., 2014; Glover et al., 2020).

Nanobiotechnology and genetic engineering combined, for instance, gene editing with CRISPR/Cas9, and open new avenues in stem cell therapies. For instance, IONPs can enhance the expression of survival and differentiation genes in stem cells, leading to better outcomes for regenerative therapies (Li et al., 2021). This interplay between nanobiotechnology and genetic engineering will likely be at the forefront of future stem cell therapies and other regenerative treatments (Jain et al., 2025). In the future, nanobiotechnology is bound

Mechanism of Action

Liposomes

Targeted nanoliposomes are used for breast cancer treatment. Their surface is functionalized with targeting agents such as small molecules, peptides, and aptamers which use passive or active targeting in which they can bind either within breast cancer-associated cells or directly to target.

In liposomal drug delivery, cell surface receptors are targeted such as CXCR4 which controls the movement of cells and cancer metastasis after binding to GPCRs (Oshiro et al., 2020). A ligand molecule CXCL12 is a chemoattractant, when a tissue has a high concentration of this molecule, tumor cells with the CXCR4 receptor are drawn to the location. In metastasized breast cancer, encapsulation of pH-responsive liposomes (CXCR4 targeted) is done with Lcn2 siRNA, where Lcn2 protein is silenced to inhibit migration of cells (Nel et al., 2023).

Chitosan Nanoparticles

These are polymeric nanoparticles that have the potential for drug delivery. These nanocarriers are used to treat Parkinson's disease. In a study, Rotigotine, a drug was loaded on chitosan NPs in human neuroblastoma cells SH-SY5Y and delivered through an intranasal route in a rat model (Afzal et al., 2022). These nanostructured lipid carriers allow the drug to go across the blood-brain barrier (BBB). When they reach BBB, stimulus from components on the surface of nanoparticles causes BBB opening resulting in promoting drug conjugates' diffusion into brain tissue. After adsorption on the cell surface, the drug is released from carriers causing an increase in the concentration gradient of the drug thus promoting diffusion of substances into the brain. Capillary endothelial cells of the brain via endocytosis and exocytosis allow penetration of substances into brain tissue (Zorkina et al., 2020). As shown in figure 2, there are multiple steps of how nanoparticles function for therapeutic purposes (Sultana et al., 2022).



Fig. 2: Flowsheet showing the mechanism of action of Nano-based delivery systems for therapeutic agents (Sultana et al., 2022)

shows that if reduced concentrations of graphene are used in gold nanoparticles in PLC (polycaprolactone) fiber scaffolds, they mimic natural ECM which increases the stimulation of cell differentiation (Jaswal et al., 2020).

Substrate Stiffness

Cells respond to external stimuli through mechanotransduction where physical signals are transduced to chemical ones resulting in cell differentiation to specific lineages (Sun et al., 2022).

Through cytoskeletal contractility, cells sense the hardness of ECM, and its high stiffness leads to BMSCs' differentiation into sweat cells (Wei et al., 2021). Osteogenic differentiation of MSCs is promoted by a harder alginate shell while the softer hydrogel directs differentiation of vascular progenitor cells to endothelial cells.

Shear Stress

The fluid flow in the tissues causes sheer stress to all types of cells. Shear stress can promote the osteogenesis of MSCs. The fate of BMSC differentiation to the osteogenic or chondrogenic cell is also influenced by the rate of fluid sheer stress. Differentiation of BMSCs to myofibroblasts is promoted by shear-stressed groove structures. As illustrated in figure 3, stem cell behaviour is influenced by diverse elements (Wang et al., 2022).

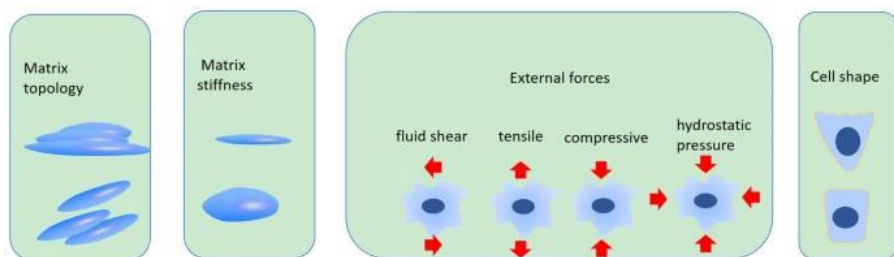


Fig. 3: Various factors that modulate stem cell behavior (Wang et al., 2022)

Types of Nanoparticles

As depicted in figure 4, nanoparticles are classified based on their origin (Khan et al., 2022).

Organic nanoparticles can be made of natural compounds such as proteins, lipids, peptides, or synthetic molecules. Among organic nanoparticles, the most common are polymeric NPs (mostly used in cancer research), liposomes, and dendrimers. Based on origin, they can be natural such as chitosan, or synthetic as synthetic polymer-based nanoparticles (SP-NPs). SP-NPs can be classified into polyesters such as poly (lactic acid) (PLA), poly (glycolic acid) (PGA), poly (caprolactone) (PCL) and polyethers such as poly (ethylene glycol) (PEG) (Ruiz et al., 2020).

Natural Nanoparticles

These include lipid-based nanoparticles such as liposomes, and solid lipid nanoparticles. They offer various advantages in terms of loading efficacy, stability, and cellular uptake (Beydar et al., 2024). Polysaccharide-based nanoparticles include chitosan nanoparticles and alginate-based nanoparticles. Natural polyelectrolyte nanoparticles such as chitosan (cationic) and alginate (anionic). Chitosan has mucoadhesive properties as it can electrostatically interact with negatively charged mucosal surfaces and enable better absorption of drugs into the intestine (De Anda et al., 2021).

Synthetic Nanoparticles

These include polymeric nanoparticles composed of synthetic or natural polymers such as PEG, and PLGA. They precisely target specific sites by navigating biological barriers (Beach et al., 2024).

Metallic nanoparticles such as gold nanoparticles, and iron oxide nanoparticles such as superparamagnetic iron oxide nanoparticles (SPIONs). They have large surface area and optical properties, minimal toxicity showing their potential in angiogenic and tumor therapy (Figure 4) (Abdelkawi et al., 2023).

Role of Nanotechnology in Skin Cancer Treatment

Melanoma (skin cancer) is considered a fatal disease worldwide. Skin is formed of two layers; mainly the epidermis and dermis (Hasan et al., 2023; Kumari et al., 2022). The epidermis is the outermost covering that serves as protection. Any change within this specific layer of skin may cause harmful effects leading to the formation of skin cancer (Jain et al., 2022; Urban et al., 2021; Zeng et al., 2023). In the past few years, the mortality rate of melanoma has increased significantly. It has been reported that the occurrence of melanoma is five-fold increased for fifty years in brown people (Saginala et al., 2021). There are two kinds of melanoma non-melanoma skin cancer (NMSC) and melanoma skin cancer (MSC). According to research, MSC is causing a high rate of mortality (American Cancer Society, 2019; Global Cancer Statistics 2018).

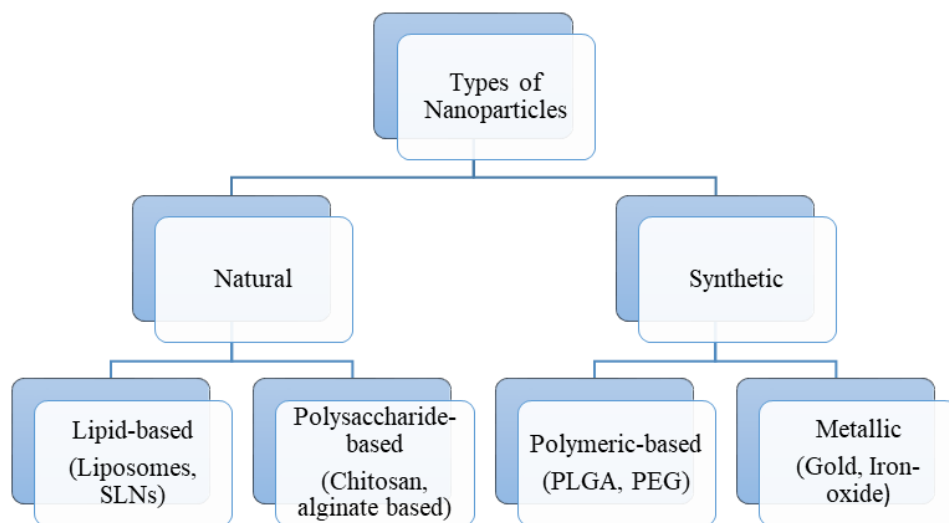


Fig. 4: Types of nanoparticles (Khan et al., 2022)

Melanoma Study in the United States of America (USA)

By the end of 2020, data collected from the global cancer burden (GLOBCAN) revealed an incredible increase in the number of deaths up to 19.3 million, and the mortality rate was found to be 10 million. The type of population and region played a major contributing factor in cancer as per GLOBCAN data (Sung et al., 2020). Non-melanoma was one of the most aggressive types of skin cancer globally found in 1,198,073 patients out of which 722,344 were men and 475,725 were women was 6.2%. Apart from melanoma, other kinds of skin cancers were 63,731 (0.6%). According to a case study carried out in the USA (2024), 150,791 women and 173,844 men were diagnosed with melanoma. It caused a huge number of deaths exceeding 57 thousand organisms (Wild et al., 2020).

Nanotechnology in Diagnosing and Treating Skin Cancer

In recent studies carried out in vitro and in vivo, nanotechnology has been found an appropriate method of treating skin cancer. Nanocarriers and nanomaterials are involved in the development of drug delivery systems causing low side effects because of their large surface and small size characteristics. Antitumor drugs are administered in nanoparticles that pass through cell membranes easily and hit the target cells particularly skin cells showing their maximum effect (Battaglia et al., 2021). The side effects of chemotherapy were reduced owing to the

increased activity of anticancer drugs and it played a great role in improving the health of cancer patients. Some other nanoparticles like liposomes, nano micelles, carbon nanotubes, nanoemulsions, and metal nanoparticles are also effective for diagnosing and treatment of skin cancer. These nanoparticles target tumor cells and increase the drug delivery system thus recovering the melanoma (Mir et al., 2022)

Lipid-Based Nanoparticles in Skin Cancer

Drug efficacy has been increased due to lipid formulations that deliver drugs to target cells and organelles thus reducing side effects. Lipid particles are spherical in shape and can dissolve and transport drugs effectively. They include liposomes, ethosomes, niosomes, and solid lipid nanoparticles having distinct characteristics and future implications (Pachauri et al., 2023)

Liposomes

Liposomes are composed of a lipid bilayer having a central space consisting of a transported drug or any other bioactive compound. The use of liposomes has greatly reduced the barriers observed in the administration of chemotherapeutic agents in chemotherapy. Many techniques have been adopted for employing liposomes in curing skin cancer. It includes the use of chemotherapeutic agents, natural polyphenols, and the use of siRNAs in gene therapies to formulate the expression of particular genes of skin cancer (Sing et al., 2023).

In the cell culture of human skin carcinoma A431, chemotherapeutic agents' activity was enhanced by the coating of DOX celecoxib. Liposomes loaded with drugs were efficient in lessening the viability of cancer cells by 99% (Cruz et al., 2022).

Another strategy is found where the surface of liposomes can be modified by binding numerous ligands to it like glycoproteins, immunoglobulin, peptides, transferrin, etc thus targeting the receptors in cancer cells. Moreover, liposomes can be used in making vaccines for curing skin cancer (melanoma).

Therapeutic use of Magnetic Nanoparticles (MNPs)

Recently, there has been a lot of interest in the therapeutic use of magnetic nanoparticles (MNPs). Early in the 20th century, Pierre-Ernest Weiss presented the fundamental theory of magnetic particles. Three important components usually make therapeutic MNPs: a coating part that enhances interactions, especially in iron oxide NPs, a magnetite core that serves as a carrier for therapies, and medicines that carry out tasks in vivo. It might have ligands that help to identify particular receptors on the outside of cancer cells. It is important to note that in recent decades, MNPs have been used more frequently to treat cancer (Barani et al., 2023). The advancement of nanotechnology has made it feasible to combine the special qualities and traits of MNPs with those of cancer treatments. MNPs are useful for identifying, diagnosing, and curing malignant tumors. The goal of creating low-toxicity superparamagnetic MNPs for biomedical devices is to reduce complications like embolization or negative cellular or molecular impacts (Bushra et al., 2024).

Conventional hyperthermia has little specificity, because of tissue nonselective heating, and it affects both tumor and healthy cells. By generating local heat and distributing heat around or inside tumor locations, NP-induced hyperthermia can get beyond these barriers. Importantly, a technique known as MNP-based hyperthermia employs MNPs to produce heat in the tumor area when exposed to an alternating magnetic field (AMF) with a frequency range of 100 kHz. The AMF facilitates the transformation of magnetic energy to thermal energy by producing electromagnetic radiation which is absorbed by MNPs. The surrounding tissues become heated as a result. This makes it feasible to precisely deliver heat to the targeted site and helps to treat it. The most promising MNP is the magnetite-based iron oxide (Fe_3O_4). Due to its exceptional biocompatibility and low toxicity, superparamagnetic magnetite (Fe_3O_4), a primary iron oxide, is widely used in biomedical applications (Montazersaheb et al., 2023).

Therapeutic use of Inorganic Nanoparticles

The inefficiency and difficulty in controlling stem cell differentiation remain a significant challenge despite the development of many innovative techniques for inducing cell differentiation. Therefore, a new and alternative approach is required to effectively control the direction of stem cell differentiation in vivo and in vitro in stem cell therapy. The therapy of stem cells may benefit from recent developments in nanotechnology that have produced a novel class of inorganic nanoparticles with special chemical and physical characteristics. Inorganic nanoparticle-based strategies against stem cells have focused on creating drug-delivering nanoparticles, using them to manipulate cell behaviors, and using them to directly induce cell differentiation within the past ten years. (Guo et al., 2022)

Numerous types of inorganic nanoparticles, including upconverting nanoparticles (UCNPs), magnetic nanoparticles (MNPs), quantum dots (QDs), gold nanoparticles (AuNPs), mesoporous silica nanoparticles (MSNs), carbon nanotubes (CNBS), and have been employed in stem cell research and applications. Multipurpose inorganic nanoparticle-based systems have been designed to better understand human diseases create therapeutic strategies for their prevention and treatment, and show significant potential in the field of stem cell biomedical applications. Furthermore, using long-term tracking stem cells in vivo has generated a lot of interest in a method to functionalize inorganic nanoparticles as a nanoprobe towards improved penetration by near-infrared light or nuclear magnetic resonance. (Ma et al., 2023)

Future Perspective

Conventional therapeutic methods and advanced nanoparticle technology have been completely studied. It suggests that though melanoma is curable in its initial stage but needs to be treated fully by the use of the latest technology which is nanotechnology. Melanoma holds about 1.7% of cancer diagnoses globally and is the fifth most occurring disease in the US (Parhi et al., 2021).

There is a dire need to address the challenges for the successful use of nanotechnology in diagnosing and treatment of skin cancer.

The International Agency for Research proposed that cases of skin cancer will reach about 30 million in the next twenty years and need to be controlled. Major contributing factors can be a deteriorated environment, population shift, and migration. Nanotechnology can be found productive in skin cancer treatment via liposomes but further study is required to meet the challenges and optimize the delivery of drug systems (Int et al., 2023).

Challenges and Limitations

Despite the immense potential, there are several challenges and limitations to stem cell therapy:

- **Immune Rejection:** One of the main challenges in stem cell therapy is immune rejection, especially when using allogeneic stem cells. Autologous stem cells, derived from the patient, are less likely to be rejected but are not always available or suitable (Haworth & Sharpe, 2021).
- **Tumorigenicity:** Pluripotent stem cells are ESCs and iPSCs which may eventually form a tumor in case they are not properly controlled. Hence, substantial attention focuses on research to ensure that the stem cells differentiate into the desired types of cells without becoming tumorigenic (Chowdhury et al., 2021).

Research is continually being conducted to overcome the existing limitations and increase the diseases that can be treated. Key areas of research in the future include:

- **Personalized Stem Cell Therapy:** Gene editing tools, such as CRISPR, may allow the generation of personalized stem cells based on the genetic profile of each patient, reducing the risk of immune rejection and increasing therapeutic effectiveness (Jain et al., 2025; Li et al., 2021).
- **Advances in Scaffold Design:** The development of scaffolds to enhance the support of stem cells in growth and integration into defective tissues will, therefore, be a vital component in improving the efficacy of stem cell treatments (Rajkumar et al., 2024).

Conclusion

Nanoscale biomedical tools are helping doctors improve how tissues heal, how stem cells work, and how we treat cancer. These tiny particles can create environments similar to natural tissues and deliver medicines directly where needed, making treatments more accurate and effective. They can also track healing in real time and help edit genes, opening doors to treatments designed for each patient. Of course, challenges remain - these materials must be safe for the body, avoid triggering immune reactions, and pass regulatory reviews. As the field grows, these microscopic technologies will likely become essential for new healing treatments.

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The Role of Nano Medicine in Controlling Vector-borne Diseases of Veterinary Importance

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Abstract

The veterinary profession has come along some tremendous advancements in terms of disease diagnosis, treatment and prevention. However, some health issues are still posing major hurdles in animals' well-being. Among these, vector-borne diseases pose major challenges for veterinary care, impact animal welfare, and cause significant financial losses worldwide. The inefficiency, environmental problems, and the emergence of resistance lead to the failure of disease and vector control strategies. This chapter is focused on the revolutionary potential of nanomedicine in resolving these therapeutic issues. The detection, prevention, control and management of vector-borne diseases are the application of nanotechnology due its unique mechanisms and nanoscale materials. The enhanced stability, immunity, and extended diffusion ability are the major concerns that lead to application of nanoscale materials in the development of nanovaccines. In this chapter we will emphasize the significance of nanotechnology in enhancing the animal health and promoting innovative strategies of preventing and treating the vector borne diseases of veterinary importance.

Keywords: Nanotechnology, Vector-borne diseases, Nanomedicine, Nanoscale materials, Nano vaccines, Nano diagnostics, Nanotherapeutics

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Introduction

Vector-borne diseases are a significant issue in veterinary medicine and affect the variety of animals, including food producing ani/mals as well as companion animals. The flies, mosquitos, and ticks are the major vectors that pose a global threat to animal health and results in significant financial losses for the livestock sector. All these vectors play major role in spreading of vector-borne diseases like babesiosis, anaplasmosis, theileriosis, leishmaniosis, borreliosis, ehrlichiosis, and rickettsiosis. The most significant of these are caused by protozoan parasites and spread by tick vectors (Little, 2008). Numerous pathogens that are transmitted by arthropod vectors, such as sand flies, fleas, ticks, and mosquitoes, cause the broad category of illnesses known as vector-borne diseases (Dantas-Torres & Otranto, 2016). The global prominence given to the 'One Health' concept of coordinated activity of those involved in human and animal health is a modern manifestation of a long tradition of comparative medicine, which has roots in ancient civilizations and a golden age during the 19th century explosion of knowledge in the field of infectious disease research (Day, 2011).

The use of nanotechnology in the medical field, where nanoscale materials are employed to identify, treat, and prevent illnesses, is known as nanomedicine (Dey et al., 2022). Nanotechnology focuses on manipulating various instruments and practical materials at the nanoscale. In 1959, American Nobel laureate Richard Feynman first proposed the concept of nanotechnology (Prasad et al., 2021). Nanotechnology has transformed almost every area of veterinary and animal science and created new opportunities for applications in molecular biology and biotechnology by producing new, small-scale materials and techniques that are beneficial for living beings. Numerous types of nanomaterials are used in disease diagnosis and treatment, medicine delivery, animal nutrition, and animal breeding. Fullerenes, liposomes, dendrimers, carbon nanotubes, magnetic nanoparticles, metallic nanoparticles, and quantum dots are among the several types of nanoparticles that are used (Prasad et al., 2021).

Nanoparticles can interact with biological systems in ways that conventional treatments cannot because of their small size and surface characteristics. This chapter examines the mechanisms, uses, and potential future developments of nanomedicine in the management of vector-borne illnesses.

Overview of Vector-Borne Diseases in Veterinary Medicine

Vector-borne diseases are any of a broad category of infectious conditions caused by pathogens that are dispersed by arthropods or other biologic intermediaries. Although transmission usually occurs when an infected bug or acarine parasite feeds on blood, infection can also occur when a vertebrate host swallows a vector or when infectious organisms in the arthropod intermediate's excrement contaminate a wound. Worldwide, vector-borne illnesses still damage animals, leading to indirect ecological and economic effects in addition to direct health effects. These illnesses frequently necessitate significant care, control, and elimination efforts in the veterinary industry (Little, 2008).

Major Vector-Borne Diseases

Anaplasmosis

Cattle and other livestock are the main victims of anaplasmosis, a disease spread by ticks and caused by *Anaplasma* spp. Ticks like *Rhipicephalus* and *Ixodes* spp. are responsible for its transmission (Silaghi et al., 2017). Bovine anaplasmosis is an infectious but non-contagious disease caused by *Anaplasma marginale*. It spreads through tick bites, the mechanical transmission of fresh blood from infected calves to susceptible cattle by biting flies, or blood-contaminated equipment such as needles, ear tagging, dehorning, and castration tools. It can result in large losses in livestock productivity and manifest clinically as fever, anemia, and lethargy (Aubry & Geale, 2011).

Usually, the infection is diagnosed using serologic evidence of antibodies, and the diagnosis is then confirmed using molecular detection techniques. The timely vaccination, vector control, prophylactic antibiotics, and ensuring the anaplasmosis free herds are the effective strategies to control bovine anaplasmosis (Aubry & Geale, 2011).

Babesiosis

Babesiosis is a significant tick born disease which is brought on by protozoan parasites belonging to the *Babesia* genus and spread by ticks. It primarily affects the cattle and dogs causes symptoms like fever, jaundice, and severe anemia (Garcia et al., 2022). The protozoal, hemoparasitic disease known as canine babesiosis sprad by ticks and can result in thrombocytopenia, splenomegaly, hemolytic anemia and severe fever in variable degree (Vishwakarma & Nandini, 2019).

An AgELISA that may be adopted for rapid diagnostic test design is presented for the early and precise diagnosis of acute infections while taking superior diagnostic methodologies into account (Irwin, 2009). Blood transfusions are used to treat the severe anemia, supportive therapy is used to restore the animal's health, antiprotozoal medicines are used to manage the parasites, and antibiotics are used to prevent secondary bacterial infection (Solano-Gallego & Baneth, 2011). Babesiosis is currently being controlled via vaccination against *Babesia* spp., particularly *B.gibsoni*, in addition to preventive measures. Along with the prophylactic measures the vaccines against *Babesia* spp., including *B. gibsoni*, are now being developed and administered to control babesiosis (Boozer & Macintire, 2003).

Theileriosis

The cattle and buffalo are most susceptible species to theileriosis which is transmitted by *Hyalomma* ticks. The swollen lymph nodes, anemia and fever are the manifestation of theileriosis which is brought on by parasites called *Theileria*. The fate of untreated animals is death in severe cases (Tilahun, 2016). The two most virulent and significant from commercial point of view are *T. annulate* and *T. parva*, that causes the tropical theileriosis and East Coast fever, respectively. The ixodid tick's species of *Hyalomma* and *Rhipicephalus* are the major vectors of tropical theileriosis and east coast fever, respectively (Kasozzi et al., 2014). Bovine theileriosis has a major global economic impact on livestock sector, prophylaxis is the best strategy to lower disease-related losses (Bhatnagar et al., 2015). The second most effective strategy to reduce the tick load is the use of chemicals acaricides is widely used worldwide. The selection of tick resistant cattle breeds is the most effective and cheapest tick control strategy for controlling the tick born infections in developing nations (Abdela & Bekele, 2016).

Vectors

The term "Vector-Borne" is frequently used to describe ta variety of pathogens and parasites that cause the most dangerous diseases in humans, animals, and the environment (Wilson et al., 2017). Flies, ticks, and mosquitoes are the major carriers of these problems. Tick transmit the babesiosis and theileriosis which are two tick-borne diseases. On the other hand, heartworm disease which affects both food producing animals as well as pets is spread by mosquitoes (Getahun et al., 2022).

Challenges in Traditional Disease Control

The traditional vector control strategies include the use of chemical pesticides, insecticides, and vaccinations. Among the several challenges that these strategies must overcome are the the development of vector resistance, environmental issues related to pesticide use, and the high expense of immunization programs (Garros et al., 2018). As a result of the demand for more targeted, efficient, and sustainable solutions alternative methodologies like use of nanomedicine, are being investigated to control these problems.

Basics of Nanomedicine and its Mechanisms in Disease Control

Nanomedicine is the application of use of nanotechnology in medicine to use nanomaterials for disease prevention, diagnosis, and treatment. Because of their novel properties such as their small size, large surface area, and ability to interact with biological systems at cellular and molecular levels, nanomaterials are very useful for medical applications, including veterinary science (Auría-Soro et al., 2019). The use of nanomedicine has been linked with target-specific drug delivery using nanoparticle formulations including liposomes, SLNs, and fullerenes, among others, and sensitive disease diagnosis using quantum dots, and magnetic nanoparticle. Furthermore, a number of nanoparticles are being investigated as potential adjuvants that can increase the efficacy of antigen presentation and prolong immunity (Mohantya et al., 2014). Nanotechnology is an emerging scientific and technical subject that has led to new and innovative techniques in many areas of medicine. Even

though they were new, Richard P. Feynman foresaw the development of nanomaterials in 1959. Nanotechnology is an emerging scientific and technical subject that has led to new and innovative techniques in many areas of medicine.

Although novel, Richard P. Feynman predicted the emergence of nanomaterials as early as 1959 (Appenzeller et al., 1991). Nanotechnology is the measurement, manipulation, and organization of materials at the tiny level. Materials smaller than 1 μm are commonly included in the scale, even though it usually refers to matter between 1 and 100 nm in size. Advances in nanotechnology have led to the creation of new nanostructures that differ from their bigger counterparts in terms of physiochemical properties and surface-to-volume ratio (Mody et al., 2010). Nanoscale biological processes are therefore excellent prospects for biomedical applications due to their diversity (Chauhan et al., 2010). Despite the fact that nanomedicine is still in its early stages and its application in the veterinary field may appear impossible, many researchers have shown promise. Nanotechnology is currently being used to treat African animal trypanosomiasis (Kroubi et al., 2010). Nanotechnology is expected to not only transform veterinary medicine but also help practitioners understand and use these technologies. Nanomedicine has the potential to be a tool for solving the issues facing modern medicine, in addition to providing endless access to knowledge about the fundamental operations of the biological system (Mohantya et al., 2014).

Types of Nanomaterials Used in Veterinary Applications

Nanoparticles: Metals, polymers, or lipids can be used to create these most widely used nanomaterials. They can be designed to administer medications or vaccines precisely (Kiruthika & Bhattacharya, 2024). These developments could lessen pain, hasten the healing of wounds, and protect our patients from viral or bacterial infections. Furthermore, these new molecules might more accurately transport drugs and DNA. Since these systems will influence how rapidly drugs or other chemicals are absorbed, transported, metabolized, and eliminated in the body, we can control the drug dynamics (Table 1) (Underwood et al., 2012).

Polymeric nanoparticles are made by combining an active molecule with a polymer. The active components are adsorbed or trapped on the surface of the polymer nanoparticle. Both natural and synthetic polymers are used in a variety of polymeric nanoparticle forms. It is simple to construct and improve polymer delivery properties, surface features, shape, and composition in order to provide the necessary drug loading, biocompatibility, targeting, degradation, and controlled release kinetics (Yang & Alexandridis, 2000).

Table 1: Here are some instances of nanoparticles that are being studied, tested, or authorized for use in animals, along with their likely uses in human and veterinary medicine (Underwood et al., 2012).

Sr.No	Nanocarriers	Veterinary Application	Animal under trail
1	Magnetic nanoparticles	MRI contrast, drug delivery (Kim et al., 2012)	Cats. (Underwood et al., 2012)
2	Liposomes	Therapeutics (Underwood et al., 2012)	Cattle, dogs, horse, Cats, birds, sheep. (Underwood et al., 2012)
3	Nanoemulsion	Drug delivery and therapeutics	Dogs, Cats (Underwood et al., 2012)
4	Nanosphere	Vaccine delivery	Horse (Underwood et al., 2012)
5	Micelle	Therapeutics	Sheep, birds, horse. (Underwood et al., 2012)
6	Dendrimers	Microbicide and vaccine delivery (Kim et al., 2010)	Pigs (Underwood et al., 2012)
7	Quantum dot	Fluorescent contrast, invitro diagnostics (Kim et al., 2010)	Cats. (Underwood et al., 2012)
8	Gold nanoparticles	In-vitro diagnosis (Kim et al., 2010)	Cats. (Underwood et al., 2012)

Liposomes: Both hydrophilic and hydrophobic molecules can be encapsulated in liposomes, which are spherical vesicles made of lipid bilayers. They have been employed in vaccine development and medication delivery (Bibi et al., 2024). Liposomes are vesicles with an aqueous core surrounded by one or more phospholipid bilayers. Both hydrophilic and hydrophobic compounds can be transported by liposomes, making them extremely versatile delivery vehicles. By conjugating to ligands or antibodies, they can be altered to optimize their suitability for a particular function. Liposomes are rarely suitable for oral use because of their vulnerability to gastrointestinal system breakdown, despite the fact that they can be used topically, intravenously, and intramuscularly (Bakker-Woudenberg et al., 2005).

They have been investigated for targeted drug delivery, gene delivery, immunization, and imaging agents with promising outcomes. In addition to customized drug delivery, liposomes are used in the treatment of cancer. Liposomes with a reasonable shelf life are now available and an affordable option for veterinary therapy due to increased liposome production for commercial use (Mohantya et al., 2014).

Dendrimers: These are nanoscale, highly branched molecules that can be functionalized to act as diagnostic agents or medication delivery systems (Sarode & Mahajan, 2024). Spherical in shape, dendrimer forms have a high molecular weight but a small molecular size, and their branch lengths are constrained by steric constraints. These structures carry medications in two ways: (a) by attaching themselves to functional groups on the surface of the dendrimer, and (b) by encasing the medications in the dendritic channels of the sphere.

One example is the development of dendrimers using polymers such as polyamidoamine (PAMAM), which provide stability, availability, and tolerability (Baker et al., 2001). Researchers think dendrimers could perform a five-step procedure for treating tumors: (i) they could find tumor cells all over the body by looking for tumor receptors; (ii) they could attach to and cross cell membranes; (iii) they could perform a chemical analysis inside the cells to inform veterinarians about the type of tumors that are present in the animal's body; (v) they could chemically verify that the process killed the cells; and (iv) they could release radioactive agents or chemotherapy inside the tumor cells (Feneque, 2003).

Solid Lipid Nanoparticles (SLNs): SLN are composed of lipids that are solid at room temperature, stabilized by a surfactant, and suspended in an aqueous solution. The therapeutic component is dissolved or dispersed inside the lipid (Mishra et al., 2010). Moreover, drugs that are hydrophobic stay stable in their lipid matrix. They have low levels of toxicity and can be made without the use of organic solvents. SLN's special capacity to transport drugs across the blood-brain barrier can impact drug delivery to the brain in a number of ways (Muller & Keck, 2004).

Mechanisms of Nanomedicine in Disease Control

Targeted Drug Delivery: To improve therapeutic effectiveness and reduce adverse effects, nanoparticles can be engineered to deliver medications precisely to infected cells or tissues (Ali et al., 2021). One of the veterinary medical areas that would benefit the most from research on nanotechnology is pharmacology. Since these systems will influence how rapidly drugs or other chemicals are absorbed, transported, metabolized, and eliminated in the body, we can control the drug dynamics (Underwood et al., 2012).

Diagnostics: Controlling vector-borne diseases requires the development of very sensitive diagnostic tools for early disease detection, which is made possible by nanotechnology (Hazra & Patra, 2023). Because nanotechnology operates at the same scale as a virus or other disease-infecting particle, it holds the potential for incredibly early diagnosis and eradication (Jain, 2005).

Vaccine Delivery: By preserving the active ingredients, boosting immune responses, and guaranteeing stable distribution, nanoparticles can enhance vaccine delivery (Liang et al., 2024). The production of a long-lasting and protective antibody against a pathogen is the primary objective of vaccine science; the adjuvant and antigen are crucial components of this process. Safer synthetic and recombinant alternatives have replaced the old vaccination method's use of living and dead organisms. Although there are several novel antigen-carrying methods available with the advent of nanotechnology, traditional adjuvants cannot be tunneled (Nordly et al., 2009). These adjuvants based on nanoparticles can be made to have a reduced dose frequency and an easy way of administration in order to trigger a target-specific immune response. To enhance target mucosal immunity, for instance, the intranasal approach can be employed. As a result, they are perfect for veterinary species where multiple animals may need treatment simultaneously or when standard immunization techniques are difficult due to complex management systems or restricted accessibility (Underwood et al., 2012).

By mimicking pathogen-associated molecular patterns, upregulating co-stimulatory molecules on antigen-presenting cells, maintaining immunity, delivering antigens for a prolonged duration, and, finally, creating virus-like particles that mimic a virus's capsid and elicit immune responses without the infectious agent, adjuvants for nanoparticles increase a vaccine's immunogenicity (Mohantya et al., 2014).

Application of Nanomedicine in Vector Control

With cutting-edge tools like nanopesticides and repellents, nanomedicine provides intriguing ways to directly control vector populations, including mosquitoes and ticks.

Nano pesticides: Insecticides that have been developed at the nanoscale to increase their efficacy, decrease their toxicity, and prolong their duration of action are known as nano insecticides. Targeting and controlling the disease-transmitting vectors in their environment is possible with these (De et al., 2014). For instance, compared to traditional insecticides, nano silver and nano sulfur are more effective at killing ticks and mosquitos with less of detrimental environmental impacts (Abdollahdokht et al., 2022). The gap enables the use of nanotechnology and application of nano pesticides. The two main categories of nanopesticides are man-made and biological nanopesticides. Insect growth regulators, conventional insecticides, and other microbial control agents are used to prevent mosquitoes from growing and spreading. Among the innovative nano formulations that exhibit the potential as nano pesticides are nanoparticles made from plant extracts, nano emulsions containing pesticides like pyrethroids, nano emulsions containing essential oils like citronella and neem. Despite the overwhelming evidence that these nano insecticides are effective, limited research is done to examine the impacts of these substances on the life of other aquatic species. The advantages of these chemical over the conventional pesticides include their efficacy and limited adverse effects on environment (Mishra et al., 2018).

Nano Repellents: The particular compositions used to keep vectors like mosquitos away from the animals are called nano repellents. These repellents are commonly in long-lasting, slow release formulations that provide extended protection with fewer treatments (Basu & Bhattacharya, 2021). According to reports, nanomodified permethrin exhibits better larvicidal activity, shelf life, and target specificity against *Aedes (Ae.) aegypti* with minimal impact on non-target organisms than the bulk version of water-insoluble permethrin currently available on the market. These tiny, delicate particles' capacities to penetrate the negatively charged outer biological membrane of mosquito larvae reduces the quantity of active chemicals required (Ghormade et al., 2011).

Additionally, they don't harm the environment, animals, or people (One Health). By adding the aforementioned advantages of nanomaterials to novel formulations, the efficacy of adulticides, pupicides, larvicides, ovicides, and repellents can be raised. According to Sap-Iam et al. (2010), a nanoformulation is any formulation with components at nanometric sizes that is expected to release active chemicals or promote mosquito toxicity in a manner that has been previously developed for increased efficacy (Sap-Iam et al., 2010). Numerous kinds of nanomaterials with appropriate functions that contain both organic and inorganic components have been reported; these include formulations based on lipids, formulations based on organic polymers, nanoemulsions, nanosuspension, nanofibre, and inorganic metallic nanoparticles (Al-Samarrai, 2012).

Controlled release formulations allow for the precise and synchronized release of active substances to their target locations. Their large surface area and exceptional sensitivity to environmental conditions make them the ideal delivery vehicle. Several nanostructures and nanoencapsulations employed in mosquito control are studied for their physicochemical characteristics (Mandodan et al., 2023).

Effectiveness Compared to Traditional Methods: Vector control methods based on nanotechnology have shown to be more sustainable and effective than conventional chemical treatments. They provide a precise, targeted method that minimizes environmental harm and vector resistance by reducing the need for extensive pesticide application (Punniyakotti et al., 2024).

Nanomedicine in Disease Diagnosis and Treatment

By offering cutting-edge instruments for the diagnosis and treatment of vector-borne illnesses, nanomedicine is revolutionizing veterinary medicine. Diseases including anaplasmosis, babesiosis, and theileriosis must be controlled by early detection and efficient treatment. Targeted medicine delivery and extremely sensitive diagnostic testing are made possible by nanotechnology, which increases therapeutic effectiveness while reducing adverse effects.

Nano-Diagnostics for Early and Accurate Disease Detection

Blood smears, serological testing, and PCR-based approaches are the mainstays of traditional vector-borne illness diagnostics. But these techniques can be expensive, time-consuming, and may call for certain tools. By creating nano-based sensors and diagnostic platforms, nanomedicine offers the chance to improve diagnostic speed and accuracy (Singh et al., 2022). Magnetic, semiconductor, polymeric, and metallic nanoparticles have all been employed in designing nanostructures for disease diagnostics. The ability of nanoparticles to have their surfaces altered by polymers, antibodies, or aptamers extends their half-life and reduces the risk of toxicity, even if their unique optical, magnetic, and size-dependent properties make them promising candidates for disease diagnosis.

By conjugating these nanoparticles with aptamers, sensitive, highly selective, reusable, and label-free sensors with fluorescent, optical, and electrochemical detection signals have been created. Nanostructures have improved medical diagnosis by providing low-cost, reproducible, sensitive, and highly specific disease diagnosis methods through the use of sensors or imaging agents (Bansal et al., 2020). For example, gold nanoparticles have been used to create colorimetric tests that enable the rapid detection of vector born diseases like *Babesia* and *Theileria spp.* in blood samples (Tubalinal et al., 2021). Additionally, early diagnosis is made feasible by nano diagnostic technology, which is crucial for stopping the spread of infection and lessening the overall effect on animal populations. In an attempt to potentially transform the disease surveillance, researchers are examining the direct detection of disease-related molecular markers from animal samples using quantum dots, nano sensors and biosensors (Wang et al., 2017).

Targeted Drug Delivery in Treatment

The drawbacks of conventional therapeutic methods include nonspecificity, limited bioavailability, poor solubility, and short circulation half-life. Due to all of these considerations, substantial dosages of therapeutic medications are required, which might result in cytotoxicity and other systemic side effects (Bansal et al., 2020). The capacity of nanomedicine to precisely transport the medication to the infection site, increasing therapeutic efficacy, is one of its main benefits. The effectiveness of treatment for vector-borne diseases can be increased by encapsulating and releasing drugs in a regulated manner using nanoparticles like liposomes and dendrimers (Chenthamara et al., 2019).

For instance, to guarantee that the medication is concentrated at the site of infection and reduce systemic toxicity, anti-babesia can be directly injected utilizing nanoparticles into erythrocytes infected with *Babesia* parasites (Couto et al., 2021). Additionally, using nanomaterials to deliver medications lessens side effects by enabling the administration of lower amounts (Chenthamara et al., 2020).

Examples of Nanomedicine Applications in Treating Vector-Borne Diseases

Numerous vector-borne illnesses are being effectively treated with nanomedicines. Studies on babesia infections have demonstrated that by more precisely targeting the parasites, a nanoparticle-based delivery system can increase the effectiveness of anti-babesia medications (Pandian et al., 2021). Additionally, nanotechnology has demonstrated the potential to cure and control *Anaplasma* infections by guaranteeing the bioavailability of medications and enhancing their stability (Kumar et al., 2024).

Nanovaccines: Prevention of Vector-Borne Diseases

Nanovaccines, which employ nanotechnology to improve vaccine administration and efficacy, provide a number of advantages over traditional vaccines. A promising strategy for preventing viral and non-communicable illnesses is the use of mucosal nanovaccines. Recent years have seen the successful usage of nanoparticles in immunization due to their unique properties. When employed as antigen transporters, many of these materials have a positive effect on vaccine effectiveness. Mucosal vaccines are the most practical immunization strategy because they are easy to administer (improving patient comfort and compliance), allow for the elicitation of relevant immune responses both at the site of administration and in distant compartments, and may therefore protect the main pathogen entry portal (oral, nasal, and genital mucosae) (Rosales-Mendoza et al., 2019).

Nanotechnology in Vaccine Development

Vaccines that are easier to administer, more stable, and have a longer shelf life can be developed thanks to nanotechnology. Antigens can be encapsulated by nanoparticles, guaranteeing a regulated delivery to the immune system. This strengthens the immune system and may lessen the need for booster doses (Peek et al., 2008). Additionally, by targeting certain elements of vector-borne diseases, such the surface proteins of parasites like *Babesia* or *Anaplasma*, nanovaccines can strengthen the immune system and offer long-term protection (Kumar et al., 2024).

Nanovaccines have the potential to enhance immunological memory, boost and accelerate immune responses, and enhance antigen presentation (Pandian et al., 2021).

Safety Concerns and Toxicity Issues

The possible toxicity of nanoparticles is one of the main issues with using nanomedicine on animals. Nanoparticles can readily interact with biological systems due to their small size, which may have negative consequences. Nanoparticles due of their small size can build up in organs including liver, spleen, and kidneys and contribute to long term damage (Ali et al., 2021).

Ethical Considerations

It's important to think about the moral ramifications of employing nanotechnology on animals. Thorough research and ethical guidelines are required to address worries about animal welfare, possible injury, and the wider environmental implications of nanoparticles (Coles & Frewer, 2013). The long-term impacts of nanomedicines on ecosystems and wildlife are also debatable.

Future Prospects and Challenges

Because of its novel approach to treating vector-borne diseases, nanomedicine has enormous potential for the future of veterinary research. However, before nanomedicine is widely adopted, a number of issues need to be resolved. Notwithstanding the possible advantages, a number of issues keep the nanomedicine from being applied more frequently in veterinary care. Ethical concerns including public acceptance, strict regulations, and costly development costs limit the potential of nanomedicine. Furthermore, because nanomaterials' extensive use may have unforeseen implications, their environmental impact requires careful investigation (Jahanmahin & Borji, 2023). Personalized medicine, in which treatment plans are customized for specific animals based on their genetic profiles, is one of the most intriguing uses of nanomedicine that researchers are currently investigating. Additionally, there is rising interest in using nanomaterials to create real-time diagnostic systems and intelligent vaccines that might completely transform veterinary care (El-Sayed & Kamel, 2022).

Conclusion

Although there is a lot of advancement in disease diagnosis and its therapeutic management but there are many challenges for veterinary care including vector born diseases that cause significant economic losses globally every year. The development of nanovaccines, target drug delivery systems, and rapid and improved diagnostic tools are some of the innovative approaches of nanomedicine that are ensuring the timely diagnosis, treatment, and prevention from vector-borne diseases. Because of its novel approach and nanoscale materials, nanotechnology is used in detection, control, prevention and management of the vector born diseases. The most important factors that drive the application of nanoscale materials in the creation of nanovaccines are their expended diffusion capacity, improved immunity and stability. The main concerns associated with nanomedicine are safety, regulation, and public acceptance. As more research and studies are carried out, nanomedicine has the potential to play a significant role in managing veterinary diseases, ensuring healthier animals and more environmentally friendly farming practices.

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Role of Genetically Modified Organisms in Agriculture Biotechnology and New Developments

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Abstract

Over the past 6 decades, GMOs have revolutionized agriculture through increasing crop yields and resistance to pests or diseases while boosting nutritional content. Through the discussion on genetic engineering techniques, this chapter highlights major molecular machinery (e.g., Agrobacterium-mediated transformation, biolistic and CRISPR/Cas9) that have made targeted improvement of traits possible. While these may come with some positives, GMOs also face their fair share of disadvantages (distrust from the public in regard to health aspects and environmental effects; poverty issues linked with bio-patented seeds as perhaps seen by smallholders). Advances made recently in gene editing technologies and regulatory frameworks are affecting the status of GMOS. In this chapter, we discuss public engagement and open, candid conversations to dispel fears and improve trust in biotechnology. In conclusion, GMOs are an important means to tackle world agricultural problems yet the ongoing debate is necessary in order for them to be part of farming practices on a long-term basis. This chapter discusses the advantages, disadvantages, and most current developments of genetically modified organisms (GMOs) in agriculture.

Keywords: GMOs, Environmental effects, Health concerns, Public engagement, Molecular machinery, Nutritional content

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Introduction

Genetically modified organisms (GMOs) represent an advancement in agricultural biotechnology and offer innovative solutions to pressing global issues. These days with challenges, like climate change and a growing population making food production more challenging than ever before GMOs play a vital role in enhancing agricultural methods (Paniza, 2024). The Food and Agriculture Organization predicts that food production needs to rise by 70% by 2050 to meet the needs of 9 billion individuals globally (Simane et al., 2025). Utilizing methods alone would not suffice to achieve such a milestone; hence the integration of GMOs is crucial, in striving for a sustainable future (Gbashi et al., 2021). The enhancement of crop plants, through the incorporation of genes or the control of natural gene activity has played a crucial role in advancing crop development and agriculture as a whole. Genetic modification and the alteration of plants have enabled traits such as resistance to herbicides and insects' capacity to withstand stresses and disease resilience (Abobatta, 2020). Improved nutritional content in genetically engineered crops and 525 unique modified instances across 32 different crops have received approval for cultivation worldwide up, to now.

Transgenic technology adoption has been demonstrated to lower crop production costs, decrease the use of pesticides and insecticides, enhance crop yields, and lower CO₂ emissions (Hickey et al., 2019). However, there are obstacles to the broad use of transgenic crops with foreign DNA because of worries about possible human toxicity, allergies, and environmental hazards, such as the likelihood of gene flow, negative impacts on organisms that are not the intended target, development of resistance in insects and weeds, etc., (Karn et al., 2022). Alternative methods including cisgenesis, intragenesis, and most recently, genome editing, have been used as a result of these worries. Since some of these alternative technologies can be used to create agricultural plants devoid of foreign genes, it is anticipated that these crops will be more widely accepted by consumers and receive regulatory approvals more quickly than transgenic crops (Anzalone et al., 2019). For example, cultivated plants modified to resist pests can lessen reliance, on pesticides and promote sustainable farming methods while safeguarding beneficial insects as well (Montecillo et al., 2021). These modified crops encompass Bollgard cotton and StarLink corn that have been genetically altered to generate a protein derived from the *Bacillus thuringiensis* bacterium to eradicate the intended pests. These varieties have reduced pest damage very significantly, which means the yields are higher and fewer pesticides are used (Umesha et al., 2018).

Moreover, with the CRISPR-Cas9 technology, crop development has been revamped with the ability to deliver precise edits to plant genomes. This enables the development of crops that are not only highly productive but also resilient to changing climatic conditions. For example, scientists have been able to engineer different varieties of maize and rice that require minimal water intake but can still grow well in drier conditions; this is a basic adaptation in the face of increased global temperatures and changes in rainfall (Bortesi & Fischer, 2022). Besides high yields and tolerance, GMOs are a crucial way to address nutritional deficiencies globally. Biofortification of staple crops is one strategy that can boost the nutrient content of food. For instance, Golden Rice, engineered to contain more provitamin A (beta-carotene), seeks to eliminate vitamin A deficiency in developing countries, where rice is a mainstay diet staple. Projects in this regard indicate GMO's ability to positively influence health directly but, meanwhile improve food security.

Implementing GMOs poses notable economic effects. Studies say that farmers using GMO produce earn more due to saving on inputs and being able to produce more. GMOs have positively impacted the economies of regions such as South America, enhancing the livelihoods of farmers. Agricultural biotechnology in Brazil and Argentina has increased their agricultural exports and contributed to their national economies (Basso et al., 2024). GMOs are not adopted uniformly across the world. Most countries have embraced agricultural biotechnology, but some are still very cautious and have avoided it, fearing the effects of regulations and public perception. The European Union has strong regulations, requiring approval for crops before their commercialization in the market after long-term safety assessments. Such a regulatory approach reflects caution towards biotechnology (Beghin & Gustafson, 2021). A regulatory environment like this could discourage innovation and limit the benefits of GMOs where it is needed most in agricultural production.

The other factor that determines whether GMOs are accepted or not is public perception. Many consumers fear GMOs due to the misinformation as well as a lack of knowledge about genetic engineering (Thompson, 2023). A research study has shown that a good number of people lack scientific knowledge about GMOs thus creating a reason for fear over safety and environmental effects (Smith & Brown, 2024). This points to a need for general education programs that deliver the benefits and safety of GMOs in the creation of an informed discussion about biotechnology. There should be a focus on effective communication strategies that emphasize scientific consensus on the safety of GMOs and their ability to improve food security with reduced environmental impacts. Through public engagement through open dialogue, educational programs, and outreach initiatives, the gap between scientific communities and consumers will be bridged, with trust and understanding developed (Lee, 2022). GMO integration into sustainable farming methods will be a key focus in the future. Researchers are investigating how soil health, biodiversity, and carbon sequestration can all be enhanced by genetically modified crops (Kelley, 2023). For example, increased nutrient efficiency in genetically modified crops can lower fertilizer pollution, runoff, and environmental damage (Basso et al., 2024).

Innovations in agricultural biotechnology are also focused on crops that can grow well in marginal environments, thus not further stressing prime agricultural land. This approach supports food production and promotes conservation by saving natural habitats (Lisboa et al., 2024). Furthermore, the aspect that GMOs contribute in ameliorating climate change cannot be overlooked. A change in climate character leads to extreme weather cases happening frequently, and for a good crop to flourish with such challenges, resistance will be key. Developing crop resistance through agricultural biotechnology will be fundamental because further research and developments create a resilient crop towards an altering climate to safeguard its security for generations (Umesha et al., 2018). This chapter's goal is to examine how important genetically modified organisms (GMOs) are to solving the world's agricultural problems, especially in light of climate change and the growing demand for food production.

Understanding GMOs

GMO stands for genetically modified organism, and it refers to any plant, animal, or microorganism whose genetic material has been changed with biotechnology to give the desired characteristics. This usually involves taking out certain genes that affect the way an organism looks or interacts, but then replacing them with a healthier set of instructions. The history of GMO technology begins with the identification of DNA and how to work on genetic modification in plants by the late 20th Century (Gbashi et al, 2021).

Genetic Modification Strategies

Genetically Engineered Crops

The commercial introduction of genetically engineered (GE) crops occurred in the 1990s. Because of concerns about possible harm to the environment, human health, and ethical considerations, some individuals and organizations continue to oppose the technology even after it has been in production for 20 years. However, some worry that because of strict laws and less public money for the development of more beneficial products for society, technology is not realizing its full potential to enhance human health and the environment (Aggarwal et al., 2022). New developments in genetic engineering are complicating the ongoing discussion over these and other issues pertaining to the methods used in the first 20 years of genetic engineering. Genetically Engineered Crops expands upon earlier relevant Academies publications from 1987 to 2010 by looking back at the alleged benefits and drawbacks of GE crops and projecting what the future may hold for these developing genetic-engineering technologies. This research identifies areas of uncertainty regarding the effects of genetically engineered crops and food on the economy, agronomy, health, safety, or other factors, and it offers suggestions to close these gaps in safety evaluations, clarify regulations, and enhance GE technology access and innovation (Lubieniechi et al., 2025).

Agrobacterium

A strategy for introducing genes into crops called plant transformation based on agrobacterium-mediated transformation imitates the natural agrobacterium system. Numerous crop species have been successfully genetically transformed thus far by means of this technology, demonstrating an improvement or modification for one or more traits. Compared to other transformation techniques, this one offers a number of benefits, including cost-effectiveness and robust transgene integration (Javaid et al., 2022). Nevertheless, this method has numerous drawbacks, including low transformation efficiency, transgenic integration, off targets, and the majority of crops being resistant to

agrobacterium. Therefore, in order to improve the genetic transformation efficiency of Agrobacterium-mediated transformation, it is imperative to investigate the main obstacles and potential fixes.

The hazards of Agrobacterium-mediated transformation in transgenic plants, the process used to create genetically modified crops using this technique, and the main crop species that have been successfully changed using it are all thoroughly examined. (Wen et al., 2022). The difficulties and issues surrounding Agrobacterium-mediated transformation are discussed and how they can be resolved in the future to enable successful genetic modification of crops through the use of cutting-edge biotechnology methods like CRISPR/Cas9 systems. The audience working on crop genome editing by Agrobacterium-mediated transformation will find great assistance in this review study, which also offers up numerous new avenues for future plant genetic transformation (Van Dijk, 2021).

Applications of CRISPR/Cas9 Genome Editing in Plant Species

Rice

The ability of CRISPR/Cas9 era to enhance the pleasant of agricultural goods is one in all its most extensive uses of in terms of sustainability. The first effective CRISPR/Cas9 manipulation of rice, a key food delivery for the arena's population (Fukagawa and Ziska, 2019), changed into achieved with the aid of (Miao et al., 2013), who showed that the approach will be applied for targeted changes in rice. Since this discovery, a variety of work has been finished to recognize the roles of unique genes and observe the results of gene modifications in rice with the intention of the use of the study's findings in actual global applications. A work by using (Guo et al., 2020) that hired CRISPR/Cas9 to each overexpress and do away with the OsProDH gene in rice serves as an illustration of this. The OsProDH gene produces the mitochondrial enzyme proline dehydrogenase that is accountable for breaking down proline in rice. Proline is essential for protecting flora from a number of biotic and abiotic stresses as it triggers some physiological responses within the flowers and scavenges reactive oxygen species (ROS) (Li et al., 2022).

It was discovered that rice with an OsProDH gene mutation accumulated more proline, which helped to lower the levels of reactive oxygen species (ROS) (Guo et al., 2020). Therefore, rice may be given extended thermotolerance via editing the OsProDH gene and ultimately the metabolism of proline, rice might be given more thermotolerance. Therefore, rice might be given improved thermotolerance by way of enhancing the OsProDH gene and eventually the metabolism of proline (Guo et al., 2020).

Soybean

Other notable plant species have also benefited greatly from CRISPR/Cas9-based mutagenesis, which has yielded amazing mutation efficiency. Carried out the first CRISPR/Cas9 gene edited in soybeans by deleting the gene for the green fluorescent protein (GFP). This landmark finding prompted several efforts to use CRISPR/Cas9 gene editing in soybeans. Han et al., (2019) employed CRISPR/Cas9 to cause a specific mutation in the E1 gene in order to regulate soybean flowering. They found that truncating the E1 protein accelerated the blooming period under long-day (LD) conditions, abolished the inhibition of the GmFT2a/5a gene, and boosted its expression. This alteration led to the creation of a photo-insensitive soybean variety, and it would be appropriate to introduce higher latitudes for soybeans shown in Figure 1 (Han et al., 2019).

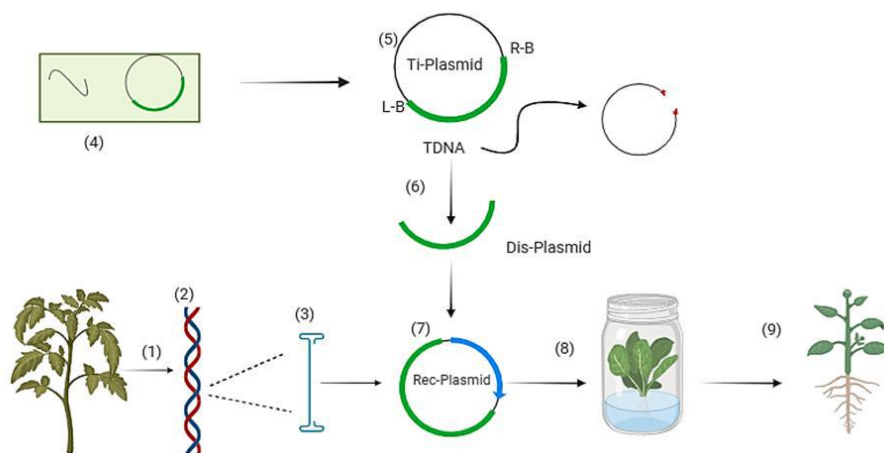


Fig. 1: Genetic modification in soybeans using Agrobacterium tumefaciens and Ti plasmid technology which is adapted to introduce desirable traits like herbicide resistance, pest resistance, or improved nutritional content (Retrieved from Bio Render).

Genetically Modified Crops

Through the use of biotechnology, genetically modified crops (GM crops) have been altered to exhibit particular desired characteristics, such as improved nutrition and resistance to pests and herbicides. Finding relevant genes, incorporating them into the plant's nuclear genome using Agrobacterium-mediated transformation and CRISPR/Cas9 procedures, and allowing the plants to regrow are some of the most crucial phases in the creation of genetically modified crops (Shehryar et al., 2020).

These crops increase the efficiency of agricultural practices as they require fewer chemicals, more specifically pesticides as demonstrated by BT cotton and golden rice. There are worries about the conservation of biodiversity, resistance management of pests, health of people consuming GM foods, and the political implications of GM agriculture including the need for stringent regulations. Overall, GM crops have proved to be a new technology in agriculture but have raised certain issues that concern the safety and risks of these crops for the environment and human health in the long run (Brookes & Barfoot, 2020).

Bacillus Thuringiensis Crops

Crops that are bacillus thuringiensis, like GMA corn or cotton, have been genetically engineered to express proteins derived from the bacterium *Bacillus thuringiensis* that kill specific insect pests. The technology has been extensively used in agriculture, especially in bacillus thuringiensis cotton and also the crops Bt corn because of their efficiency to manage key pest insects such as the cotton bollworm (*Helicoverpa zea*). Such crops, which help to reduce damage and improve production levels by reducing the use of chemical insecticides traditionally used (Brookes & Barfoot, 2018a).

One of the greatest advantages that also usually leads to direct economic and environmental benefits is reduced reliance on chemical insecticides which happened with terms Bt crops. Indeed, reductions in pesticide use with the adoption of Bt cotton have been shown to lower production costs for farmers while simultaneously diminishing environmental consequences related to chemical applications shown in Figure 2 (Pimentel, 2019). For example, Bt cotton can reduce the quantity of synthetic insecticides used and lower pesticide residues in the environment (Brookes & Barfoot, 2018b).

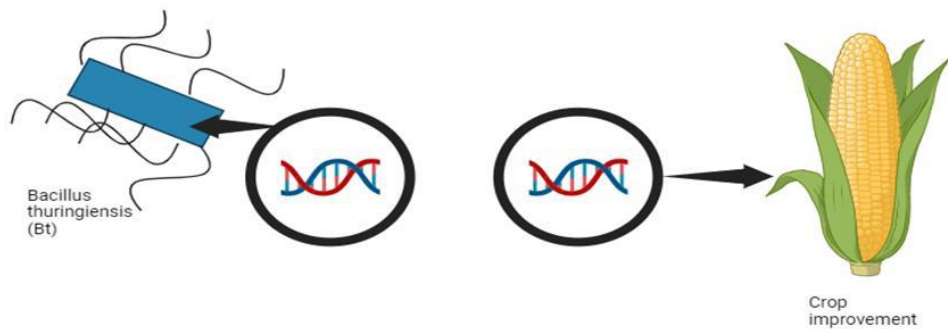


Fig. 2: The genetic modification process using *Bacillus thuringiensis* (Bt) to improve crops (Retrieved from Bio Render).

However, as with all insecticides, an alarm should sound whenever mechanisms of resistance to Bt crops are discovered. Over time, insect populations have been able to evolve resistance to the Bt proteins which can eventually render this technology ineffective. Integrated pest management strategies are essential as a solution from this risk. One of the major recommendations for refuge strategy and involves planting of non-Bt close to Bt. This also ensures that there are still some susceptible insect pests around so they do not develop resistance as easily or quickly to the Bt proteins (Nagaraj et al., 2024).

Golden Rice

Golden Rice is a genetically modified rice designed to combat vitamin A deficiency (VAD), a major public health problem affecting millions of people. Especially in developing countries. The gene responsible for the synthesis of beta-carotene comes from daffodils in genetically developed golden rice. The health of rice, is the staple food of millions of people. There is often a lack of essential nutrients in foods that rely on rice. Vitamin A is important for various physical functions, consisting of vision, immune reaction, and skin health. The World Health Organization has highlighted that VAD is a leading cause of preventable blindness in youngsters and extensively will increase morbidity and mortality from infectious sicknesses (World Health Organization, 2009).

Table 1: This table provides an overview of Golden Rice, a genetically modified crop designed to address vitamin A deficiency.

Aspect	Details	References
Purpose	Developed to prevent blindness in the young generation, a major health issue in growing countries.	(WHO, 2009)
Nutritional Impacts	Aims to increase morbidity from infectious sickness and to provide essential required vitamin A to people relies on rice as staple food.	(WHO, 2009)
Field Trials and Regulation	Regulatory our bodies in various nations have carefully assessed those trials to make certain protection for consumption and environmental impact.	(Smyth et al., 2020)
Public Perception	The debate about Golden Rice has underlined the necessity of transparency and public involvement in attempting to ease concerns regarding genetic modification.	(Yadav et al., 2024)
Current Advancements	The goal of recent developments has been to enhance Golden Rice's horticultural and agronomic performance by creating new, high-yielding, or disease-resistant cultivars.	(Zhang et al., 2023)

Golden Rice seeks to offer a sustainable answer by way of enhancing the nutritional intake of nutrition A amongst vulnerable populations. Since its inception, Golden Rice has gone through great discipline trials to assess its agronomic performance, protection, and efficacy. Regulatory While navigating a complex landscape sparked by public opinion and scientific data, our bodies in different countries have carefully evaluated those experiments to ensure protection for consumer and environmental impact (Smyth et al., 2020). Despite its potential advantages, Golden Rice has encountered strong criticism from anti-GMO activist groups. The Golden Rice controversy has highlighted the need for openness and public participation in efforts to allay worries about genetic engineering (Yadav et al., 2024). Proponents of Golden Rice, a staple in many nations, argue it is a powerful tool in the fight against starvation, while detractors maintain there are other, non-GMO crop alternatives for large-scale agriculture. With new high-yielding or disease-resistant cultivars, more recent advancements have attempted to enhance Golden Rice's horticultural and agronomic performance (Zhang et al., 2023). As more governments and organizations recognize the advantages of biofortified crops, efforts to integrate Golden Rice into regional food systems are beginning to bear fruit, propelled by both commercial and policy developments.

Biolistic Technique

The biolistic technique gives a novel solution to the mission of turning in DNA into dwelling cells and tissues. High-pace microprojectiles are employed to transport substances, which includes DNA, via membranes and cell partitions. The word "biolistics" refers to a sort of biological ballistics that is represented by way of the "shooting" of DNA into cells. Plant transformation the usage of biolistic techniques accommodates numerous steps which make contributions to its a hit final touch. In the first area, gold or tungsten debris are lined with the plasmid DNA constructs containing the target genes (Meyer et al., 2021). Subsequently, a gene gun is used to propel the aforementioned debris into plant.

This device propels the debris at an extreme speed with the use of both a jet of compressed air or small explosive materials (Gao et al., 2022). When particles are hurled at the goal plant tissue, they pass the cell wall and cellular membrane boundaries, as a result facilitating the doorway of DNA into the plant cells (Sheng et al., 2023). This allows the incorporation of recent talents with the altered DNA which could grow to be a part of the host plant's genetic records (Deng, 2024). Afterwards, such cells are implanted into the correct growth medium, so as to regenerate entire plants thru culturing techniques (Niu et al., 2021). This method has been applicable to many types of organisms, and so remains a critical component of plant agricultural technology.

The biolistic process has a number of basic advantages over other methods of plant transformation shown in Figure 3. Regardless of the species or type of tissue, the biolistic approach seems to work well, is quick and easy to use, and should make it easier to directly alter totipotent tissues like pollen, embryos, meristems, and morphogenic cell cultures. Furthermore, it seems that organelle transition is a unique application for the biolistic process. The biolistic process has two drawbacks: it's still in its early phases of development and needs specialized equipment. As a result, delivery efficiencies remain below those possible in highly optimized transformation methods such tobacco agrobacterial infection or electroporation. Additionally, prospective users should be ready to invest some effort in customizing current procedures to their particular species or target tissue (Bate et al., 2021).

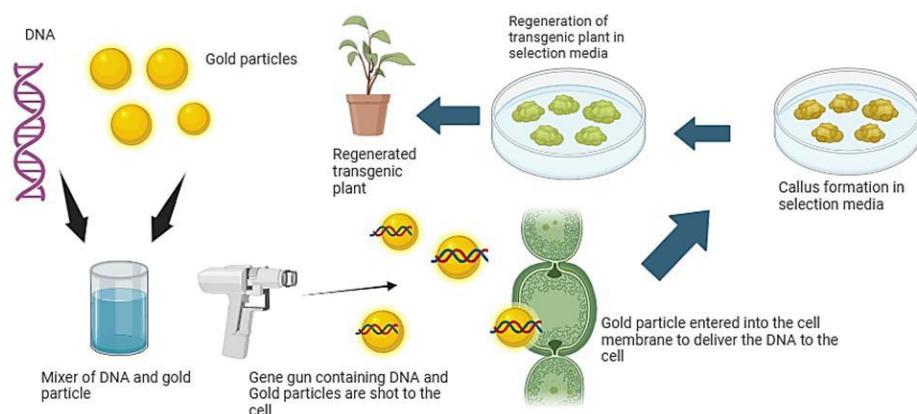


Fig. 3: The schematic diagram shows the method of genetic transformation of the plant. It illustrates the bombardment of gold particles carrying the gene of interest onto cultured plant cells to regenerate transgenic plants (Retrieved from Bio Render)

Public Perception and Ethical Consideration

The public discourse on genetically modified organisms (GMOs) in agriculture is dominated by opposing viewpoints on their dangers and advantages. Their religious ministry has, however, somewhat influenced support for bio-resources. They argue that in this world where individuals are protected, eradication of hunger, control of malnutrition, alleviation of diseases, and enhancement of health and quality of human life are possible for everyone. Emerging technologies, however, have not received universal acceptance. Some insist that we cannot help humanity without endangering public health and cultural ecology. Others are just opposed to that research for religious and ethical reasons. Mixing of gene from different species is regarded by some as "playing God" or violating the "Natural Order" (Lala, 2020).

Biosafety of (GM) crops is an emerging field which encompasses scientific inquiries, ethical concerns as well as policy and regulatory strategies aimed at evaluating and controlling risks of harm to humans or animals such as food and animal feed concerns as well as to the environment from the use of modern biotechnology products (Ewa et al., 2022). Bio-policy refers to the rules, norms, and ethical considerations that govern the development, production, and use of biotechnology products. This encompasses social and political mechanisms that help shape and administer national and international policies on biotechnology. A primary focus in this framework is the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement, which is a fundamental legal instrument for harmonizing international standards for the protection of intellectual property rights. Every country that is a member of the World Trade Organization (WTO), which deals especially with international trade of agricultural products, must implement a patent system in all members and the TRIPS Agreement also cuts across modern biotechnology. Patent systems are made to advance inventions by way of monopolizing the innovations for a limited time.

Conclusion

To sum up, GMOs are a necessary step forward in agricultural biotechnologies that have the capacity to increase crop productivity, its toughness and even nutrition value. However, there are still some problems concerning health, environmental and ethical aspects that the public has. This calls for an open and active informed dialogue. Recent updated information including the very latest tools such as gene editing applications especially CRISPR/Cas9 clearly indicate that there is more to GMO technology than meets the eye. As we define these issues, building confidence and comprehension over biotechnology will be fundamental in the encouragement of the use of GMOs in the current agricultural practices as a way of food security and nutrition's problem. Other than that, looking into the problem objectively as opposed to one sided belief of who is right or wrong avoids imbalances in GMO implementation.

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Integrating Nano-Biotechnology and Biotechnology: Advancements and Applications in Biomedical and Health

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Abstract

Nano-biotechnology comprises the grouping of nano-based materials with biotechnological applications to one of the major fields that has been widely revolutionized in this universe. Nano-biotechnology encompasses nano-based materials which are primarily based on the use of nano-diamonds, carbon nanofibers, quantum dots, carbon nanotubes, and bucky-balls which are majorly used in the field of medicine to support early detection of disease, to treat diseases in a specific or targeted location, tissue regeneration and in biomedical imaging. Current researchers also indicated that the amalgamation of biotechnology and nanotechnology has aided the expansion of point-specific diagnostics and tailored health-detecting structures. In the agricultural, environmental and food industries, the use of nano-based bio-sensors have highly signified the technological ground because of their sensing effects. The functional effect of such nano-scaled materials is very accommodating in giving the exterior surface characters to nanomaterials for increasing the presentation and firmness in numerous areas. Nanotechnology is majorly concerned with ethical dilemmas which usually need to be addressed. This chapter highlights the incorporation of nanotechnology and biotechnology with innovations in the health industry and impacts of nanomaterials while treating health crises.

Keywords: Nano-biotechnology, Nano-diamonds, Carbon nano fibers, Quantum dots, Carbon nanotubes and Bucky-balls

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Introduction

The reality of this universe is based on the fact that an unplanned discovery of this universe became the source of attraction for researchers and scientists known as Big Bang Theory. This theory demonstrated that the world popped out as a wobbly and uneven micro-sized eager element which was called an atom (Malik et al., 2023). Little piece of this unstable component shaped the whole world and researchers and scientists are now more enthusiastic to discover some particles that are like to this little element such as micro particles (Zhang et al., 2022). The mystery of these little particles assures that these active particles even though smaller in size proved very effective in many industries. The mystery of nanoparticles has come to know with the existence of atoms (Farrokhi et al., 2024). By working more on these mysterious elements, researchers came to know about the existence of some particles that were shorter in size than atoms. These smallest elements were given the name of Nano-particles or nano-elements (Ahire et al., 2022). Richard P. Feynman was the first scientist who projected these microelements. These nanoparticles are the smallest and have many advantages in many emerging fields such as nano-biomedicine, nano-robots, and many other sub-fields (Moeinian et al., 2023). The major discovery of these elements led to the most important field of science which is known as Nano-biotechnology. Nanotechnology involves the combination of nanoparticles and technology to produce those items that are the hotspots for future perspective (Chehelgerdi et al., 2023). The demand of nano-biotechnology is very high concerning future. An atom usually comprises a size of 3 angstroms (3Å) while the size of a nanoparticle usually occurs as 10^{-9} of a material. In the early times, it was also considered that these nanoparticles were the spare part of atoms which has been separated by uneven distribution (Joudeh et al., 2022). The technology of nanoparticles has gained its importance to overcome so many future loads. The future is more depending on such types of technologies that pave the way easily for people (Martínez et al., 2022). The early diagnosis and detection of diseases, treatment of cancer, and pharmaceutical findings are now getting even better by using nano-biotechnology. On focusing more on the area of nanotechnology, the treatments are being improved and also many fields are related to being treated with these nanoparticles. Nano-technology and biotechnology are getting more in touch with each other by when there's come such conditions that are unable to be solved by using less efficient technologies (Suhag et al., 2023). The future demands are high enough to cope with the disease with other medical technologies because nanoparticles have gained importance in providing the way easy treatments. Their combined effects are usually increasing their trust on people to get more of their use (Pokrajac et al., 2021). There is a major improvement in techniques like PCR-based diagnosis, agriculture-based pathogen detection, sensors technology, imaging technology and drug discovery, high throughput discoveries and these techniques are now developing their designation as a Nano-based treatment. These Nano-based treatments prove very efficient in fulfilling future stresses (Dessale et al., 2022).

2. Application of Nano-Biotechnology

Using nanotechnology and biotechnology as a connected field doesn't only mean making the lives of people better but also increasing such technologies as in daily life use because such nanotechnologies are very efficient in giving the best results describe in Table 1 (Rajput et al., 2024). Now these nanomaterials have many significant applications in fields like manufacturing of different products, clearance of leftovers, wear and outfits, foodstuff, cosmetics, and even in today's life side by side shown in Figure 1 (Bayda et al., 2020). Numerous medicinal prospects are made possible by the special properties of ingredients at the nanoscale, including the capacity to modify and customize their physico-chemistry at the scale where bio-molecular interactions take place (Xia et al., 2022).

Table 1: Overview of Applications of Nano-Biotechnology

Applications of Nano Biotechnology			
Areas of application	Examples	Advantages of applications	References
Nano-based drug delivery	Nanomedicine, Nanotubes, Nano capsules	Specific targeted treatment decreases the rate of mutations.	(Bayda et al., 2020)
Biosensors nanotechnology	Nano-bio detectors	For the diagnosis any disease at early stage	(Rajput et al., 2024)
Nanobased biofertilizers	Nanotubes, quantum technology, particles of gold and zinc	For detecting pathogens on crops, to protect crops from any kind of pesticides	(Suhag et al., 2023)
Nanobased environment cleanness	Nanobased filters, zinc oxide	Very suitable for removing pollutants from environment.	(Chehelgerdi et al., 2023)
Nanoctecnological robots	Graphite tubes	Widely used to support human health.	(Farrokhi et al., 2024)

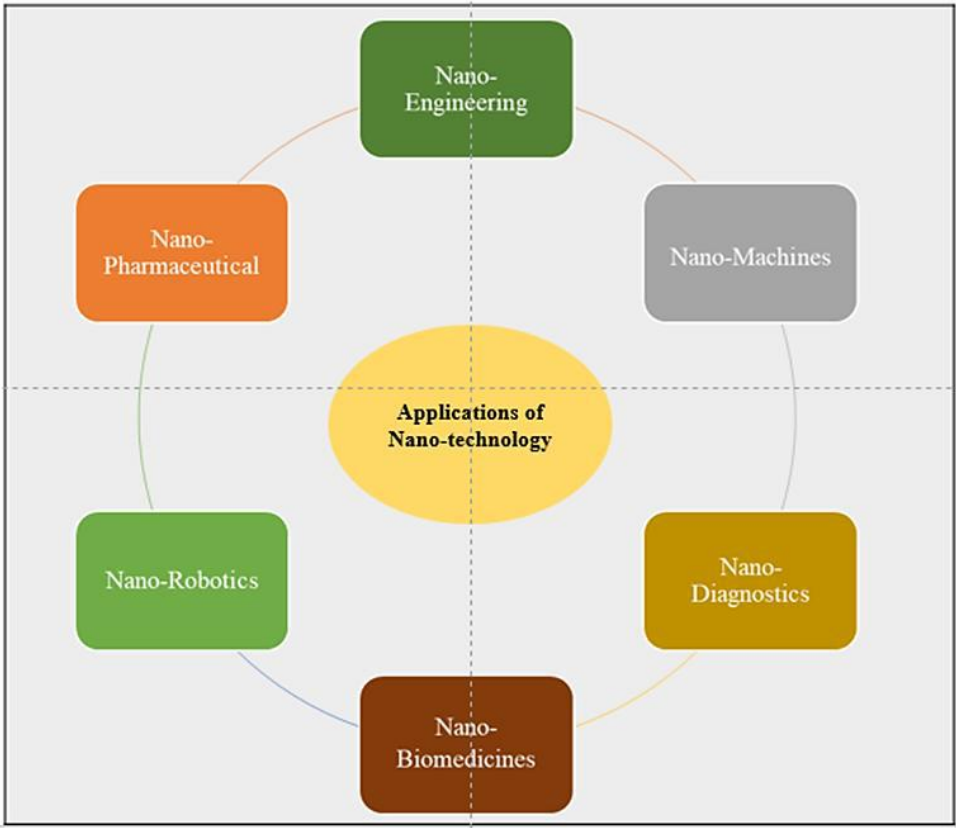


Fig. 1: Applications of Nano-biotechnology (Rederived from Biorender)

2.1. Carbon Nanomaterials

Carbon nanomaterials are the most emerging application of nanomaterials that gives a wide range of different techniques such as regeneration of tissues and cells, medicinal implants, delivery of certain drugs and vaccines, and also in some other important applications (Choudhary et al., 2024). Maximum size range of these carbon nanomaterials is from 1-100nm. Nano-biotechnology has been prominent as a most evolving field that has developed the treatment and analysis of illnesses and this is all happens because of the expansion and growth of carbon-nanomaterials approach with possible submissions for treatment of disease recovery and identification (Yan et al., 2023). Old CNMs were less efficient but the introduction of higher nano-scaled particles has become the source of more efficacy of outcomes. Carbon nanomaterials have a blend of possessions that are modified via production procedures to improve various characteristics like drug efficacy, optical commotion, biocompatibility and immunogenicity (Zhong et al., 2022). The material's high degree of control over many important properties gives it a benefit over metal-established biomaterials like titanium. There is an excellent example of titanium-based nanomaterials in treating the targeted drug site that proves very promising in giving higher results (Mamidi et al., 2020). Carbo nanomaterials has so many

categories and these include carbon foam, fullerene or bucky-ball, nano-diamond, amorphous nano-carbon, single and multi-walled carbon nanotubes, quantum dots by graphene (Debnath et al., 2021). Carbon nanomaterials have many novel characters that may be applied to many vast biological fields. CNM has also gained an excellent approach to various anti-inflammatory and anti-cancerous stuffs (Mohanaraman et al., 2024). Further findings also conclude that carbon nanomaterials are more focused to being contaminated by various elements such as the production of metal ions (Behera et al., 2022). Overview of the Types of Carbon Nanomaterials shown in Figure 2.

2.1.1. Functionalization of Carbon-Nanomaterials

However, the effect of carbon nanomaterials increases the efficacy of delivery by decreasing the extended maintenance in the body (Behera et al., 2022). Some reports also propose that the involvement of carbon nanomaterials with reactive oxygen species may develop cancer cells by damaging the genetic material i.e. DNA and metabolism of lipids. It is also found that amplified amount of reactive oxygen species by graphene materials also bring changes in the metabolic movement of macrophages and destroys the many mitochondrial films which ultimately leads to programmed cell death (Varol et al., 2022). Carbon nanomaterials make their efficacy better usually by labeling various elements if they have some toxic effects such as they mark or tagging different proteins, DNA, amino acids, and drugs, and then function by decreasing the poisonousness of such elements (Peng et al., 2020).

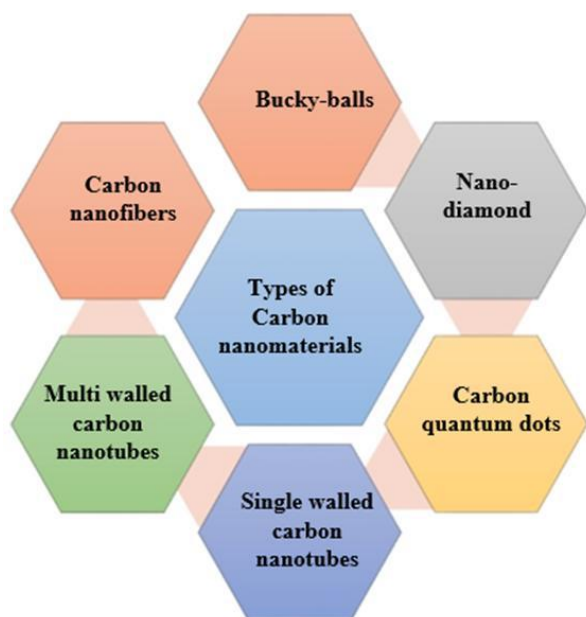


Fig. 2: Overview of the Types of Carbon Nanomaterials (Retrieved from Biorender)

most important form of carbon nanomaterials that occur in the size of usually 8nm and are covered with unique effective coatings of the group that prove helpful in decreasing the oversized connections. These nano-diamonds or even artificial nano-diamonds have low cost (Inal et al., 2023). Such suitable properties of these nano-diamonds with a medical point of view (Mohamed et al., 2024). Nano-diamonds have a very novel property such as they can carry substantial drug loads (Saldmann et al., 2020)

2.2. Fullerenes

Buckyball is a type of carbon molecule that has many irreplaceable structural and electronic possessions and has novel applications in the field of medicine due to its outstanding abilities of being hydrophobic and configuration (Nurzynska et al., 2022). Particles of fullerene have gained its potential as an obstruction of HIV and also against many antibacterial and antiviral mechanisms (Mishra et al., 2021). One of the major advantages of using fullerenes is that these bucky-balls do not show any kind of toxicity, excluding the effects of its severity and non-severity. This is one of the benefits that these buckyballs proved effective in using favor of solubilization, physicochemical characteristics, and decreasing the behavior of toxicity shown in Figure 3 (Ghosh et al., 2023).

2.3. Nano-Diamonds

The discovery of the Nano-diamonds is similar to the structure of diamond-shaped material. Nano-diamonds mimic the structure of diamond particles to perform their work. In the structure of Diamonds, the involvement of a covalent bond with attached carbons to the single one makes it as well as it provides the hard nature to such diamonds (Pan et al., 2023). The structure of nano-diamonds is more similar in way to diamonds because they are also very strong, possess many unique characteristics, has a blend of mechanical strength, sparking nature, and novel thermos-conductive properties. Nano-diamonds, the

2.4. Carbon Quantum Dots

Carbon quantum dots are widely used in the size range of less than 10nm and has extensive use in the areas of research because of their immense properties as they are nonhazardous and give fluorescence effects. Quantum dots are usually Nano-dots that has novel optics properties and because of their small sizes or dots, their activities are restricted (Desmond et al., 2021). Nano-scaled quantum dots get more similar to smaller carbon quanta. The characters of the Graphite carbon dots are also involved with these quanta (El-Shabasy et al., 2021). Carbon quantum dots have become the point of hotspots because of highest level of pressure and temperature ranges are used to make graphene, cellulose and other such stuff by using these carbon quantum dots. There fluorescence effects give 2 major phases; one of which is the radiation of band-gap fluorescence and the other is from the exterior i.e. surface phenomenon (Yang et al., 2023). Reactive oxygen species are also very stable with such CQD (Zou et al., 2020). Carbon quantum dots are more reliable to use in many fields. Carbon quantum dots has also

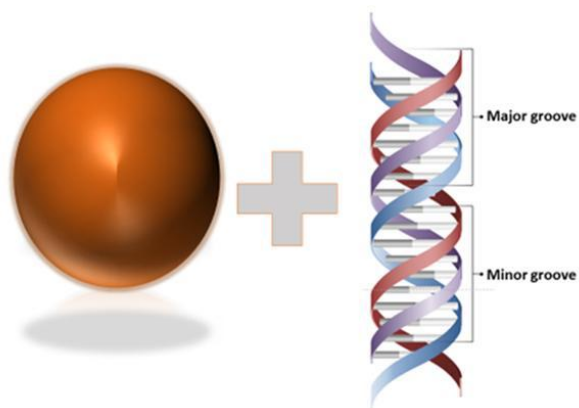


Fig. 3: An overview that represents the combination of buckyballs and biotechnology (Retrieved from Biorender)

important applications in the area of electric gadgets. The area of biomedical science is dependent on the use of carbon quantum dots to get considerable results because of unique fluorescence effects. They are widely used in the diagnosis and treatment of cancer, for precise delivery of medicines, solar power utilization, photo-driven reaction systems, and also for optical devices (Alaghmandfard et al., 2021). Combined Applications of Buckyballs, CNTs and Quantum Dots describe in Table 2.

Table 2: Combined Applications of Buckyballs, CNTs and Quantum Dots

Combined Applications of Buckyballs, CNTs and Quantum Dots				
CNTs	Carbon quantum dots	Fullerene	Relative advantage	References
Tissue Regeneration, Targeted delivery	Cancer Imaging	On site drug equilibrium	Combined effect in different therapies.	(El-Shabasy et al., 2021)
Batteries	Solar energy efficacy	Storage of certain gases potential	Mixed effects on energy conservation	(Joudeh et al., 2022)
Pollutants Identification	To measure pathogens in water	To determine the level of contamination	Integration to find pollution level and toxicity.	(Pan et al., 2023).

2.5. Carbon Nanotubes

The other name for carbon nanotubes is famous bucky-tubes that usually have a hollow or cylindrical appearance made with nano-carbon related particles. Carbon-nanotubes are similar to the structure of simple tubes but these tubes are long and fine with attached carbon molecules in them (Norizan et al., 2020). These hollow carbons are blended upon the tubes and provide unique features by treating many diseases. Double-walled nano-based carbon tubes usually involve two graphene tubes in their production while multi-walled nanotubes involve many cylinder-shaped explosives of graphene sheets. In the areas of research, the double-walled carbon nanotubes are widely used because of their precise monitoring to detect the signals in many electric or medical surroundings (Duoc et al., 2020). Many other phenomena which are known as laser-induced material removal, pressurized carbon reaction, and vapor phase deposition method or vapor deposition by chemical method have been used for the production of such nanotubes (Nikolaev et al., 2023). Among all these methods, chemical vapor deposition has gained much potential because of its positive attitude towards nano-based carbon tubes. Those nanotubes that come to existence by using this method provide many aids by possessing high enactment of length and augmenting morphological properties (Fatehbasharad et al., 2023). These nano scale carbon tubes are widely utilized in the field of medicine because of their highly tuneful traits. Many surgical tools have been designed using carbon nanotubes (Aoki et al., 2020).

2.6. Carbon Nanofibers

Carbon nanofibers come with a stable class and have confident conductive nature. Their physicochemical properties have a vast potential in medicine as they have an easy way to fields of pharmaceuticals, mechanism, and action of drug and their delivery, transfer of different DNA segments or genes to other living beings, for investigation of bio-sensors as well as in many other industries (Omoriyekomwan et al., 2021). Carbon nanofibers have been quickly evolving because of novel thermal, optical and structural properties. Other than that, carbon nanofibers offer a huge dimension for a surface area that makes them bendable for fulfilling the demands (Abdo et al., 2021). CNTs are also widely used in the textile factory and they are so cheap when contrasted with carbon nanotubes. Carbon nanofibers are produced through gas-vapor phase deposition method and point departure electrospinning. One of the biggest examples of carbon nanofibers involves the production of bio-sensors. The functional activity of CNF makes them unique part to dealing with higher demands (Gaur et al., 2021). Developing Level of Nanotechnology for Nanotubes and Nanofibers describe in Table 3.

Table 3: Developing Level of Nanotechnology for Nanotubes and Nanofibers

Developing phases of Nanotechnology for Nanotubes and Nanofibers			
Phases	Nanotubes	Nanofibers	References
Concept stage	Carbon and graphite nanotubes	Drug transport across the whole body	(Gaur et al., 2021).
Experimental stage	Stimulus related to carbon tubes i.e. devices	Regeneration of tissue and medical scaffolds.	(Sharifianjazi et al., 2021)

3. Drug Delivery Systems of Nanomaterials

The world is facing so many problems due to increased amount of cancer; a lot of lives have been lost. To combat this problem, nanotechnology has proved very beneficial to give a soothing effect throughout cancer treatment. Delivery of drugs to the targeted location has become possible by using nanomaterials shown in Figure 4 (Dutta et al., 2021). One of the important components called as magnetic nanomaterials when combined with some other materials such as an introduction of RNA or some chemo-therapeutic antidote or drugs give auspicious effect to treat cancer and minimize the side effects of chemotherapies (Pusta et al., 2023). Drug delivery mechanism is important for humans as well as for animals to treat different diseases and there are different routes to transfer the drug like pulmonary or nasal routes. Graphene or carbon-based nanoparticles are also widely being used (Bhardwaj et al., 2023). Damage to the skin and assembly of wounds sometimes seriously effect a patient's life. To normalize the situation, nano-based materials show excellent effects towards healing of injuries. Nanoscale therapy represents as a prominent tool in such regard (Liu et al., 2023). Other than all, there is another eye-catching approach related to these nanoparticles involve hollow structure nano-based materials that corroborates very promising towards the areas of medical grounds. The function of these nanomaterials combined with a cavity and shell-like structure that give great surface area, shows the lowest density medium, and also enlarges the mass transmission. Such characteristics give leverage to activities like the transmission of drugs, providing outstanding dealings, and transportation of diverse elements (Li et al., 2023).

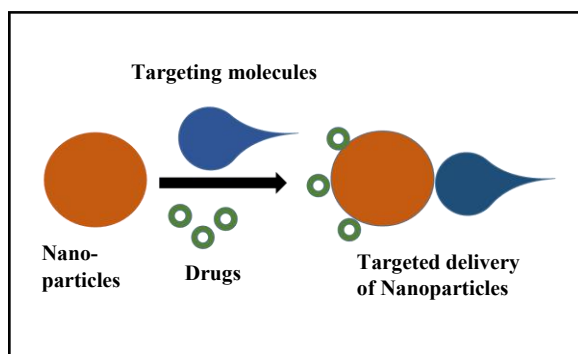


Fig. 4: Target delivery of Drugs Nanoparticles (Retrieved from Biorender)

4. Tissue Engineering

Nanoscale materials signify the most progressive technique to dealing with those patients who have suffered from the disaster of organ failure. One of the major applications of nanotechnology in this regard is the production of engineered tissues that has provided the solution to such loss (Zheng et al., 2021). A protruding type involves the polymeric bio-materials that are highly used because of their unique properties, malleable structure-activity, flexible nature, functional activity, solid power-driven asset, and appropriate living atmosphere. Nanomaterials also provide a high spot for making the tissue engineering activity better. Therefore, the improvement of biologically active compounds and porcelains has favored the use of tissue engineering (Khan et al., 2023). Tissue engineering technique specifically necessitates the usage of a permeable framework, which assists in the 3-dimension pattern or template for preliminary cellular connection and consequent muscle development mutually within the lab and outside the lab. Production of many organs such as artificial

kidneys, liver, heart and the production of human body parts were made possible when tissue engineering techniques were more intact with the help of biotechnology (Halim et al., 2021). The combined effect of these nano-based particles on the making of tissue engineering helps more productivity in the medical field. Scaffolds are the primary source of obligatory provision for cellular activity to ascribe, produce and preserve their discriminated purpose. People are more reliable in using nano-scaled scaffolds because their efficacy is far better than simpler one. Nano-scaled scaffolds show promising effects in the treatment of many health-related issues (Chimerad et al., 2023).

5. Biosensors

Biosensors are also one of the most significant types of nanotechnology that usually sense the biological phenomena of materials. Biosensors are exactly similar to simple sensors. As simple sensors detect the sense of being sensitive and toxicity to certain conditions, biosensors are alike to these but these include some living forms that sense (Nagraik et al., 2021). Biosensors has a great use in so many industries like in medical, agriculture, the environment and even in food industry described in Table 4. With a medical point of view, to know the amount of being uncharacteristic happening or any other kind of change in the body, it measures the signals by using nanoscale technology (Karnwal et al., 2024). By conclusion the introduction of biosensor as it a device that includes transducer that generate the warmer, electrical or ocular indicator. The use of carbon nanomaterials played an important role in improving the methodical presentation because of the upsurge in an electro-chemically energetic shallow zone by utilizing fluorescent activity as well as in the production of biosensors especially electro-chemical and ocular biosensors (Ramesh et al., 2022). As cancer is one of the major causes of death in today's world so nano-scale biosensors prove to be an outstanding tool for cure cancer by giving early detection of cancerous cells in a patient so on time the patient's therapy can be started. Biosensors usually act as bio-markers and a combination of different nanoscale materials like CNTs, CNF, and Carbon Quantum Dots and more prominent graphene is being used to detect the cancer in lungs, breasts and even in the colon (Sharifianjazi et al., 2021). Other than cancer, HIV is also a great concern which ultimately leads to AIDS. A major drawback of HIV testing kits is that these kits are not being able to detect early infection of the virus which ultimately increases the exposure of diseases. Those HIV kits are built by using old methods. To combat this alarming situation, nano-based biosensors provide great easiness in such regards. HIV based nano-based kits show great suitability towards the treatment of HIV. These specific biomarkers attach to the specific location and produce a fluoresces effect and detection of virus molecules becomes possible on the very initial phases. The fluorescence effect that produced after detection saves a lot of time of researchers for diagnose the certain conditions (Farzin et al., 2020).

Table 4: Availability of Biosensors in different forms

Different forms of biosensors with their examples		
Type	Example	References
Diagnostic Biosensors	Pathogen detection, Pollutants detection	(Nagraik et al., 2021)
Magnetic Biosensors	Biomolecules identification	(Ramesh et al., 2022)
Updraft Biosensors	Temperature measurement	(Farzin et al., 2020)

Ethical Concerns Related to Nano-based Biotechnology Materials

It is not a matter of fields but the fact about technologies, and every technology have its pros and cons and even ethical trepidations. As nano-biotechnology has played a significant role in providing the easiness to the lives of people their ethical concerns are also with-it side by side (Yousaf et al., 2024). cancer detection at the start of its spreading, the mutations diagnosis, disease recognition and targeted drug delivery methods have brought about a very calming effect by using nano-carbon tubes, nanofibers, bucky-balls and many more (Mohi-ud-din et al., 2020). Different nanotechnologies have different concerns but the Ethical concerns of these nanomaterials are also found along with its advantages. A major ethical concern in medicine is that sometimes those nanoparticles that are used in the treatment of diseases may gather in some parts of body or in organs that lead to damage to those parts by introducing toxicity to them (Arnold et al., 2022). Labeling of nano-based particles products is important because people become well aware of such products and use them according to the label. But there is also a concern that some companies provide risks by giving misinformation on providing miss labeling (Ukochovwera et al., 2023). There is still lacking of public acceptance about these nano-scaled particles. Some crops are also having nano-scaled labeling but people feel fear to talk

about these labeled crops. Toxicity of such nano-elements bring very undesirable effect on health. There should be an informed consent that provides before treatment as approval for dealing with disease. Biosensors-based nano-techniques that used those sensors to detect the privacy of people and then misuse it, brings up a major ethical concern (Grunwald et al., 2020).

Conclusion

To overcome the challenging issues of today's world in different fields, especially in medical lines, Nano-based particles, and biotechnology together make a prominent field which is known famously as nano-biotechnology as one of the protuberant fields. Nano-biotechnology has been developed as one of the major fields of today's times and provides many benefits by giving with it outclasses advantages in the field whether it is related to medicine or agriculture, textile or food. The demand of nanoparticles is being increased day by day as different types of nano-based particles are effective in different fields for performing different valuable tasks. Near in the future, there will be more demands of these little particles to make the lives of people easier. With time, these nano-based techniques are getting better and people are usually more rely on these nano-based technologies.

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The Synergy of Nanotechnology and Biotechnology in Promoting Holistic Health

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Abstract

The combination of nanotechnology and biotechnology has modified healthcare by developing innovative keys for holistic health. Nanotechnology facilitates precise and effective therapeutics through its controlled release systems, nanoscale drug delivery methods, and advanced diagnostic instruments. Biotechnology makes genetic engineering, biopharmaceuticals, and microbiome engineering advancements to modify treatments according to each person's health demands. Together, these fields facilitate mental health, chronic disease management, and immune system expansion with the help of personalized, focused methods. Nanobiotechnology encourages developments in tissue engineering, regenerative medicine, and functional foods to magnify overall health. Regardless of the barriers including regulatory issues, ethical difficulties, and approachability issues, the synergy of nanotechnology and biotechnology represents groundbreaking probabilities for personalized, eco-friendly, and holistic healthcare resolutions. The development of these technologies accelerates improvements in precautionary care, medicines targeting entangled medical issues, and real-time health monitoring with the surety of a future where healthcare coordinates with the rules of holistic health.

Keywords: Nanobiotechnology, Holistic approaches, Nanomedicine, Nanomaterials in health, Nanotechnology

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Introduction

1. Nanotechnology and Biotechnology in Health

Biotechnology is an innovative, interdisciplinary domain that influences various sectors, including agriculture, veterinary science, medicine, pharmaceuticals, and fine chemicals production. It is emerging as a pivotal technology for the transition to a carbon-free society and for addressing critical societal challenges such as health protection, food and energy supply, and environmental conservation (Martin et al., 2021). Nanotechnology represents a revolutionary approach in contemporary technology, significantly impacting medical devices such as imaging probes, drug delivery systems, and diagnostic biosensors within the pharmaceutical sector. Nanoparticles (NPs) are defined as particles with sizes ranging from 1 to 100 nm (Omietimi et al., 2023).

Holistic health is a comprehensive approach to individual well-being that encompasses illness prevention, alternative treatment modalities, and strategies for attaining optimal health and life satisfaction. The term "holistic" was introduced by Jan C. Smuts in 1926, derived from the Greek word "holos," signifying that a living organism transcends the mere sum of its components (Gross, 1980). An integrated approach in healthcare amalgamates several disciplines and technologies to address and support the comprehensive spectrum of an individual's health. For comprehensive health, this entails employing modern instruments such as nanotechnology for precision and efficacy in therapy while harnessing biotechnology to tailor solutions to specific requirements. Contemporary diagnosis techniques for the majority of ailments rely on the presentation of observable symptoms prior to medical practitioners identifying the patient's specific ailment. However, once those symptoms manifest, the likelihood of therapy efficacy may diminish (Fakruddin et al., 2012).

The pathophysiological circumstances and anatomical alterations of diseased or inflamed tissues may create numerous opportunities for the advancement of diverse targeted nanotechnological devices. Drug targeting can be accomplished by using the unique pathophysiological characteristics of sick tissues (Vasiret al., 2005). Nanoparticles can efficiently transfer pertinent medications to the brain, circumventing the blood-brain barrier (meninges) (Martin et al., 2021). Loading drugs onto nanoparticles alters cellular and tissue distribution, resulting in a more targeted delivery of physiologically active chemicals, hence improving medication efficacy and diminishing drug toxicity (Feng et al., 2004).

2. Nanotechnology in Health Applications

Nanomedicine

➤ Nanoscale Drug Delivery and Controlled Release System

Nanoparticles as treatments can be administered to specific locales, including those that are not readily accessible by conventional medications. If a medicinal agent can be chemically conjugated to a nanoparticle, it can then be directed to the disease or infection site via radio or magnetic signals. These nanodrugs can be engineered to "release" solely in the presence of certain molecules or upon the application of external stimuli, such as infrared heat (Olalekan et al., 2023). Simultaneously, adverse side effects from powerful drugs can be mitigated by decreasing the effective dosage required for patient treatment. Encapsulating pharmaceuticals in nanoscale materials (including organic dendrimers, hollow polymer capsules, and nanoshells) allows for significantly enhanced control over release mechanisms. Pharmaceuticals are engineered to deliver a therapeutic payload (radiation, chemotherapy, or gene therapy) in addition to serving imaging purposes (LaVan et al., 2002). Recent years have seen the introduction of DNA-based medication delivery systems, including DNA weapons and DNA vaccines. An emerging field of DNA nanotechnology is being introduced in the nanomedicine industry, based on analogous principles (Liu et al., 2023). Drugs can be encapsulated within nanoparticles made of biodegradable polymers, facilitating the controlled release of the drug as the nanoparticles degrade. The conditions leading to particle degradation can be modified by altering the chemical bonding characteristics within the particle (Lewin, et al., 2000).

➤ Vaccine Delivery

The most exhilarating and demanding application of nanotechnology in medical sciences is the prospective utilization of nanosystems as vehicles for vaccination administration. A vaccine is a formulation designed to induce immunity to a disease by promoting the synthesis of antibodies. The augmentation of adjuvant efficacy via micro- and nanoparticulate delivery systems is particularly promising, as synergistic effects frequently occur, yielding immunological responses beyond those induced by the adjuvant or delivery system in isolation (Mohanty et al., 2009). Micro- and nanoparticles facilitate the improvement of vaccine absorption by specific cells via the modification of their surface characteristics. These essential vaccine components could enable the creation of innovative vaccines for viral and parasite illnesses, including hepatitis, HIV, malaria, and cancer. Vaccine delivery techniques are typically particulate (e.g., emulsions, microparticles, and liposomes) and possess dimensions analogous to the diseases that the immune system has evolved to combat. Particulate systems of one micron in size have numerous benefits for vaccine administration (Jiang et al., 2005).

➤ Gene Delivery

Nanotechnology is advancing rapidly, significantly influencing the field of medicine, especially in gene therapy. This process entails the insertion (or occasionally the deletion) of segments of genes in patients with diseases to facilitate their cure and promote a healthier life. The introduction of genes into individual cells is facilitated by viral vectors, including retroviruses, adenoviruses, adeno-associated viruses, and commonly used viral vectors (Anand et al., 2022). The physical features of nanoparticles, such as shape, size, charge density, and colloidal stability, are critical factors in assessing their effectiveness as prospective nonviral gene delivery vehicles. A variety of inorganic compounds, including calcium phosphate, gold, carbon materials, silicon oxide, iron oxide, and layered double hydroxide (LDH), have been investigated as potential candidates for gene delivery (Mohanty et al., 2009).

Diagnostics

Ideally, diseases ought to be detected and treated before the manifestation of symptoms. Nucleic acid diagnostics will be essential in this process, enabling the identification of infections and diseased cells at an early, asymptomatic stage of disease progression, hence facilitating more effective therapy. Contemporary technology, exemplified by polymerase chain reaction (PCR), is advancing testing and devices; however, nanotechnology is broadening the available possibilities, resulting in enhanced sensitivity, improved efficiency, and more cost-effectiveness (Fakruddin et al., 2012). A significant application involves nanoparticle-based diagnostic imaging, wherein nanoparticles are conjugated to specific biomarkers to augment imaging techniques such as magnetic resonance imaging (MRI), computed tomography, and positron emission tomography (Medarova et al., 2007), thereby enhancing their sensitivity, accuracy, and specificity (Singh and Amiji 2022). Metal nanoparticles can boost the quantity of immobilized biomolecules in sensor construction. Due to its exceptionally high surface area, colloidal gold has been utilized to improve DNA immobilization on a gold electrode, hence reducing the detection limit of the developed electrochemical DNA biosensor. Nanoparticles are the primary catalysts of next-generation multimodal technologies due to their extensive surface area, which allows for the functionalization of various reporters and surface ligands to enable site-specific localization and stimuli-responsive behaviour (Mohanty et al., 2009).

Biotechnology in Health and Medicine

Genetic Engineering and CRISPR

Genetic engineering is a scientific discipline that alters the hereditary characteristics of an organism's genetic material via natural processes or laboratory cloning (Uzogara, 2000). CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) is a potent genome editing technology that has transformed the realm of genetic engineering. Recently, CRISPR has surfaced as a promising instrument for the treatment and prevention of diverse genetic and non-genetic diseases (Olalekan et al., 2023).

➤ Role in Disease Prevention and Personalized Medicine

Besides its capability to treat genetic disorders, CRISPR has been investigated as a means to avert disease onset. Numerous infectious disorders result from organisms that have adapted to circumvent the immune system, rendering treatment challenging (Doerflinger et al.,

2017). Researchers have utilized CRISPR to alter the genomes of these diseases, rendering them more vulnerable to the immune system and hence more amenable to prevention (Bikard et al., 2014). CRISPR can change the genomes of mosquito populations, rendering them resistant to the malaria parasite, therefore diminishing their capacity to spread malaria, dengue disease (Hammond et al., 2016), and Zika fever (Hoffmann et al., 2021). CRISPR-based methodologies are being devised to identify and eradicate viral DNA, including HIV and hepatitis B, from infected cells (Olalekan et al., 2023).

CRISPR systems have been employed to identify novel therapeutic targets (Dong et al., 2019). Identify pathogenic genes to build illness research methodologies (Yan, et al. 2018) and formulate treatments for diverse ailments (June, 2019). Numerous clinical trials are in progress to assess the potential and security of CRISPR-based therapies. The transplantation of cells with the CCR5 gene artificially destroyed has shown a significant therapeutic benefit towards infection by HIV-1 (Gupta et al., 2019). CRISPR systems can also be utilized to validate potential targets for novel pharmaceuticals. employed CRISPR-Cas9 mutagenesis to examine a series of cancer medication targets at various phases of clinical trials. The suppression of these presumed targets did not diminish certain medications' anti-cancer efficacy, suggesting unforeseen targets (Lin et al., 2019).

Biopharmaceuticals and Vaccines

Bio pharmaceuticals and vaccines signify pioneering progress in biotechnology, providing precise, efficacious, and safer methods for disease prevention and treatment. Their advancement has profoundly influenced contemporary healthcare (Hogan & Pardi, 2022)

➤ Advances in Biologics

Biologics are medical products obtained from live creatures, encompassing proteins, antibodies, and gene therapies. They are engineered to target specific biological processes. Over 25 antibodies have received approval for human therapy, while more than 240 are presently undergoing clinical development (Chan and Carter 2010).

Biosimilars

Economical substitutes for biologics that enhance access to life-saving therapies while maintaining efficacy. In contrast to biosimilars, bio-betters are engineered to be enhanced iterations of the original molecule, focusing on factors such as cost, patient convenience, the product's safety, or effectiveness (Sassi et al., 2015).

Advances in Vaccines

Vaccines constitute a significant advancement in science and health, aiding individuals globally in the prevention of infectious disease transmission.

Various forms of nanoparticles, including those made of gold, dendrimers, carbon, polymers, and liposomes, have been utilised thus far. All can induce the synthesis of cytokines and reactions to antibodies.

mRNA Vaccines

The swift advancement of mRNA vaccines, exemplified by those for COVID-19 (Pfizer-BioNTech, Moderna), showcased the capability of this platform to deliver prompt and efficacious responses to emerging infectious illnesses (Hogan and Pardi 2022).

Viral Vector Vaccines

Platforms utilised in AstraZeneca and Johnson & Johnson COVID-19 vaccines administer genetic material to elicit an immune response (Lundstrom, 2021). Engineered microorganisms are designed to synthesise medicinal chemicals, including anti-inflammatory substances and vital vitamins, directly within the gut. Modifying microbiomes to address illnesses like as obesity, diabetes, and certain malignancies by reinstating microbial diversity and functionality (Foo et al., 2017). Table 1 provides an overview of applications of nanotech and biotech in holistic health.

3. The Synergistic Role of Nanotechnology and Biotechnology

Targeted and Personalized Therapies

Personalised medicine is frequently referred to as precision medicine. Clinical, pharmacological, and diagnostic strategies for better illness care tailored to individual genetic differences in patients the integration of nanoscale delivery methods for drugs with biotechnological innovations has advanced the creation of targeted and personalised medicines, transforming contemporary healthcare. Nanotechnology-driven drug delivery methods, including liposomes, nanoparticles, and polymer conjugates, permit meticulous regulation of drug release and biodistribution, thereby improving therapeutic effectiveness and reducing systemic toxicity. Moreover, biotechnological platforms, including liquid biopsies, imaging techniques, and circulating tumour DNA analysis, permit real-time assessment of therapy efficacy and disease advancement, allowing for prompt modifications to therapeutic protocols (Contera et al., 2020). Biotechnology enables the transition of targeted medicines from preclinical investigation to clinical application, where they are included in personalised treatment protocols. Complementary diagnostics, pharmacogenomic testing, and genetic profiling technologies allow clinicians to identify individuals most likely to benefit from targeted treatments and customise treatment regimens accordingly (Matsushita et al., 2002).

Regenerative Medicine and Tissue Engineering

Tissue engineering is defined as the application of engineering ideas and life sciences methodologies to generate biological alternatives for the repair, maintenance, or restoration of tissue function (Vacanti and Langer 1999). The primary objective of tissue engineering and

regenerative medicine is to create functional alternatives for the restoration, repair, or replacement of damaged tissues and/or organs. Nanotechnology facilitates the creation of nanospheres that replicate certain bodily tissues, such as bone and heart tissues. Substantial discrepancies in cell attachment, production, and separation were noted following randomisation (Lamers et al., 2010). The nanosized scaffold facilitates the effective adhesion of a fibrin clot, enhancing the migration of osteogenic cells to the tailored exterior (Mageret et al., 2011). Due to their diminutive size and therefore elevated surface area, they are extensively utilised for controlled drug release, leading to enhanced drug-loading efficiency (Maheshwari et al., 2012). Nanoparticles can be utilised locally in bone tissue engineering (BTE) to promote tissue regeneration, improve osseointegration of implants, and avoid infections (Tautzenberger et al., 2012). Tissue engineering scaffolds serve to deliver biochemical parameters and cells for cellular movement and connection, provide temporary functionality during tissue regeneration, delineate an area that influences the formation of regenerating tissue, and facilitate the diffusion of essential nutrients and metabolic products for cells (Sokolsky-Papkov et al., 2007).

Table 1: An overview of applications of nanotech and biotech in holistic health

Category	Area of interest	Major Contributions	Examples	References
Nanotechnology	Nanomedicine	Precision drug administration, regulated release, and minimised adverse effects.	DNA nanotechnology for vaccinations and nanoscale carriers for chemotherapy.	(Lewin et al., 2000; LaVan et al., 2002; Liu et al., 2023),
	Gene Delivery	Accurate administration of therapeutic genes to designated organs.	Nanoparticle-mediated CRISPR gene therapy.	(Mohanty et al., 2009).
	Vaccine Delivery	Augmented immunity, effective delivery to target cells	Nano-adjuvants for vaccines against malaria, HIV, and cancer.	(Jiang et al., 2005).
	Diagnostics	Early disease identification, enhanced sensitivity, and imaging techniques.	Nanoparticle-augmented biosensors for oncological biomarkers.	MRI, (Medarova et al., 2007; Singh and Amiji 2022)
Biotechnology	Genetic Engineering and CRISPR	editing of genes for the prevention, and treatment, and investigation of diseases.	Altering the CCR5 gene for HIV resistance and employing CRISPR-based therapies for genetic conditions.	(Gupta et al., 2019; Olalekan et al., 2023)
	Biopharmaceuticals	Targeted therapy utilising biologics, such as monoclonal antibodies and biosimilars.	Pembrolizumab (Keytruda) for oncology, biosimilars for autoimmune conditions.	(Sassi et al., 2015)
	Vaccines	Advancements in mRNA vaccines, viral vector technology, and personalised immunisations.	COVID-19 mRNA vaccines (Pfizer, Moderna), viral vector vaccine (AstraZeneca) and immunotherapy vaccines.	(Lundstrom, 2021; Hogan and Pardi 2022)
	Probiotics microbiome engineering	and Gastrointestinal health, immunological enhancement, and psychological well-being through regulation of the gut-brain axis.	Formulated microbes and enhancements in digestive and cognitive health.	(Drisko et al., 2003; Foo et al., 2017)

Bio-Nano Sensors

A sensor is an electrical device that detects events or changes in its environment and transmits this data to a processor. Nano-biosensors (Nano-BSE) are a category of biosensors being developed under the impact of nanotechnology (Sreejith et al., 2024). Nano-sensors can be employed to monitor several factors such as glucose, cholesterol, and salt. Nano-sensors can also be employed to detect pathogenic tumours and other harmful agents. The current application is an innovative method for delivering drugs within the human body, primarily utilising molecular communication. A nano-biosensor is highly beneficial for illness screening, health monitoring, and precise diagnosis. Nanobiosensors facilitate the avoidance of numerous invasive treatments in patients with severe illnesses, thereby streamlining monitoring and enhancing cost-effectiveness (Pramanik et al., 2020).

4. Applications in Holistic Health Promotion

Mental and Physical Health

Nanoparticles may enhance the pharmacokinetics and bioavailability of pharmaceuticals. Examples of targeted drug delivery include liposomes, virosomes, polymeric nanoparticles, and nanosuspensions. Nanoparticles differ from conventional small molecules in their structure and may exhibit novel therapeutic capabilities. Nanoscale drug carriers administer neuroactive pharmaceuticals directly to the brain, surmounting the blood-brain barrier to address depression, anxiety, and neurological conditions such as Alzheimer's and Parkinson's disease (Anand et al., 2022).

Modelling the central nervous system (CNS)

Nanoparticle assemblies may serve as models for artificial intelligence and maybe mental disease (Fond et al., 2013).

➤ Chronic Disease Management

Cancer

Lung cancer is a major cause of mortality from cancer and presents significant treatment challenges, primarily due to late-stage detection.

Guinart and associates elucidate the intricacies involved in the early detection, diagnosis, and treatment of lung cancer, while examining the various applications of gold nanoparticles to mitigate these challenges. These applications include utilising biosensors for non-invasive disease diagnostics, inhaling functionalised gold particles with specific medication payloads to diminish cancer growth while minimising side effects, and employing photothermal therapy (Contera et al., 2020).

Tuberculosis

Tuberculosis causes millions of deaths worldwide; its treatment requires many drug regimens over extended periods, and noncompliance can lead to multidrug resistance (MDR) in the *Mycobacterium tuberculosis* organism, resulting in MDR-TB and heightened morbidity and mortality. Alzahabi and associates elucidated the recent investigation into the application of nanomaterials (both organic and metallic) as carriers for the administration of current and innovative tuberculosis medications, utilised alone and in conjunction, with the treatment of TB. They also emphasise the incorporation of nanoparticles, such as silver, which impart supplementary antibacterial capabilities to augment the medication formulation's antimicrobial efficiency (Alzahabi et al., 2020).

➤ Immune support

Porous polymeric nanostructured implants serve as a platform for the continuous and regulated release of medicines and other treatments, hence eliminating the need for repeated administration. Long-lasting vaccine implants for single-dose immunisation are being utilized (Contera et al., 2020).

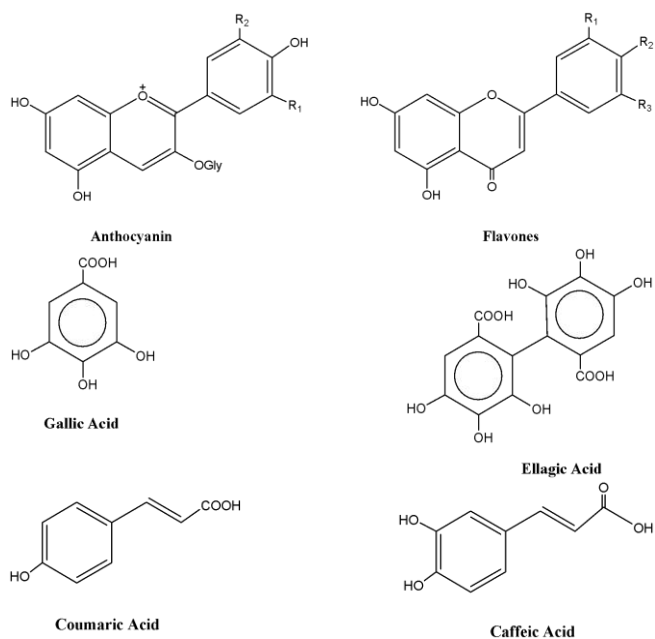


Figure 1: Structures of some Polyphenols (Anand et al., 2022)

Curcumin is a type of polyphenol. It is a component of turmeric recognised for its capacity to mitigate inflammation (Figure 2). Scientific research reveals that curcumin exhibits anti-inflammatory benefits comparable to commonly used nonsteroidal anti-inflammatory drugs, including indomethacin, Vioxx, Celebrex, and ibuprofen in specific contexts. An advantage of employing curcumin is the diminished incidence of adverse effects, including gastrointestinal pain and cardiovascular complications. Curcumin nanoparticles enhance the anti-inflammatory and antioxidant characteristics of turmeric (Graumlich, 2001).

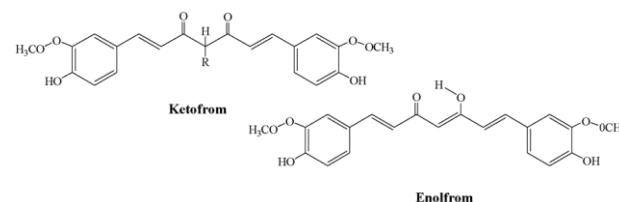


Figure 2: Chemical Composition of Curcumin (Pandey et al., 2020)

Nanoencapsulation effectively enhances the solubility of polyphenols (Figure 1), mitigates their degradation, reduces toxicity, and regulates their active uptake and biological reaction. Nanoencapsulation refers to a variety of approaches grounded in chemical, physical, and physiochemical considerations. (Ghayour et al., 2019) Described the nano-capsulation of quercetin and curcumin in casein-based delivery systems. The encapsulated polyphenols inhibited the advancement of tumour cells relative to the non-encapsulated counterparts. Curcumin-NPs and proanthocyanidin-NPs shown significant acetylcholinesterase inhibitory activity and beneficial neuroprotective effects against A1-42-induced toxicity (Chen et al., 2020).

Elements of the standard diet that may confer health advantages beyond essential nutrients. Functional foods encompass soy, almonds, chocolate, and cranberries. Biotechnology and genetic modification processes are being refined in specific regions to enhance the production and development of nutritious foods, as well as to elevate the amounts and efficacy of biologically active compounds in food plants (Niba, 2003). Methods utilised in genetic modification encompass mutant breeding, enhanced conventional breeding, transgenic alterations, DNA insertion, gene transfer, and somatic hybridisation (Bouis et al., 2003).

Crops are genetically modified to possess elevated concentrations of vital nutrients, exemplified by golden rice fortified with vitamin A to address malnutrition. The micronutrient concentration in goods can be enhanced through the incorporation of genes that generate the desired nutrient. This applies to staples that are generally lacking. The incorporation of the soybean ferritin gene into rice enhances the iron content of the grain (Goto et al., 1999; Ghafoor et al., 2024). Biotechnologically produced probiotics enhance gastrointestinal health and general immunity. When paired with prebiotics, they promote a balanced microbiota, enhancing digestion and mental health via the gut-brain axis. Genetic modification can enhance the availability and value of protein in food crops (Niba, 2003).

5. Challenges and Ethical Considerations

It is well acknowledged that monitoring human and animal exposure to environments potentially polluted with nanomaterials is necessary

to assess any detrimental effects. The issue escalates in complexity within intricate matrices such as food. Nanoparticles (NPs) are often administered through intravenous injections straight into the bloodstream, which disperses the NPs, complicating their retention and interaction with the target site. Consequently, a high-concentration medication is employed, which may fail to yield the intended therapeutic outcomes (Salar et al., 2024). Quantum dots, which contain cadmium, a cytotoxic metal, are a type of nanomaterial. Consequently, the emission of cadmium, whether from the degradation of particles or the progressive leaching of deposited quantum dots, is a considerable worry (Ghafoor et al., 2024). The primary environmental issue is that the minuscule nanoparticles may infiltrate water sources, jeopardizing the health of both humans and animals (Oberdörster et al., 2006). Nanoparticles pose significant dangers regarding their:

- Capacity to disseminate across the environment, including the possibility of long-range transport (Dispersal).
- Capacity to induce detrimental effects on environmental organisms (Ecotoxicity).
- Capacity to endure within the environment (Persistence).
- Capacity to bioaccumulate or bioconcentrate in upper trophic level organisms (Bioaccumulation).
- Capacity to eliminate or revert their initial entry into the ecosystem (Reversibility) (Grieger et al., 2010).

The technology must prioritize the four fundamentals of bioethics. Firstly, autonomy: acknowledging individual liberties and the significance of free will. Secondly, non-maleficence: refrain from purposefully inflicting pain, especially harm resulting from incompetence. Third, beneficence: the obligation to "promote well-being." Fourth, justice: guarantee equitable allocation of advantages and burdens among all impacted individuals (Ghayour et al., 2019).

Modernisation of biotechnology must consider the institutional necessities and cultural inclinations of any community impacted by the commodification and implementation of its products. Neglecting to do so will generate obstacles and impediments to the adoption of technology and advantageous utilisation (Chen et al., 2020). The values and trust substantially affect public opinions of biotechnology (Pauwels, 2013). Critical perspectives on biotechnology have been noted among stakeholder groups where cultural values shape opinions on biotechnology and gene editing. Understanding and respecting the diverse risk cultures (moral perspectives and values within and among communities concerning the perceived hazards and opportunities presented by new technologies) where biotechnologies will be implemented is crucial. These concerns collectively represent the potential public backlash against any biotechnology implementation, where specific organisations and NGOs may contest the use of biotechnology and perhaps contravene international laws and accords (Trump et al., 2023).

6. Future Directions in Nanobiotechnology for Health

Nanoparticles are utilised for illness diagnostics, medicine delivery, gene therapy for cancer, pulmonary disorders, and the prevention of various infections. Liposomes are coated with polyoxyethylene, inhibiting their opsonisation and subsequent absorption by macrophages (Senior et al., 1991; Chen et al., 2020). Quantum dots, owing to their prolonged stability, high sensitivity, and multi-contrast imaging capabilities, are employed for in vivo cancer detection and diagnosis (Morrow et al., 2007). Nano-biosensors are advantageous for the early detection of cancer. They can also be efficiently employed for tracking of cancer agents, including environmental contaminants, viruses, and carcinogenic gases (Mody, 2011).

The extensive body of research on the integration of nanotechnology with biology demonstrates that nano-pharmaceuticals and nano-diagnostics provide novel insights in healthcare. Consequently, these advancements are utilised in the biomedical sector in many capacities. Several medical items are already demonstrating potential advantages in the field of nanomedicine (Mohanty et al., 2009).

Nano-biotechnology has the potential to drive innovations by significantly contributing to diverse biomedical applications, including medication delivery, gene therapy, molecular imaging, biomarkers, and biosensors. One of the primary research objectives at now is target-specific medication therapy and strategies for early detection and treatment of diseases (Sahoo and Labhasetwar 2003). The majority of medical devices and treatments are at least ten years from market availability. Consequently, the manipulation of pharmacological targets and the implantation of devices necessitate a sophisticated technical infrastructure, such as nanotechnology, along with intricate regulatory oversight (Hamad-Schifferli et al., 2002). Future Innovations include nanoscale drug delivery systems, bioengineered therapeutics, and nano biosensors that facilitate accurate treatments, real-time monitoring, and early illness diagnosis. Ongoing breakthroughs in nanomedicine have expanded its use across various medical fields. The potential future use in diagnostic and regenerative medicine is presently under investigation. In diagnostics, the identification of sick cells would be expedited, enabling their treatment promptly before dissemination to other bodily regions. Moreover, persons experiencing significant traumatic injuries or compromised organ systems may derive advantages from nanomedicine.

Conclusion

The synergy of nanotechnology and biotechnology represents the groundbreaking ability to transform overall health. By combining nanoscale precision with molecular intuition from biotechnology, these fields tackle complicated health issues through innovations in the supply of medicine, diagnostics, regenerative medicine, and personalised therapy. Nanotechnology accelerates precise targeting, balanced drug delivery, and improved diagnostic precision, whereas biotechnology promotes developments in genetic moderation, biopharmaceuticals, and microbiome engineering. Together, they promote protective care, intensify treatment outcomes, and encourage mental and physical health. Regardless, unblocking the complete possibility of these advancements helps tackle problems like safety issues, regulatory troubles, ethical complications, and equitable access. Developments in research show that the combination of nanotechnology and biotechnology is assured to provide advanced conclusions for a future denoted by personalised, efficient, and holistic health, thus establishing the quality of life for people throughout the world.

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Molecular Biology of Stem Cell Therapeutics in Cancer Treatment: Underlying Potential Applications

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Abstract

Numerous populations of tumor cells that may survive, develop, and proliferate under specific circumstances make up cancer. Resistance to treatments and cancer recurrence might result from the often insufficient and nonspecific target therapy. The scientific study of stem cells was recognized as a viable approach to creating more potent anti-cancer drugs in the last few years. Regeneration, migration toward tumor locations, differentiation into many cell types, and modulation of adjacent cells are some of the amazing properties of stem cells. These abilities can be used in regenerative medicine, targeted medication administration and even the production of immune cells to combat cancer. This chapter has examined the molecular processes in connection with the application of several types of stem cells to cancer treatment, with an emphasis on how they could enhance treatment results, current advancements in medical or therapeutic applications, such as immunological modulation.

Keywords: Cancer treatment, Stem cell biology, Mechanisms, Potential Applications, Therapeutics

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Introduction

Scientists have pointed out that stem cells have provided substantial insights into morphological, developmental as well as physiological aspects of 'stem cell niche' its generation, support as well as tissue and organ repair potentiality in situations of damages. Because they may be able to promote the multipotent differentiation of stem cells, both in vivo and ex vivo into functional offspring that could assist mankind in repairing its defective tissues and organs, recent advancements in the stem cell biology are quite popular and holds significant therapeutic value (Siegel et al., 2016). The concept of an adult stem cell as a slowly dividing cell that is capable of differentiating into various mature cell types is relatively recent: the idea of a stem-cell 'lineage' is also novel – but compelling given that, for the most part, the multipotent adult stem cells are present in most tissues as well as organs of the body. These are stem cells derived from amniotic membrane, embryos, fetal tissue, and the UC. These include gastrointestinal system, pancreas, kidneys, lungs, liver, adipose tissues, muscle tissue, skin, eyes, bone marrow (BM), brain, heart, ovaries, prostate, breast, and testes (Vanneman & Dranoff, 2012).

Therapists may be able to tailor out more effective therapy regimens if they have a primarily understanding of cancer biochemistry. The treatment strategy depends on the kind and grade of cancer and goal of treatment. The first method of direct excision of solid tumors in one region is the surgical. The therapy can help to get rid of tumors by destroying the DNA of cancer cells. Chemotherapy utilizes very poisonous drugs to arrest or slow down growth of cases (Arnold et al., 2020). Immunotherapy, which encompasses adoptive cell transfer, checkpoint inhibitors, monoclonal antibodies, and cancer vaccines, has become a major cancer treatment with much improved clinical outcomes (Young et al., 2018). Nevertheless, the major limitations associated with current treatments include inability of current therapies to accurately identify and home in on tumor areas other than effector CAR cells; hence, present low efficacy, therapy resistance, and lead to tumor relapse (Cui et al., 2021).

In the meanwhile, the perspective in fight against cancer is stem cell treatment, which means all the treatment methods using stem cells. Due to that, it may enhance the efficiency of other drugs affecting tumors and reduce side effects (Zhang et al., 2017). Preclinical studies are now being conducted on a number of stem cell-based approaches, which present both significant opportunities and difficulties for cancer therapy (Zhou et al., 2021). Thus, it is necessary to evaluate more results to check their relevance for the further clinical study. The goals of this work are to introduce various forms of stem cells and discuss how they work to destroy cancer cells. We will also give you an update on recent advancements and the negative effects of this treatment. Additionally, this study will offer broad suggestions for the future.

Types of Stem Cells for Cancer Treatment

Stemness in anti-tumor therapy depends on different abilities depending on the stem cells' ability to move, to differentiate or replicate.

Pluripotent Stem Cells (PSCs)

ESCs, which are taken from inner cell mass of embryo is capable of developing all the variety of cells other than those forming the placenta. But there does not seem to be a vast use of ESC in clinical research due to ethical concerns. The discovery of Yamanaka factors in 2006 to create pluripotent stem cells from somatic cells in lab culture grew to become a primary development of cytology (Timmermans et al., 2009; Knorr et al., 2013). Like ESCs, these iPSCs resolve the ethical conundrum of destroying embryos. These days, HESCs and iPSCs are both useful tools for producing effector T- as well as NK cells and developing anti-cancer vaccines (Ouyang et al., 2019).

Adult Stem Cells (ASCs)

ASCs have the potentials capacity to differentiate into a variety of specific tissue and organ cell lineages. These cells that are mostly used in treatment of cancer include hematopoietic stem cells (HSCs), neural stem cells (NSCs), and MSCs. HSCs are mainly in bone marrow and are capable of producing all the body's adult blood cells. At the time of writing, the FDA has only certified that HSCs from cord blood can be used as stem cell therapies in disorders of the blood system, leukemia; multiple myeloma (Copelan, 2006). MSCs are particularly important in terms of tissue repair and regenerative medicine, and may be located in many different tissue types and organs of the body. They may exhibit exponential growth in vitro and differentiate into distinct cell kinds including osteoblasts, adipocytes as well as chondrocytes. Due to specific bio-and-immunological characteristics, MSCs have been employed to solve various tumor indications by transferring curative substances or as supporting injections (Christodoulou et al., 2018; Lin et al., 2019). Apparently originating from the brain and nervous system, NSCs are capable of autonomic proliferation and differentiation into glial and neurons (Kanojia et al., 2015).

Cancer Stem Cells (CSCs)

Regular stem cells and precursor cells can be transformed into cancer stem cells (also called tumor-initiating cells, cancer stem cells, or stem-like cells) by epigenetic modification. They often located in the tumor tissue; hence they are responsible for tumor growth, spreading and relapse. Consequently, focusing on CSCs might have the potential to treat numerous solid cancer kinds (Samadani et al., 2020). By concentrating on CSCs, scientists hope to develop more effective treatments that not only shrink tumors but also eliminate the root cause of metastasis and recurrence, offering a possible approach to treating many solid tumor types (Chang, 2016).

Mechanisms Underlying the Action of Stem Cells in Cancer

Stem Cell Homing and Integration in Cancer Treatment

When malignant tumors are treated with extremely high doses of chemotherapy to kill every cancer cell, leukocytes and blood-forming cells are either totally or partially killed. Some patients require intravenous injections of autologous or allogeneic HSCs at some point. Through a mechanism known as homing, these HSCs are believed to swiftly move into certain bone marrow (BM) stem cell niches. When the transplanted HSCs come into contact with BM, they undergo the engraftment process, which leads to the development of specialized blood cells (Chatterjee et al., 2021). The principal molecular means underlying the HSC homing process, the direct binding of the gradient SDF-1 created by the BM SCNs cells to the stem cell CXCR4 receptor. Extracellular ATP or UTP, ceramide-1 phosphate, sphingosine-1 phosphate, Ca²⁺, and H⁺ ions are additional molecular signaling molecules (SEITZ et al., 2005; Juarez et al., 2012). Moreover, HSCs need to interact with the endothelium through VLA-4/5, LFA-1, CD44, and the synthesis of the extrinsic matrix-degradable enzyme MMP-2/29 in order to move through blood arteries (Wang et al., 2023).

Stem Cells in Tumor Growth and Migration

Numerous cell types move led to the tumor microenvironment, which is defined by an accumulation of extracellular matrix (ECM) along with secreted paracrine substances. These cell types include endothelial cells, infiltrating immune cells, and MSCs. Because of their persistent oxidative stress, inflammation, and hypoxia, tumors are viewed as chronic wounded tissue that never heals. It is thus postulated that MSC migration to ischemia or injured areas as similar to MSC delivery into the tumor milieu. Actually, by secreting various chemoattractant substances, tumor cells and immune cells linked to malignancy can aid in this process (Pattabiraman & Weinberg, 2014). MSC migration into the tumor microenvironment is facilitated by the secretion of SDF-1, CCL-25, CXCL16, and IL-6 by osteosarcoma, myeloma multiplex, breast cancer, and prostate cancer cells, for instance (Sun et al., 2014; Jiang et al., 2019). Immune cells that are present in the tumor via secreting cytokines that favors inflammation including IL-1 β and TNF- α which in return attracts MSC inside the tumor and also prompts their differentiation. At the tumor site MSCs differentiate into myofibroblasts or endothelial cells that play a role in growth of tumor stroma (Sullivan et al., 2014).

Signaling Pathways in Cancer Stem Cells (CSCs)

Several key pathways involved in CSC function:

- Wnt/ β -catenin pathway
- Notch signaling
- Hedgehog signaling
- PI3K/Akt/mTOR pathway
- TGF- β signaling

Some of the molecular pathways which regulate regular growth of stem cells include these pathways. The constant alterations of those signaling processes will give rise to CSCs and then, cancer cells. Due to the relative high capacity for self-renewal, differentiation, CSC is

beneficial for growth, recurrence and metastases of tumor. These cells may also be the reason why the cancers are so invulnerable to normal treatments. Hence, understanding of the properties of CIKSCs is crucial to achieving the goal of finding a perfect cancer treatment (Matsui, 2016; Battle & Clevers, 2017).

Some of the tumor types in which CSCs have been identified include cancers of the gastrointestinal tract, leukemia, brain, breast, and lungs. They are single and characterized by techniques like metabolic/functional profiles, and surface proteins. CSCs exhibit similar features and functions of normal stem cells from which they are originated. However, some of the specific surface markers which are used to identify CSCs originate from highly dissimilar cancers including; CD133 (HSC marker), CD44, Lgr5, CD24 and EpCAM (Yang et al., 2020; Zhou et al., 2021). Furthermore, CSCs that has low proliferation rate, high glycolytic activity, immune tolerance and therapy resistance. Oncofetal and cancer/testis antigens are TAA which are normally produced only during germ cell differentiation throughout the embryonic development are some of the CSC specific immune TARAs that can be targeted for immunotherapy.

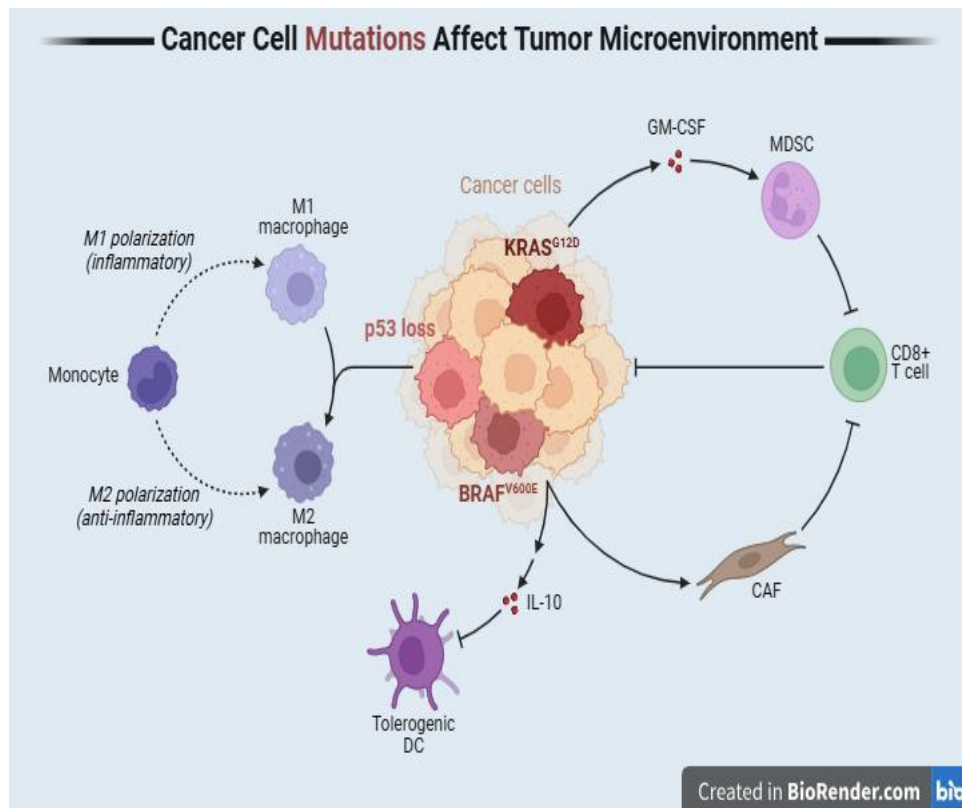


Fig. 1: Tumor Formation and its Complex Microenvironment

CSCs are generated when normal stem cells or precursor/progenitor cells have an epigenetic change (Figure 1). These cells play important function of stemness, initiation of tumor, their maintenance and also metastasis. Cancer associated immune cells such as T-cell, Macrophages (MΦ), Dendritic cell (DC), Cancer associated Fibroblasts (CAF) are present in the tumor niche but tumor cells and SCs. In addition, all of those cells secrete chemo attractant factors (CXCL16, SDF-1, CCL-25, IL-6, TNF-α & IL-1 β) which are involved towards the migration of MSCs towards the tumor cells and these all are involved in tumor progression.

The Potential Applications of Stem Cell Therapy in Cancer

Numerous approaches, including immunological effector cell synthesis, MSC injection for post-cancer treatment, HSC transplantation, stem cells as treatment vehicles, and cell vaccines, have been used to treat cancer using stem cell therapy.

HSC Transplantation

HSC transplantation, a routine treatment for leukemia, multiple myeloma and lymphomas following cycles of extreme intensity radiation and chemotherapeutic intervention. Furthermore, this procedure is currently being studied more actively in clinical trials for many cancer types when combined with immunotherapy or chemotherapy like the brain tumor, neuroblastoma, sarcoma, and breast cancer (Casper et al., 2010; Cieri et al., 2021).

MSC Transplantation after Cancer Treatment

Regular tissue injury and injury to the hematopoietic system often arise by intense cancer treatment involving tumor excision and doses of the treatment. There is convincing evidence that the infusion of MSCs improves the overall treatment result by preserving the indeterminate state and proliferation of HSCs. Moreover, in patients who suffer from refractory GVHD, the MSCs with immunosuppressive properties may indeed treat the fast and intensive immune reactivity. Co-transplanting MSCs and HSCs has produced encouraging results in recent clinical trials with no associated side effects (Méndez-Ferrer et al., 2010). Steroid-resistant GVHD adult patients are still receiving MSC derived from

mesenchymoangioblast through multi-center to determine the safety, tolerance and efficacy of MSC infusion. Furthermore, there are indications that MSCs can hasten the repair of injured tissues and organs and may even improve on the body's capability to withstand high dose chemotherapy as a means of increasing the effect of this nontoxic agent on tumors (Lan et al., 2021).

Stem Cells as Potential Therapeutic Carriers

The use of stem cell in cancer treatment is justified by the following reasons: For therapeutic molecules, some of their proposed advantages included:

- (i) Protection from rapid biological degradation
- (ii) Reduction in incidence of systemic toxicity
- (iii) Elevation of local therapeutic concentration due to inherent tumor tropism of stem cells.

The quantity of stem cells in the tumor's microenvironment determines how well this system fights tumors.

Genetically Modified Stem Cells

In order to increase the production and release of soluble factors such as prodrug-converting enzymes, chemokines, or tumor-toxic cytokines, this technique relies on the direct viral transduction of stem cells, including MSCs and NSCs. The former approach is commonly referred to as suicide gene therapy. Furthermore, they have persistent stem cells and may generate enzymes that change inert substances or prodrugs into active molecules that are even harmful to cancer cells (Chu et al., 2020). Furthermore, stem cells have the genetic capacity to create secretable cytokines and chemokines. TRAIL has a limited half-life because of the tumor-toxic TNF- α -related ligands that cause apoptosis after systemic delivery. Surprisingly, research has demonstrated that NSCs, which act as a gene courier that continuously regenerates TRAIL, can slow the progress of brain tumors and improve treated mice's life (Lan et al., 2021).

Nanoparticles (NPs)-Carrying Stem Cells

For a long time, NPs have been used to transport anti-cancer medications. The primary disadvantages are their unregulated absorption by normal cells, lack of targeted action, and quick elimination from the body. The ability of stem cells to easily transport NPs to tumor locations is intriguing. With this method, NPs may be absorbed into the cytoplasm or attached to the cell membrane's outer surface. Depending on their size, concentration, nature of the surface, and incubation time, NPs can be swallowed by active endocytosis or passive absorption. The two main issues are possible toxicity to the cell carrier and drug loading (Ertas et al., 2021). Additionally, stem cells can aid in tissue repair and regeneration, particularly after cancer treatments. Because autologous stem cells—those generated by the patient's personal body—reduce the risk of immunological disapproval, this approach is more customized and effective (Lin et al., 2023). The use of stem cells and nanoparticles shows enormous potential for developing more accurate, targeted cancer therapies with fewer side effects, however research and clinical trials are still ongoing. However, before this technology is used in clinical settings, issues like maximizing the makeup of nanoparticles and guaranteeing their effective loading with therapeutic compounds need to be resolved (Rosenblum et al., 2018).

Stem Cells as Carriers for Oncolytic Viruses (OVs)

These molecules increase in particular cancer cell, particularly over yielding vesicles (OVs). There is still the belief that in response to the OVs, tumor cell lysis occurs and that subsequent warning signals alert the immune system for enhanced control of malignant cells. While naked OVs can easily be identified and expelled from the body by the immune system. The stem cells might be presented as potential OV delivery and tumor-area safeguard vehicles. Similarly, MSCs were shown as efficient for loading attenuated oncolytic HSV and oncolytic OMV, and thus, the animals develop hepatocellular carcinoma and GBM (Marelli et al., 2018; Ghasemi Darestani et al., 2023).

Stem Cell-Derived Exosomes as Therapeutic Carriers

Exosomes have been used to contain a variety of cancer-fighting medicinal materials, including proteins, miRNAs, and small compounds. When compared to other manufactured nanoparticulates, these natural carriers provide a number of benefits, such as a higher loading capacity for the payload, improved internalization into tumor cells, and more stable and reasonably biocompatible nanoparticles. Additionally, it may be easily altered by adding certain proteins or ligands to the surface to improve the tumor microenvironment targeting effectiveness (Sun et al., 2021). Exosome loading of stem cell-derived anti-tumor mRNAs or siRNAs has been achieved, as in a traditional transfection method. For instance, exosomes released by marrow stromal cells containing miR-146b were recovered by Katakowski et al. In a rat model of a primary brain tumor, research found that injecting these exosomes directly into tumors inhibited the development of glioma xenografts. In a different study, exosomes released by MSCs that expressed miR-122 markedly increased the drug's anticancer activity on a model of hepatocellular carcinoma. Similarly, bladder cancer cells' polo-like kinase 1 gene was successfully silenced by siRNA mediated by MSC-derived exosomes (Wang et al., 2017; Burgos-Ravanal et al., 2021). There are two ways to load small molecule medications into exosomes: The first is that the human pancreatic cancer cell line's ability to proliferate was significantly suppressed by the exosomes of MSCs primed with paclitaxel. The study also showed that stem cells have the ability to absorb extracellular materials, load them onto exosomes, and then release them into the culture medium through the process of exocytosis (Lou et al., 2015; Zhang et al., 2022).

Stem Cell Source for Production of Immune Cells

Immunotherapy to cure anticancer has been in operation, and it involves the natural killer cells and chimeric antigen receptor T cells. Often the patient's own cells used to drive these clinical grade immune cells, stimulate them, transduce using CAR designs, amplify and then re-infuse the cells. This suggests that it is still challenging to control the number and quality of cells utilized in immunotherapy, especially in things like extensive chemotherapy or old age. Moreover, these CAR immune cells suggest in vivo anti-tumor efficacy, but it is usually limited due to their tendency to differentiate rapidly into short-lived effector cells (Bayik & Lathia, 2021). The differentiation process involves culture

of stem cells in growth media providing cytokines that trigger T or NK cells. Some of the examples of such cytokines are FLT3L, IL-15, IL-3 as well as IL-7 and SCF to enhance the growth of NK cells. T cell development was induced from hESCs as well as OP9 bone marrow stromal cells by culturing both in medium containing IL-7, SFC and FLT3L (Iriguchi & Kaneko, 2019; Leone & Powell, 2020). Interestingly, CAR induction on HSCs seems to be more beneficial for cancer therapy. In bone marrow, transplanted CAR-HSCs would differentiate and give rise to a range of immune cells with fitted CAR. These cells when coordinated would have improved immunity to attack and eliminate cancer (Lan et al., 2021).

Stem Cell-Based Anti-Cancer Vaccines

Since CSCs have been established to have a central role in the tumor progression and metastasis, targeting them would enhance the treatment regimens which are developed in the war against cancer. Of the various approaches targeting CSCs, anti-cancer vaccines are particularly rewarding due to their strong immunogenicity that may be derived from oncofetal peptides or CSC/ESC/iPSC based whole cells. Vaccine preparation commonly involves antigens and dendritic cells; such cells are employed to activate engineered T-cells for adoptive cell therapy or to induce naïve T-cell responses (Gjorgieva Ackova et al., 2016).

Due to the presence of tumor heterogeneity and rapid escape mechanisms, the oncofetal peptide-based vaccination is unable to induce immune responses adequate enough for tumor control when administered singly. The vaccines derived from whole cell lysates could be far superior to these. However, the fast emergence of CSCs knowledge still poses a challenge of extracting a few CSCs from the tumor tissue thus disallowing the use of CSCs as vaccine sources (Lu et al., 2018). Even more applications of cancer treatment could be identified if vaccines were produced from many antigens derived from ESCs or iPSCs. These two are the risks for tetraomic development and autoimmunity ignition. A higher number of immune cells combined with serum cytotoxic cytokines to support the idea that allogeneic ESCs autologous iPSC-based vaccinations were effective in eradicating tumor recurrence in mice as compared to xenogeneic ones (Arjmand et al., 2024). Vaccine treatment may not be effective due to preformed tumors, containing extremely immunosuppressive microenvironment, therefore, these vaccines should be employed only as a prophylactic measure. To increase anti-tumor immunity other therapies including chemotherapy, radiation treatment, surgery, inhibitors and adjuvants must be used (Bernardes de Jesus et al., 2020; Kishi et al., 2021).

Conclusion

Although HSC transplantation has shown beneficial in instances of hematologic malignancies, such as leukemia, myeloma multiplex, and lymphomas, GVHD is still a major concern for certain patients. It is important to note that different kinds of stem cells have been employed in different ways for anticancer therapy. Moreover, the carrying and actions of MSCs and NSCs, and their exosomes have been examined in comprehensive detail to deliver the therapeutic agents towards tumors in animal models; but the only application of stem cell carriers as a treatment modality called “suicide gene therapy” is listed to trials. Despite its benefits seen in preclinical and clinical studies, there are several critical barriers to overcome of stem cell treatment. In other words, while today the stem cell technologies demonstrated quite high efficacy of tumor therapy, more research is required to make their application safer and more effective for clinical trials. Furthermore, more primary studies would be performed to elucidate how stem cells communicate with tumor progression and metastasis under specific circumstances, so that the best stem cell engineering strategy could be chosen. Surprisingly, when combined with other drugs, including immune checkpoint inhibitors, the response to tumors with micro metastases and immune-mediated tolerance to cancer cells may be superior to current treatments for establishing cancer-free outcomes and preventing recurrence due to immune suppression and heterogeneity of the solid tumor environment.

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Future Trends in Lab Grown Meat from Stem Cell

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Abstract

As the population increases the demand for meat also increases, people are well aware of their nutritional needs and meat is a rich source of protein. But people are also concerned with the animal's welfare and want to fulfil their needs. To overcome this problem lab-grown meat from stem cells is a good initiative which will also increase as people's demand and awareness increase without sacrificing animals. Lab-grown meat from stem cells is actively researched as it represents the cellular product of cellular agriculture due to ethical concerns, environmental factors, and global food security. For market entry understanding stem cell meat and establishing the safety regulations and standards are necessary and crucial. To develop high-quality cultured meat at a wide scale we need high throughput technology but also consider the fact lab-grown meat is still in the early stages because of consumer acceptance and limitations in technology. Understanding the techniques, technology and regulations of cultured meat will open new ways for cellular technologies and help the growth of country's economy.

Keywords: Lab-based meat, Cultured meat, Animal welfare, Stem Cell, Livestock industry, Future trends

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Introduction

The most important source of feed for humans is meat which is “muscle tissue of slaughtered animals” (Heinz & Hautzinger, 2007) because of its nutritional properties and benefits for human health (Wyness et al., 2011). Approximately world population by 2050 will be almost 10 billion and there will be not enough production from conventional methods to fulfil the nourishment requirements of people globally (Eibl et al., 2021). The renowned British statesman, Winston Churchill (Churchill, 2016) indicated that in the future tissues of chicken muscles would be grown independently, by eliminating the devoid to raise chickens. This groundbreaking idea set the beginning of a journey into the realm of cultured meat production. Various researchers have described the possibility of growing meat in labs, as years pass, paving the way for an insurgent approach to food technology. Known as cultured as well as in vitro meat, under controlled conditions cultivated animal tissues grow in laboratories in this method. This provides the solution for many challenges related to traditional meat (Wang & Rudnicki, 2012).

One of the most potential solutions to solve the future problems of food security is cultured meat, which is the spiralling field of agribiotechnology, uses culturing microbes, animal & plant tissue and cells to produce agricultural products (Rischer et al., 2020). Like for the meat industry, consumer satisfaction and preferences are the most important concerns. Consumers' beliefs and behaviour mainly affect the product itself because of the negative image like its connection with the living animal, environmental issues, ideological and moral concerns and the slaughter conditions. So, changes in food production are required as unconventional protein-rich products are increasing in popularity among consumers. Because changes in the eating behavior enforces livestock farming and agriculture to bring the evolving period (Sharma et al., 2015). Foodborne illness is caused due to inappropriate animal welfare conditions so, cultured meat will reduce the growth of animals on farm so there will be no problem with animal welfare and reduce chances of foodborne illnesses from harmful pathogens like Salmonellosis and *E. coli* (Ben-Arye & Levenberg, 2019).

Cultured meat serves different advantages like competition to other protein products, needs no large space for animal upbringing, is more economical and reduces food-borne illness (Benjaminson et al., 2002). So, ongoing experiments on initial stem cells under control conditions to grow small cell tissues. As enriched protein diet is essential for humans that will be provided by cultured meat and conventional meat cannot fulfill these requirements.

Driving Factors behind the Growth of Lab-Grown Meat

In 2013 Lab-grown meat was first introduced, but did not receive global commercial approval until 2020 when Singapore became the first country to approve the sale and utilization of lab-grown chicken meat. Key factors driving its development include ethical behavior and animal welfare, consumer health, the safety of food, and environmental sustainability. The introduction of lab-grown meat aims to support a sustainable food supply, especially during periods of booming population and global crises, like pandemics (Warner, 2019; Chong et al., 2022).

Advantages

1. Increased Meat Production: Addresses the growing demand for meat.
2. Customizable Nutrition: Can be developed as a functional food with a tailored nutrient profile to meet dietary needs.
3. Ethical Benefits:
 - Reduces animal sacrifice and cruelty.
4. Environmental Benefits:
 - Lowers greenhouse gas emissions and production of ammonia from farming livestock.
 - Reduces the carbon footprint of animal husbandry.
5. Food Safety and Public Health:
 - Reduces the risk of foodborne illnesses due to the absence of antibiotics.
 - Lowers the risk of zoonotic disease transmission.

Challenges

1. High Production Costs: Currently expensive compared to conventional meat.
2. Environmental Concerns: May still produce significant levels of carbon dioxide.
3. Health Risks: Potential unknown health effects, such as the risk of cell line deregulation leading to cancerous cells.
4. Cultural and Religious Barriers:
 - Conflicts with dietary laws, such as Halal requirements in Islam and prohibitions against beef and pork in Hinduism.
5. Technological Limitations:
 - Limited production quantities.
 - Dependence on animal serum for culture medium, making it not entirely slaughter-free.
6. Consumer Acceptance:
 - Taste and texture do not yet fully replicate conventional meat.

Environmental Sustainability

Excessive meat consumption has significant environmental consequences. The main contributor to global warming is the meat industry, as it requires to fulfil livestock needs substantial resources, like soil and water, while also generating large amounts of (GHG) greenhouse gas emissions (Ben-Arye & Levenberg, 2019; Ben-Arye et al., 2020). 95% of greenhouse gas (GHG) emissions come from livestock farming, which includes methane, carbon dioxide, and nitrous oxide. Activities such as fertilizer application, manure management, land grazing, and enteric fermentation in animals are the reason for these emissions and implemented significantly to degradation and environmental pollution (González et al., 2020).

Aggressive livestock farming is the main cause of air, water and land pollution. High concentrations of environmental ammonia (NH₃) are released by livestock farming, which arises from the breakdown of uric acid in animal dung and urine through urease activity. Air and water pollution are the results of these emissions and can have harmful environmental effects (Jacobsen et al., 2019). In livestock manure management ammonia is a common odor-causing substance, and in composting areas concentrations reach up to 4100ppm. In present challenges for waste management in livestock farming these high ammonia levels can contribute to air pollution (Wang et al., 2021).

Although animal products account for fewer than 20% of the global supply of food energy, their production has disproportionately negative impacts on natural resources. Greenhouse Gas Emissions: Food production and consumption are responsible for approx. 13.7 million metric tons of CO₂ commensurate with, contributing around 26% of all human-induced greenhouse gas emissions. Terrestrial Acidification: The food supply chain contributes to 32% of global terrestrial acidification, impacting soil health. Eutrophication: It accounts for about 78% of eutrophication, which disrupts aquatic ecosystems by promoting excessive nutrient accumulation (Searchinger et al., 2018). Deforestation for livestock pastures and animal feed production is a major environmental issue, particularly in regions like South America. Countries such as Brazil, with its extensive tropical forests, have experienced significant deforestation, where large areas are cleared to create pastures for livestock and soybean fields used for animal feed. This practice contributes to biodiversity loss, carbon emissions, and disruption of ecosystems (Nepstad et al., 2014).

Cultured Meat

Under controlled laboratory conditions lab-grown meat is created completely by using animal cell culture methods. This process combines bioengineering, tissue engineering, biological chemistry, and techniques of chemical and bioprocess engineering (Ben-Arye et al., 2020). (Figure 1). Cells, signals, and scaffolds are three key components required for tissue engineering. First of all, select the most suitable type of cell and it is crucial as a starting point. Next, choose a biocompatible tissue scaffold to provide structural support that will enable the cells to grow and transform properly. Finally, at the last step it is essential to supply the cells with appropriate nutrients and signaling molecules to make sure the proper growth and development of the cell (Hamdy, 2023; Santos et al., 2023). The making of the first hamburger from lab-based meat marked a significant turning point in the historical events of the food industry, igniting the development of this innovative technology in the years that followed in the future. Besides this, meat production was entirely dependent on traditional animal husbandry, a system that not only consumed natural resources at unsustainable rates but also contributed to some of the planet's most crucial environmental challenges.

To expand the lab base meat many startups and research teams around the world are working today, aiming to make this technology widely accessible to consumers. The majority of these efforts are carried out in the United States and the (EU) European Union (Rubio et al., 2020). In late 2020, the Singapore Food Agency (SFA) made history by granting regulatory approval to Eat Just Inc, allowing the inauguration to sell lab-base chicken meat. This allows the first time a government authorized to commercialize the lab-grown meat. Firstly, the product

was sold in the restaurant for around \$23 USD. By contrast, the very first lab-grown beef burger, created in 2013 by the Dutch startup Mosa Meat, came with a production cost of approximately \$330,000 USD (Morais-da-Silva et al., 2022). Brazil, a leading global producer and exporter of meat, is now home to research groups conducting pioneering studies on cultured chicken meat. These efforts aim to include sensory and nutritional analyses, which are anticipated to be completed by 2024 (da Silva & Conte-Junior, 2024). To achieve a high-quality result in lab-grown meat, advanced technology is essential at every stage of the production process.

Stem Cells

To make lab-grown meat, scientists discovered different stem cells. Researchers first discovered Myoblast or satellite cells. Adult stem cells from tissue play a crucial role in helping muscles repair after an injury. However, maintaining their growth potential in cell culture has proven to be challenging (Mauro, 1961; Collins et al., 2007). When cultured in large quantities, satellite cells readily differentiate into myotubes and additionally developed muscle fibres. This characteristic makes them an ideal cell origin for constructing tissues of muscle. Recent findings on mature satellite cells reveal that few are particularly efficient at the repair and regeneration, further highlighting their potential in tissue engineering (Pallafacchina et al., 2013; Kaczmarek et al., 2021).

Stem cells exhibit a range of characteristics, from totipotency (capable of developing into a complete organism) to monopotent (having power in one way only), in a hierarchical order. Selecting the appropriate cell type is critical for producing lab-based meat through in vitro cell culture. Additionally, replicating the in vivo environment, known as the stem cell niche, is crucial for maintaining cells in vitro. Typically, the physical substrate that supports cells is replaced by scaffolds, while body fluids supplying nutrients are substituted with culture media (Tewary et al., 2018). Somatic muscle is composed of various types of cells. Muscle fibres are formed when muscle cells from embryos and young animals divide, transform, and fuse with each other, creating large cells that contain multiple nuclei. Attempt to stimulate the growth of more muscle fibers often fail because cell nuclei in most of the muscles remain lifeless and do not divide. While cells of embryonic stem can grow and differentiate into various cell types, this process is challenging to induce, limiting the number of cells that can be harvested. It is unclear whether embryonic stem cells can continue to grow rapidly and become somatic muscle cells or if they will differentiate into other cell types. Therefore, the most promising cells for lab-based meat production are expected to be those derived from the muscles of embryos or young animals (McFarland et al., 1991).

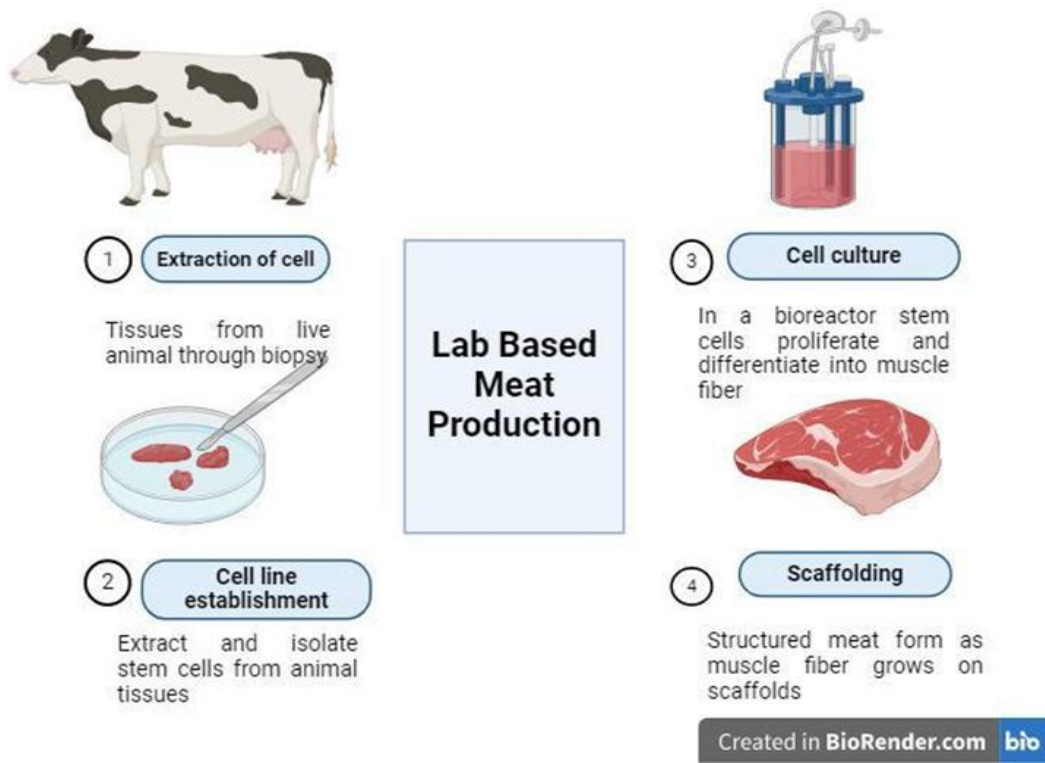


Fig. 1: Structure for lab-based meat production

Cell Culture

Cell development normally occurs in cell culture media including (DMEM) Dulbecco's Modified Eagle Medium and (MEM) Minimal Essential Medium. Fetal bovine serum (FBS) and/or horse serum are used to boost these media, which provide essential growth factors that support and encourage the growth of cell. To support cell growth, providing additional growth factors that aid in the growth and differentiation of cells other cell cultures have also incorporated chicken embryos as a natural essence (Stephens et al., 2018; Srutee et al., 2022). To manage metabolic processes and assist the differentiation of muscle cells, hormones like insulin and dexamethasone are commonly added to the cell culture media. The formation of muscle tissue and the development of cells are guided and supported by these hormones. To maintain the optimal pH of the cell culture medium HEPES and bicarbonates buffering agents are crucial (Tyagi & Mani, 2023). To ensuring cell viability and function it is important, as changes in pH can negatively impact cell growth and activity.

To simulate the intrinsic environment of cells, cell culture medium solution was designed carefully due to its complexity. To assist the growth of cells and their functions it supplies essential nourishment, growth factors, and other components needed. On this basis for the production of cultured meat, the medium is specifically adapted to support the growth and differentiation of muscle cells, facilitating the growth of the tissue of muscle that closely looks like natural meat (Lee et al., 2023).

Table 1: Lab Based Meat Challenges in Industry

Limitations in Technology	Laws and Legislations	Consumer Acceptance
- Cell line - Media of cell culture - Scaffold and Biomaterials - Bioreactors	- Food Labeling - Risk Assessment	- Food Neophobia - Economic Anxieties - Socioeconomic in Meat Consumption

Scaffolds and Biomaterials

In the industry of lab-based meat, evolutions in scaffold technology are crucial to copy the 3D structure and feel of real meat. The formation of efficacious scaffolds remains a significant technological challenge in lab-grown meat production. Current scaffolds used in muscle tissue engineering can only achieve thicknesses of a few mm (around 3 mm) and often exhibit derelict mechanical properties, which limit the attachment of cells and multiplication (Stephens et al., 2018; Seah et al., 2022). In in vitro (artificial insemination) culture, scaffolds serve as biomimetic materials that replicate the in vivo (in living organisms) stem cell niches by giving a 3D clammy surface (Figure 2). This helps the morphogenesis of stem cells and the maturation of tissues, unlike the 2D cultures using traditional tissue culture plates.

To arrange artificial tissues from stem cells in vitro hydrogel and porous scaffolds are commonly used. Hydrogel is a hydrophilic polymer and is particularly effective for generating self-arranging artificial tissues or organoids, from stem cells. These scaffolds enable stem cells to follow their revolutionary programs, facilitating in vitro morphogenesis by copying in vivo micro-environments (Ostrovidov et al., 2014; Hofer & Lutolf, 2021). It's essential to adhere to specific guidelines for scaffold use when producing lab-grown meat. Scaffolds must be biocompatible, meaning they are safe for the body and capable of degrading over time. They should have appropriate strength and structure to support cell growth. If we compare 2D and 3D culture systems, 3D fat production enhances both the effectiveness and the degree of discrimination. While the 2D culture commonly results in lipid accumulation of multi-layer. Large, unilocular lipid droplets can be produced in the 3D system, which are features of mature adipocytes. Additionally, 3D culture induction promotes a higher discrimination rate compared to traditional monolayer cultures (Ma et al., 2018; Dohmen et al., 2022).

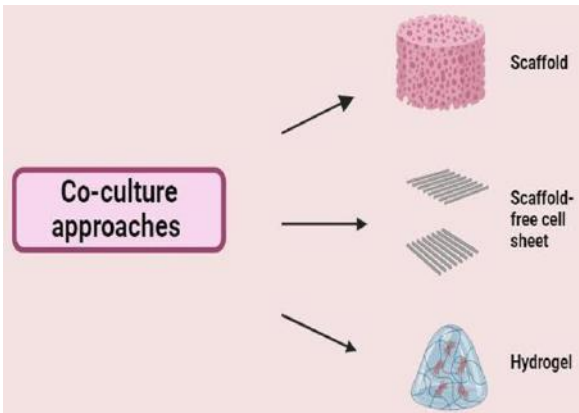


Fig. 2: 3D culture technique for the cultured meat process

Scaffolds must have the correct size and texture, adapted to the desired function. Based on the specific requirements for muscle tissue formation of features of the scaffold should be carefully selected (Levi et al., 2022). On other hand, plant-based protein scaffolds have gathered significant scientific interest due to their huge accessibility, lowness, biological acceptance, and considerable nutritional value. Moreover, they offer benefits for environmental sustainability and animal welfare. However, one limitation of using plant-based scaffolds is their relatively poor mechanical properties and their ability to carry the growth and effective development of muscle tissue can be affected by this. This issue can be resolved through several approaches, such as using processes like chemical, physical, or enzymatic crosslinking, or by incorporating materials with better mechanical properties. The most commonly used plant-derived proteins for scaffold production are zein and soy proteins (Ben-Arye & Levenberg, 2019).

Consumer Perception

An innovative alternative to traditional meat is lab-grown meat, which raises the question of how will consumer react or what will be their perception. Industry plays an important role in consumer acceptance because of consumer perceptions associated with food technology and consumer's trust in the industry (Siegrist & Hartmann, 2020). Diseases that spread from animals to humans and that are resistant to antibiotics are also concerns of consumers so the best possible option is cultured meat which also fulfills demand for meat in the world (Tuomisto, 2019; Tuomisto, 2021).

(Table 1) Lab-grown meat makes sure it is safe to eat and good quality that is checked by the digital systems which prevent bacteria to enter in the food when prepared. To check if meat tastes good and fulfills nutrients' requirements after its preparation we need to use a control system (Bhat & Fayaz, 2011).

Conclusion

Lab-grown meat from stem cells is a revolutionary change in the meat industry in the way we produce meat and consume it. The demand for sustainable and ethical alternatives to traditional meat production becomes necessary as the globally, population continues to grow and intensify environmental challenges. The advancements in cell culture techniques, stem cell research, and bioreactor technology have brought cultured meat closer to commercial viability, offering the potential to reduce usage of land, consumption of water, and emissions of greenhouse

gas but also addressing animal welfare concerns. But with that there are still significant challenges to overcome, such as scaling production, reducing costs, and navigating regulatory landscapes and consumer acceptance. However, the rapid pace of innovation in this field, alongside growing consumer acceptance and investment, signals a bright future for lab-grown meat. As technology evolves and new solutions emerge, cultured meat could play a crucial role in ensuring food security, improving sustainability, and reshaping the global food system. The next few years will be pivotal in determining how this technology integrates into our diets, ultimately transforming the way we think about meat and its place in the world.

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Mechanistic Exploration of Gold Nanoparticles as Adjuvants in Enhancing Vaccine Responses to Infectious Pathogens

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Abstract

Improvement in the development and administration of vaccines has incorporated with the use of nanoparticles. In this regard, Gold Nanoparticles (GNPs) are considered for numerous good reasons. They are resistant to chemical reactions, can bind to small molecules and are relatively easy to produce hence being suitable for vaccine engineering. Also, GNPs are useful in disease diagnosis and research because of their swift circulation in the body and their response to detection. Among their properties, the immunostimulant effects and increasing the efficiency of vaccines are most valuable. These GNPs can also incorporate antigens, which will guarantee the delivery of vaccines to a particular target tissue. When formulated with antibodies they can be targeted at delivering to a tissue or cell. These characteristics include size, structure, cost, and optical properties governance of their interaction with the immune system. Some findings indicate that GNPs can act to activate immune cells that include dendritic cells, T cells and B cells. This chapter's main goal is to demonstrate how GNPs are used to create nanovaccines that protect against a variety of infectious agents, including bacteria, viruses, and parasites. Even though GNPs have drawbacks and a low but noticeable amount of toxicity, their advantages make it worthwhile to devote more time and effort to creating innovative vaccine approaches.

Keywords: Nanoparticle immunology, Gold nanoparticle, GNP, Nanovaccine, Nanovaccine immunity

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Introduction

The vaccines have come a long way from the infectious diseases to cancer vaccines. This development is primarily attributed to the growth of nanotechnology. Nanoparticles (NPs) have been proven useful in vaccines production. Another crucial component of vaccine development is selecting the proper adjuvant — the substance used to jump start an immune reaction. Scientists have investigated various nanoparticles in order to evaluate their immunomodulatory potential in other disease models. These nanoparticles not only enhance the immunogenicity of the vaccine, but also have the function of delivery for the vaccine. Distribution technique, shape, size, and amalgamation of the antigen into the NP have an impact on the proficiency of it (Comber & Bamezai, 2015; Salazar-González et al., 2015). Much research has been conducted in the recent years to understand how nanoparticles modulate immune system and how they can enhance immunity, minimize adverse reactions and eliminate side effects (Frey et al., 2018; Kelly et al., 2019). Out of all the tremendous number of nanoparticles that have been involved in various vaccine endeavors, one can distinctively remember gold nanoparticles (GNPs). Because of their facility in their labeling with antigens & due to their ease in chemical point of view, GNPs are useful in preparation of vaccinations (Fai & Kumar, 2021). Some of the unique properties that are attributed to high surface area volume ratio of GNPs are peculiar plasmonic excitation, strong binding affinity and electronic structure (Personick et al., 2011). Additionally, it allows GNPs to engage with many types of ligands and functionality groups to improve the steadiness of the functionalized GNPs. Due to low toxicity of colloidal gold, magnetic and optical characteristics, it is applied in the treatment of multiple diseases (De Matteis et al., 2020). In some trials, multifunctional GNPs have been used in aggregation with FDA-endorsed antibiotics and antimicrobials (Fan et al., 2019). Also, GNPs conjugated with antigenic peptides have been able to effectively elicit high titer pathogen specific antibodies (Quach et al., 2018).

To achieve a specific and planned release at the intended target site, the researchers can employ GNP based systems to deliver drugs or antigens (Lee et al., 2018). These GNPs can be modified in a way that particular molecules or antibodies can attach themselves to the GNPs' surface in order to significantly increase the selectivity with which they bind target cells. Gold nanoparticles upon interaction with biological systems lead to some changes in that system as well as in themselves as indicated by figure 1. It increases the immune reaction at the area of

point injection while decreasing detrimental effects in other areas of the body (Kalishwaralal et al., 2020). Moreover, GNPs have additional immunoadjuvant effects that enhance the immune reaction. Researchers have the potential to authorize the immunogenicity of GNPs by altering shape, charge, size and surface disposition when explore a biological system (Dykman & Khlebtsov, 2019).

Key Characteristics and Roles of Gold Nanoparticles in Vaccine Development

As potent antigen trailers in immunization, gold nanoparticles (GNPs) are also extensively used. They could be considered perfect because they are easily formed, have unique chemical and physical properties and are reasonably non-toxic (Fan et al., 2020). Resultantly, these nanocarriers need to be directed straight at the definite immune cells or locations. The immunological response or vaccination requires the provocation of immune-related genes, antigen processing, antibody generation, cytokine creation and T cell activation, all of which are facilitated by this direct transport (Pati et al., 2018). GNPs fall under the class of tiny, highly surface-aread nanoparticles that can breach barriers and blood arteries. Their chances of attaining their destination are increased because they can be captivated by cells (W. Wang et al., 2020). Furthermore, GNPs are environmentally assisting because of their degradability in water and their chemical inertness. They may be modified with other peptides and compounds, thus they can be presented in various forms and to be slightly more sophisticated. Also, nanoparticles are stable, which enable broad areas of utilization as shown in figure 2 (Amina & Guo, 2020).

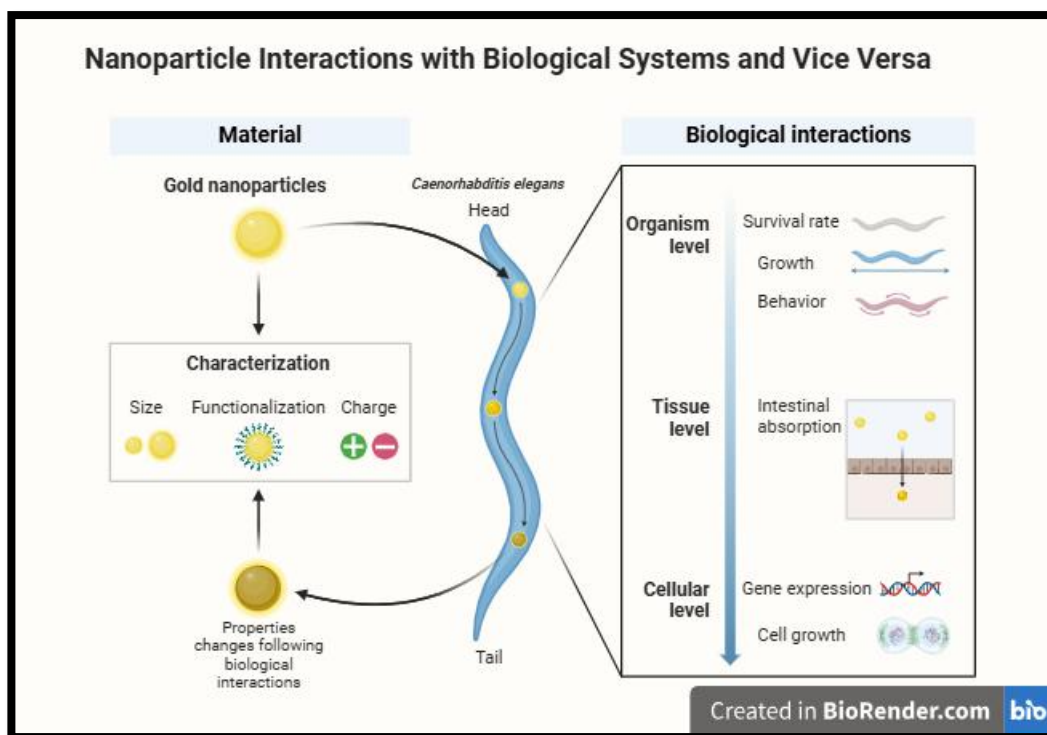


Fig. 1: Change in properties of Gold Nanoparticles upon interaction with Biological Systems and vice versa

Viral genes can be utilised in vaccine production to incorporate GNPs into viral structures called virus like particles (VLPs) (Wang et al., 2016). It can also be adsorbed to proteins and polysaccharides before use as an antigen. According to past research, the gold sugar nanoparticles have immunomodulatory effects. Furthermore, GNPs also boost the immune system which makes them preferable in preparing vaccines. Due to these characteristics, GNPs are presented as the media technology desired to be applicable in medication delivery, injection, and disease diagnosis (Dykman, 2020).

Impact of Gold Nanoparticle Morphology on Immune Responses

The size and form of the GNPs have great influence on the manner in which they behave in a host's immune system. Most of these characteristics determine the manner of functioning of these proteins as the enhancer and in modulation of the immune system for various illnesses (Kohout et al., 2018). For example, in bone marrow-derived dendritic cells (BMDCs), the rod-shaped GNPs increase interleukins, particularly IL-1b and IL-18. However, when normal cells, granulocyte macrophage colony-stimulating factor (GM-CSF), IL-6, and IL-17 are present, the spherical GNPs are active in activating cytokines (Cai et al., 2022). (Niikura et al., 2013) studied on the impact of shape of GNPs; spherical, rod and cube on the immune system. Comparing their study's findings, the scientists noted that these nanoparticles' capacity to generate antibodies or TNF α depends critically on their surface area to size ratio. When it came to cytokines like IL-6 and IL-12, the largest GNPs-about 40 nm in size-were more effective than smaller or other nanoparticles. The antibodies that GNPs form, are similarly prejudiced by their chemical makeup. It is conjectured that changes to the particle surface, such as roughness, antigen coating or hydrophobicity influence the type and degree of immunity (Farfán-Castro et al., 2021). Besides, the location of GNPs within cells is also inclined by their size. For instance, the larger nanoparticles, with a size of between 5.5 and 8.2 nm, aggregate in the cytoplasm; and 2.4 nm nanoparticles are internalized through endocytosis. However, GNPs with size >18-20 nm do not enter the cells at all (Mulens-Arias et al., 2020).

Effect of GNPs on Dendritic Cells, Macrophages, and Natural Killer Cells

Dendritic Cells

Dendritic cells (DCs) are critically important for initiating immune response and GNPs exert a robust immunomodulatory effect on DCs. Researchers can attach several chemicals to the GNPs surface in order to thus support the immune response system and make it even more clumsy to the target DCs. (Cunha-Matos et al., 2016). In one study, animals containing *Listeria monocytogenes* antigens received DCs which have been loaded with GNP. This strategy generated an effective Th1 immunity which was attracting CD8+T cells and killer cells and the vaccine was much more effective than conventional approaches, proving the GNP system's capability of strengthening the immune system (Rodriguez-Del Rio et al., 2015). An endotoxin- like effect is observed in BMDCs that release proinflammatory cytokines such as IL-6, TNF- α , and IFN- γ when they take up GNPs. These cytokines participate in initiating as well as maintaining immunological reactions (El-Sayed et al., 2021). In addition, GNPs can stimulate neutrophil to release extracellular decoy that causes immune reaction through DNA receptors such as Toll-like receptor 9 (TLR9) (Staroverov et al., 2019). It has become evident that GNP coatings interfere with how well they interact with dendritic cells. Namely, it points at GNPs that may interact with monocyte-derived dendritic cells (MDDCs), if the latter are coated with polyethylene glycol (PEG) or polyvinyl alcohol (PVA) or both. Although the PEG coating improved the aspect of cells creating TNF- α , it reduced the quantity of GNPs these cells could uptake. On the other hand, GNPs conjugated with PVA or PEG-PVA blend caused higher levels of IL-1b release which was in equal proportion to the amount produced. However, neither of these coatings seemed to have a direct effect on the MDCs themselves; namely, their phenotype or functionality (Fytianos et al., 2015)

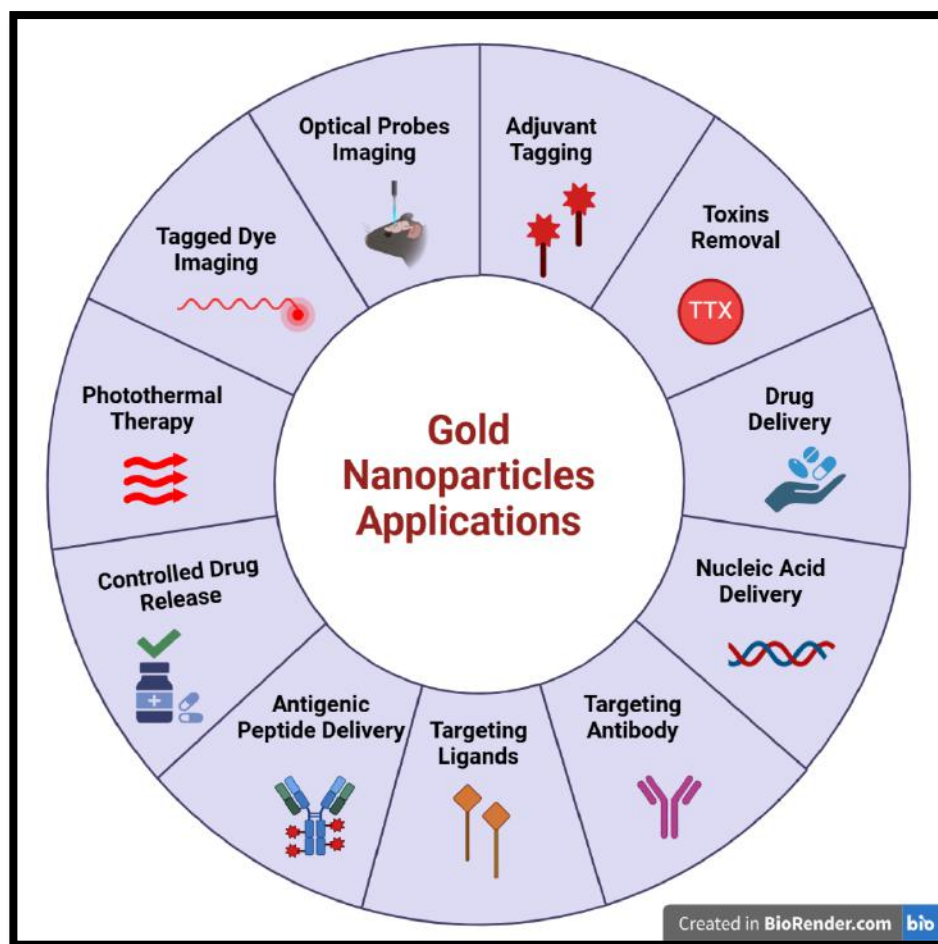


Fig. 2: Applications of Gold Nanoparticles

Macrophages

Macrophages have a versatile role in distinguishing and creating the immune system, as well as preventing diseases from arising. (L. Wang et al., 2020). It has also been discovered that the internalization of GNPs enhances the macrophage ability to communicate with other cells, a key characteristic of tissue repair and regeneration (Luan et al., 2020). Notably, GNPs inhibit the ability of macrophages to store proinflammatory cytokines. GNPs were reported to have similar impact on the spleen cells that are sensitized with LPS, which attacked the immune system, or show that they can modulate excess inflammation (Kingston et al., 2016). The capture of free radicals from these cells is again an important attribute of macrophages of GNPs. For instance, GNPs have been found to reduce the levels of Reactive Oxygen Species (ROS) in LPS stimulated mouse macrophages in a concentration dependent-manner. This decline is related to the decrease of the synthesis of other cytokines, such as TNF- α and IL-17 involved in inflammation. They describe how GNPs may function as guardians of inflammation and present a new treatment approach (Jiao et al., 2016).

Natural Killer Cells

In the circulation, natural killer cells (NK) originating from the lymphoid progenitor lineage are strictly required for immunological shadowing. To induce infected cell death, they release perforins and granzymes. To guide the targeting of GNPs to NK cells, the mechanism of NK cell mediated antibody-dependent cellular cytotoxicity (ADCC) has been planned out. This is the manner through which antibody-tagged GNPs utilize as well as interact with NK cell receptors. This enhances the activation of NK cells to deliver performances (Jiao et al., 2016). A new approach of immunotherapy is a technique for employing PEGylated polyamidoamine dendrimers confined in GNPs to direct human ferritin heavy string into NK cells (Qu et al., 2019). Such an agent, when used to treat NK cells in vitro, gives GNPs a new shape that behaves anti-inflammatory, excitedly reducing IFN- γ emission (Elbagory et al., 2019).

Use of GNP in Antiviral Immunization

The researchers specifically prefer to use errand gold nanoparticles because of their multidisciplinary and viral vaccine characteristics. Their capacity to deliver and address particular cells makes them a unique method for vaccine manufacturing. In addition to enabling the transport of antigens, these nanoparticles provide the attached or core formulations optimal antiviral protection and enhance immune response. Besides their immunomodulatory properties, GNPs support the release and delivery of antigens for continuous effective immunization. Due to their qualities, they are an indispensable component of today's vaccines and a dynamic factor in the virus disease control system.

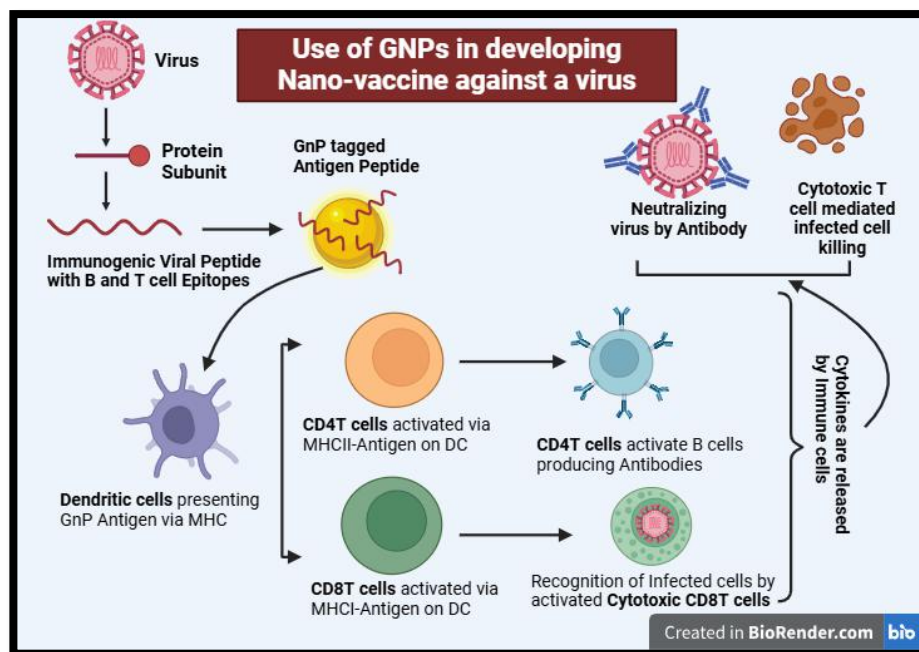


Fig. 3: A schematic representation of the use of GNPs in developing nanovaccines against a virus

Figure 3 explains how any conserved, immunogenic peptide that is separated from a virus and attached to GNPs to form a nanovaccine is studied on mice. Even when the vaccine is given, dendritic cells transport the peptide to CD4 helper T cells and CD8 cytotoxic T cells, resulting in immunological initiation. This causes B cells to become activated and helper T cells to thrive clonally, which produces certain antibodies. While cytokines produced during this immune response help in forming either Th1 or Th2 responses depending on the degree of inflammation, cytotoxic T cells trace and eradicate infected cells. Long-lasting immunity is recognized by the development of memory B and T cells and the efficient neutralization of the virus by the formed antibodies. This ensures a rapid immune response to future infections by the same virus, possibly averting severe illness (Carabineiro, 2017).

1. HIV

The envelope glycoprotein of the human immunodeficiency virus (HIV) known as gp120, has a significant cluster of mannose-rich glycans, which is identified by 2G12-like antibodies. Gold nanoparticles that could link with 2G12 were formed using a monolayer covering of self-assembled oligomannosides, which looked like gp120 (Abia et al., 2013). Furthermore, GNPs coupled to thiol-terminated oligosaccharides have been employed in the formation of HIV vaccines (Chiodo et al., 2015). When coated with a synthetic fractional structure of several mannosidases, GNPs with a size of 2 nm show exceptional binding to anti-HIV antibody-like 2G12. Alpha helices or beta strands can be formed by conjugating the third variable region (V3 peptide) of HIV1's gp120 to GNP. In addition to manufacturing a large quantity of particular neutralizing antibodies in rabbits, this increases their steadiness against peptidase dilapidation in any form (Xu et al., 2012).

2. Hepatitis B

Gold nanoparticles (GNPs) have been publicized to be an auspicious platform for diagnosis and cure of hepatitis B. One such ground-breaking tactic involves extraction of hepatitis B virus (HBsAg) DNA from epidermal cells with a GNP coated gene gun that has been shown to be a calming strategy (Negahdari et al., 2019). The second important application involves the use of GNPs as an adjuvant with plasmid DNA

encoding HBsAg, injected into mice. Incorporation of GNPs not only increases the immune response but also expedites antibody production such that animals reach peak antibody levels sooner than with standard methods. Additional in vitro studies have also shown further advantages. When RAW 264.7 macrophages were treated with HBsAg conjugated gold nanocages, antigen uptake and processing capacity were increased. Along with this secretion of interleukin-4 (IL-4) further implies an increased immune response. In addition, new progress shows that GNPs are particularly useful for the detection and identification of HBsAg, which represents a new and powerful method for monitoring hepatitis B infection (Kim et al., 2018).

3. Hepatitis C

Using conductive plasmonic gold nanoparticles (GNPs), a research team has unveiled a new approach to a highly effective hepatitis C DNA vaccine. The formation of pores in the cell membrane allows this unique opening, which greatly increases absorption of the DNA vaccine. The findings were surprising: The mice in the group that got GNP had the gene at 100 times the level of the control group that didn't get GNP. Mice treated with GNPs also have enhanced immune responses, with markedly increased humoral (antibody-mediated) and cell mediated immunity (Draz et al., 2017).

4. Dengue

Domain III envelope glycoprotein derived from serotype 2 of the dengue virus to bind gold nanoparticles (GNPs) of different sizes (20, 40 and 80 nm) was used. Subcutaneous administration to BALB/C mice 3 times was done. The results were encouraging: Mice developed serotype specific neutralizing antibodies and were highly immunized. The researchers then judiciously adjusted the height and size of the GNP, and they found this transformed the vaccination level in the animals. Moreover, the treatment results in profound changes in the immune system: spleen cell proliferation and activation as well as helper T cell and cytotoxic T cell expansion. In mice, synthesis of important cytokines such as IL-4 and IFN- γ was also increased (Quach et al., 2018). In another experiment, GNPs were joined with small interfering RNA (siRNA) that targeted dengue virus. This approach increases the anti-inflammatory effect by improving the stability and delivery of siRNA (Paul et al., 2014).

5. Influenza

Gold nanoparticles (GNPs) have been subjected to significant research in developing anti-influenza drugs. The conserved N-terminal extracellular domain of the influenza virus matrix protein 2 (M2e) peptide was used and linked to 12 nm GNPs (Tao et al., 2017). BALB/C mice were twice vaccinated with GNP conjugates. The results were encouraging: Mice that produced more IgG1 and IgG2 antibodies had better protection when challenged with the deadly PR8-H1N1 virus (Tao et al., 2014).

Many other vaccination processes have been developed to combat viral pathogens. A few of these are highlighted in Table 1.

Table 1: Use of GNP-based Nanovaccines against Viral Pathogens

No.	Antigen Type	AuNP Formulation	Immune Reaction Observed
1	Spike protein from Avian Virus-like Coronavirus	particles synthesized with 100 nm AuNPs	Improved antigen targeting to lymphoid tissues, enhanced spleen T-cell activation, higher antibody titers, and mitigated infection symptoms (Chen et al., 2016).
2	Gastroenteritis virus proteins	Conjugated with 15 nm AuNPs	Elevated levels of IL-6, IFN- γ , and IL-1 β , enhanced macrophage and lymphocyte activity, and stronger humoral immunity through spleen follicle increase (Staroverov et al., 2011).
3	Glycoprotein from Nanorods respiratory syncytial virus		Stimulated immune cell expansion, including activation of primary T-cells by dendritic cells (Stone et al., 2013).
4	Rabies virus glycoprotein (Moscow strain 3253)	Conjugated with 15 nm AuNPs	Elicited production of virus-neutralizing antibodies with high specificity (Bawage et al., 2016).
5	West Nile virus	Various shapes: 20-40 nm nanospheres, nanorods, and nanocubes	40 nm nanospheres produced the highest antibody titers; nanorods showed greater cellular uptake by dendritic cells and macrophages (Niikura et al., 2013).

Use of GNP in Antibacterial Immunization

Gold nanoparticles (GNPs) have been developed as an important vaccine and antigen delivery tool against a variety of bacterial diseases. A few of them are highlighted in Table 2. In some cases, they act as boosters to boost immune responses. For example, antibody against the N-terminal domain of the flagellin domain of *Pseudomonas aeruginosa* in combination with Freund's adjuvant and GNPs significantly augmented the IgG response. Similarly, combining 15 nm GNPs with two antigens from *Francisella tularensis* induced anti-tularemia sera by eliciting antibodies. GNPs were also used for the first time as an adjuvant to generate antibodies against surface antigens of *Yersinia pseudotuberculosis* (Staroverov et al., 2003). In addition, F1 antigens were coated with 15 nm GNPs and studies were performed on *Yersinia pestis*. This process led to high levels of IgG2a, interferon gamma and Th1 cell infiltration and hence improved immune responses (Gregory et al., 2012). Surface antigens of *Salmonella typhimurium* were coated with GNPs and were shown to have improved immunogenic properties after viral clearance. Additionally, GNPs from the capsular polysaccharide of *Neisseria meningitidis* were treated with non-immunogenic sugars to increase T cell activity, MHCII expression and overall immune responses (Fallarini et al., 2013).

Use of GNP in Anti-Parasitic Immunization

Stimulating the host's immune response, GNPs have become an important area of research on parasitic diseases. Many other vaccination

processes have been developed to combat parasitic pathogens. A few of them are explained in Table 3. In one study it was found that GNPs are capable of activating MHC I and II which are responsible for antigens presentation to the immune system. This stimulation activates a response from the leading actors of the immune system, CD4+ and CD8+ T cells. It was touched that the GNPs could enhance the host's immunity against parasitic infections and synthesize high titer of species specific antibody (Parween et al., 2011; Kumar et al., 2015).

Table 2: Use of GNP based Nanovaccine against Bacterial Pathogens

No.	Antigen Type	AuNP Formulation	Immune Reaction Observed
1	Listeriolysin O peptide from <i>L. monocytogenes</i>	Conjugated with AuNP	Increased CD4+ and CD8+ T-cell populations, NK cells, and dendritic cells; stimulated cytokine production (IL-12, TNF- α , IFN- γ , MCP-1) (Calderón-Gonzalez et al., 2016).
2	Outer membrane vesicles from <i>E. coli</i>	Conjugated with 30 nm AuNPs	Prompted rapid maturation of dendritic cells, higher-quality antibodies, and strong Th1/Th17 immune responses via IFN- γ and IL-17 (Gao et al., 2015).
3	Tetanus toxoid (<i>Clostridium tetani</i>)	25 nm AuNPs combined with saponin-based adjuvants	Oral delivery significantly improved mucosal immune responses in the presence of plant-derived adjuvants (Liu et al., 2018).
4	Tuberculin (antigens from various mycobacteria)	Conjugated with 15 nm AuNPs	Promoted robust antibody responses against diverse mycobacterial strains (Staroverov & Dykman, 2013).

Table 3: Use of GNP based Nanovaccine against Parasitic Pathogens

No.	Antigen Type	AuNP Formulation	Immune Reaction Observed
1	Recombinant protein from <i>Schistosoma mansoni</i>	Gold nanorods conjugated	Activated Th1 response; increased IFN- γ production by CD4+ and CD8+ T-cells; up-regulated MHCI/MHCII expression and IL-1 β synthesis (Assis et al., 2018).
2	Surface protein Pfs25 from <i>P. falciparum</i>	Gold nanospheres, nanostars, nanocages, and nanoprisms	Produced high-affinity antibodies using nanospheres and nanostars with the highest reactivity; This demonstrated efficient suppression of parasite migration to mosquitoes (Kumar et al., 2015).
3	Merozoite surface protein fragment (19 kDa) from <i>P. falciparum</i>	17 nm AuNP combined with Alhydrogel®	Stimulated immune reactions against low immunogenicity peptides; preventing the invasion of parasites in-vitro (Parween et al., 2011).

Discussion and Future Perspectives

This chapter contends that gold nanoparticles hold a great promise in preventing and managing many diseases. GNPs have been on the rise in the synthesis and use in nano vaccine research and are considered as a possible solution to address some of the world's most deadly diseases. For this reason, GNPs are considerably safe for use by humans and this makes them a common ingredient in vaccines against many diseases ranging from infectious to cancerous diseases. GNPs are exceptional, and their affluence of application and manipulability are tremendously attractive to researchers. For example, GNPs are conjugated to isotopes, fluorescent tags or optical probes, and high-resolution optical imaging techniques are used to protect specific cells with antibodies or ligands. GNPs have also been shown as effective for use in biosensors and microscopy for detecting bacterial infections. GNP conjugated vaccines have been shown to give 100% survival rates against lethal viruses in animal studies. Yet many obstacles remain for the successful application of GNPs in vaccine development and clinical practice. First, we need to have a uniform, large scale production system for GNPs. It has been previously mentioned that charge, size and shape of GNPs can impact cell interaction, and thus these variables need to be considered carefully when manufacturing. GNPs from 15 to 50 nm have been most studied and nano shells have been used in many of these studies, but other shapes such as nanocages, nanorods and nano cubes have not been explored. This leaves a missing piece of our understanding of how different GNPs of different sizes and types impact the system.

One area that needs further research is the way that GNPs affect immune cells. Many exciting questions will be answered by detailed studies of how functional and nonfunctional GNPs interact with immune cells. GNPs biodistribution needs to be further investigated, particularly on non-targeted organs and cells. Studies tend to focus on organs, cells or infected pathogens, but overlook the possibility that GNP might accumulate in other organs. This brings us to the next important consideration: nanotoxicology. As GNPs are not irreversible, methods to reduce their toxicity or improve their elimination from the body need to be developed.

Conclusion

The peculiarities of GNPs such as increased number of accessible surface for a given volume, chemical inertness, low biotoxicity, and ability to modulate immune reaction make them a breakthrough in immunotherapy and vaccinology. Due to their diverse roles, these molecules may serve as immune enhancing agents and antigen carriers that enhance the efficacy of vaccines and decrease toxicity. Moreover, varying the size, morphology, and surface properties of GNPs, it is possible to stimulate powerful immune reactions with different types of immune cells such as natural killer cells, dendritic cells or macrophages. GNPs are incorporated into anti viral vaccines such as the flu vaccine, Hepatitis, Dengue and HIV, via enhancing antigen dispersion, promoting immune stimulation and increasing the duration of protection. Furthermore, because of their flexibility, they can couple with parasitic and bacterial antigens and encapsulate into virus like particles, which affords them potential for future enhancement in therapy as well as diagnosis. However, there are some challenges that have to be faced, for instance, one needs to produce GNP with high uniformity and scaled up production, toxicity and biodistribution, avoiding biocorona formation, which may compromise the efficacy of the nanoparticles. Further, for its broader applications, further research is required to understand more about the effects of GNP with immune cells and efficiency trials are needed to determinate the right dose and protocol to follow in order to avoid risks.

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Nanotechnology: A Broad Spectrum Weapon against Antimicrobial Resistance

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Abstract

Antimicrobial resistance (AMR) is a major public health concern and it exhibits potential threats to environment and health. Due to the AMR, the use of conventional ways of treatment and many therapeutic drugs are of no use which led to the exploration of nanomaterials as an alternative. Nanoparticles are substances with size ranges between 1 nm to 100 nm and are classified into different types based on their size, properties, and shapes. There are different ways of the production of NPs such as top-down approach and Bottom-up approach which are further divided into different processes for the development of NPs. Although the mechanisms of action of nanoparticles are not yet confirmed or poorly understood, the studies show different ways through which these nanoparticles work against pathogens. Different mechanisms of action of NPs include oxidative stress and production of ROS, release of metal ions, disruption of cell membrane of bacteria, and eradication of biofilm etc. This chapter explores different ways of development of NPs, various types of NPs and the mode of action used by NPs to combat AMR as it can be used and explored in future for their amazing characteristics.

Keywords: AMR, Nanotechnology, Nanoparticles, Top-down and bottom-up approach, Membrane disruption, Oxidative stress, Metal ions

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Introduction

The modes of action of antibiotics are either inhibiting bacterial growth or directly killing bacteria (Fischbach & Walsh, 2009). These drugs work by targeting essential components of microbial metabolism, disrupting the formation of functional biological molecules (Linares et al., 2006). In the present situation, the efficacy of antibiotics has reduced significantly due to the developing resistance of microbes (Peschel & Sahl, 2006). Nowadays, the major threat to human health is the continuous rise of drug-resistant microorganisms. According to reports, antibiotic-resistant infections affect over 2 million people annually in the United States, resulting in more than 23,000 deaths (Munir et al., 2020). The motto 'No action today, no cure tomorrow' was used by WHO on World Health Day 2011 (Willyard, 2017). It also mentions that the mortality rate from antibiotic resistance is higher in developing nations compared to developed ones (Prestinaci et al., 2015). Long-term drug therapy is crucial for infections caused by multidrug-resistant bacteria, costing approximately 55 billion dollars annually in the USA, according to reports, making it very costly (Laxminarayan et al., 2013). Moreover, the inappropriate use of antibiotics and prolonged treatment for multidrug-resistant bacteria are major causes of resistance. *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter* are some of the major multidrug-resistant bacteria (Chambers, 2001; Perez et al., 2007; Lister et al., 2009). The increasing issue of bacterial multidrug resistance has encouraged research for novel materials that are more effective compared to conventional antibiotics and antimicrobial medications. Researchers increasingly look to nanotechnology as a viable alternative, primarily because of the exceptional physicochemical properties shown by nanoparticles (NPs) (Valodkar et al., 2011; Loza et al., 2020). Nanoparticle (NP) treatments, nanostructured coatings for indwelling and other medical devices, and nano drug delivery systems are some of the possible means to control antibiotic resistance. Nanomaterials, with at least one dimension in the range between 1 and 100 nm, are referred to as nanoparticles (Khan et al., 2019). Because of their extremely high surface area-to-volume ratio and small size, nanoscale materials have attracted a lot of attention. This ratio is improved when materials are shrunk to the nanoscale, giving the resultant nanoparticles (NPs) remarkable chemical activity, solubility, flexibility, and a variety of morphologies with different modes of action (Padmavathy & Vijayaraghavan, 2008). Drug delivery routes, direct antibacterial compounds, and nanostructured layers for medical devices are some of the approaches by which nanoparticles could be used to combat antibiotic resistance. Many types of NPs, such as organic polymers, inorganic metals, and nanostructured materials, are being made for a variety of biomedical applications. They have been established to

exhibit antibacterial activities in laboratory and animal studies, and they could act as a replacement or addition to conventional antibiotics (Tiwari et al., 2012). Nanoparticle efficiency is determined by size, form, and physicochemical character. Scientists discovered that shrinking substances to the nanoscale totally changes their character, such as optical behavior and reactivity. Due to their strong bactericidal action, nanoparticles have emerged in the biomedical field as emerging next-generation antimicrobial drugs. By combining nanotechnology with standard treatments, new means of attacking antibiotic resistance might be found while enhancing patient success (Simon -Deckers et al., 2009; Ssekatawa et al., 2020).

Preparation Methods of NPs

There are different methods used for the production of NPs, but mainly these methods fall under two classes for instance; (1) Top-down approach (2) Bottom-up approach (Wang & Xia, 2004). Based on different properties such as operation, protocols used to synthesize them, and conditions of reaction, these two main classes are further divided into different subclasses (Figure 1) (Tiwari et al., 2012).

Top-down Approach

This method is based on a destructive approach in which larger molecules decompose to make smaller units of these molecules. These smaller units are then employed to make NPs of suitable sizes. Different decomposition techniques are adopted in this method of NPs synthesis which mainly include grinding or milling and physical vapor deposition (Iravani, 2011). Using the top-down approach coconut shell (CS) NPs are produced. In the production method of CN, the milling method is used to finely grind the raw CN powder for a specific interval of time. In this method, ceramic balls and planetary mills are used for milling purposes (Bello et al., 2015). Another example of NPs production from top-down method is the synthesis of spherical magnetite NPs in the presence of organic oleic acid from natural iron oxide ore. The size of these NPs ranges from 20 to 50 nm (Priyadarshana et al., 2015). Another example of top-down approach is the development of colloidal carbon spherical particles in which sizes of the particles are controlled. In this technique, continuous chemical adsorption of polyoxometalates (POM) is done on the interfacial surface of carbon. The continuous adsorption process on the carbon surface results in the aggregation of carbon into smaller spherical particles. These smaller particles have high dispersion capacity and narrow size distribution (Garriague et al., 2004). Recently another top-down approach called laser fragmentation is employed to make highly photoactive Co_3O_4 Nps. In this method, powerful laser irradiations produced well-uniform NPs with excellent oxygen vacancies (Zhou et al., 2016). The size of these NPs ranges from $5.8 \text{ nm} \pm 1.1 \text{ nm}$.

Bottom-up Approach

In the bottom-up approach, relatively simpler substances are employed for the synthesis of NPs that's why this technique is also known as the building up approach. Sedimentation and reduction techniques are examples of this approach. Different protocols such as sol gel, spinning, biochemical synthesis, and green synthesis are employed in the bottom-up approach (Iravani, 2011). TiO_2 anatase NPs with graphene domains is an example of bottom-up approach (Mogilevsky et al., 2014). Solvent-exchange method is also used recently for the production of limit sized low density lipoprotein (LDL) NPs. These LDL are employed for medical cancer drug delivery applications as they have high hydrophobic capacity (important for drug delivery purposes) (Needham et al., 2016). Another example of bottom-up approach is the synthesis of monodispersed spherical bismuth (Bi) NPs with good colloidal capabilities. The size of these NPs produced from bottom-up approach ranges between 100 nm to 500 nm (Wang & Xia, 2004). Green and biogenic synthesis fall under the category of bottom-up approach which has drawn the attention of researchers as these methods are cost effective, environment friendly, and less toxic. Different biological systems are employed in these techniques for instance plant extracts, Aloe vera, bacteria, yeast, and human cells (Parveen et al., 2016).

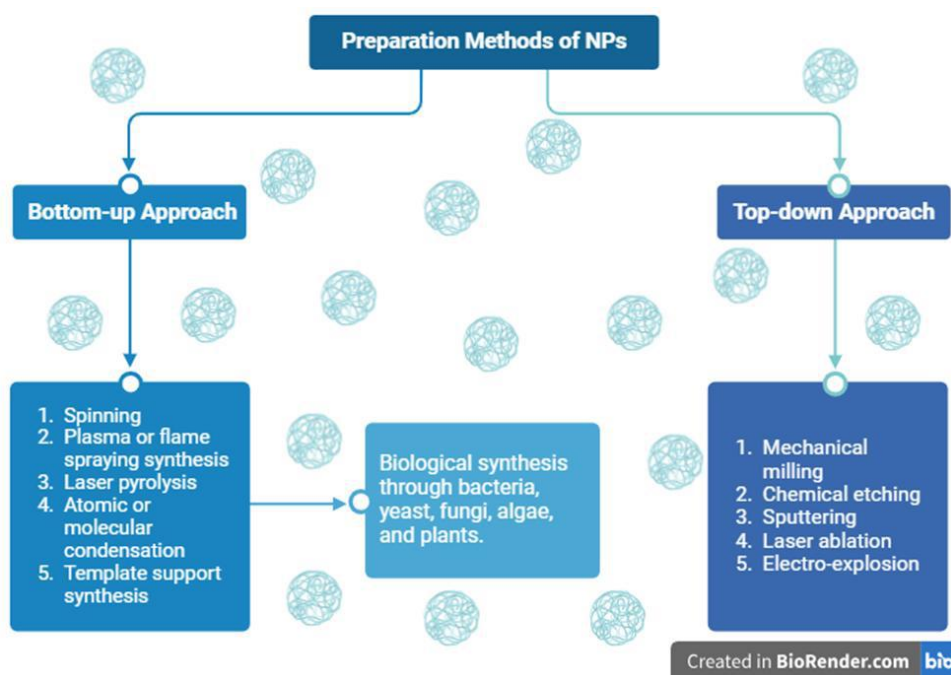


Fig. 1: Methods of preparation of NPs.

Antimicrobial Mode of Action of Nanoparticles

Nanotechnology has become one of the best methods to combat AMR and challenges associated with it. There are a number of ways through which the Nanoparticles work to increase the potency of drugs and decrease the chances of resistance (Figure 2) (Ozdal & Gurkok, 2022).

Disruption of Bacterial Membrane Integrity

The primary physical barrier for any antimicrobial agent is the bacterial membrane so first to penetrate the cell wall of a bacterial cell it is necessary to develop a NP with such effective features. One of the best NPs, AuNP is investigated and considered the best to work as an antimicrobial agent (Bilal et al., 2017; Tao, 2018). The AuNPs attach to the bacterial membrane via electrostatic interactions and finally cause the disruption of the integrity of the bacterial cell membrane (Kundu, 2017). Other than that, Nps changes the membrane potential and hinder the activity of ATP synthase which ultimately result in the reduction of major metabolic activities. AuNPs also cause the disruption of bacterial structure as the cell loses its integrity. Other than AuNPs, GBNs (graphene-based NPs) are also known for their mechanisms of bacterial cell membrane disruption. These GBNs also called as "nano-knives" and MoS₂ and MnO₂ having sharp edges are also famous for their work as they cause physical harm to lipid bilayer of bacterial cell membrane (Lu, 2017). After cell membrane, biofilm is another way through which bacteria become resistant to various drugs. Different drug delivery systems have been studied which can be used for the destruction of biofilm. In a study, it has been seen that use of silver NPs, capped with rifampicin, reduces the formation of biofilm in different bacteria such as *Klebsiella pneumoniae* and MRSA. It also increases the antimicrobial activity which helps to eradicate the already present biofilm in these strains of bacteria (Farooq et al., 2019).

Formation of Reactive Oxygen Species (ROS)

Oxidative stress due to the production of reactive oxygen species (ROS) is an important mechanism of NPs against bacteria. In normal circumstances, the balance is maintained between the production and clearance of ROS in bacterial cells. While during the excessive production of ROS, the bacterial cell promotes the process of oxidation. The oxidation reaction causes the disturbance of balance and causes oxidative stress which results in the damage of bacterial cell components (Li et al., 2012; Peng et al., 2013). Different types of NPs cause the production of different ROS such as calcium oxide and magnesium oxide NPs produced O₂ and zinc oxide NPs generate H₂O₂ and OH. Whereas copper oxide NPs produced O⁻², OH, H₂O₂ and O₂ (Malka et al., 2013).

Release of Metal Ions

The release of metal ions is another antibacterial mechanism of NPs. In this mechanism, the metal ions are released from the inorganic NPs which are then absorbed in the bacterial cell membrane and cause its disruption. Other than membrane disruption, these metal ions also cause damage to biomolecules of bacteria such as amino, thiol, and carboxylic functional groups. For instance, the antimicrobial activity of AgNPs is attributed to the Ag⁺ release (Hsiao et al., 2015). These silver ions perform their function by blocking the catalytic activity of enzymes, replication of DNA, and disrupting the synthesis of cell walls of Gram-positive bacteria through their interaction with sulfhydryl groups (Baptista et al., 2018). Zinc NPs work by producing zinc ions which destroy the membrane integrity by making a bond with the thiol group of cell membrane (Stanić & Tanasković, 2020).

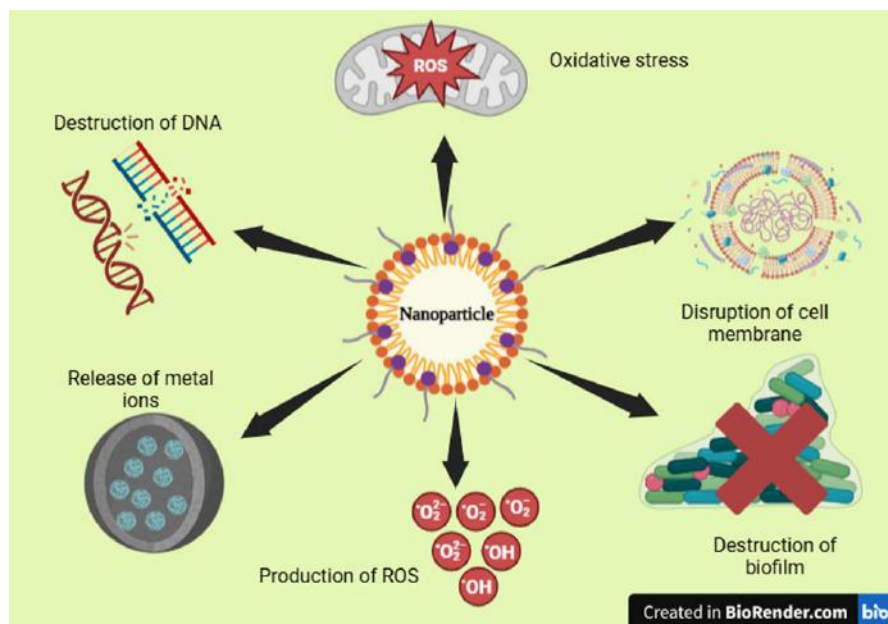


Fig. 2: Mechanism of action of NPs.

Types of Nanoparticles used against AMR

As a potential weapon against AMR, Nanotechnology presents a novel way to fight against AMR. This is done through a number of ways including development of innovative nanoparticles which are then used for drug delivery purposes, antimicrobial agents, and different tools used for diagnostic purposes. Some of the important classes of nanoparticles are mentioned subsequently (Figure 3) (Bharti & Kumar, 2025).

Metallic Nanoparticles

The nanoparticles made of metals are called metallic nanoparticles. Among these metallic nano-sized particles, silver-based nanoparticles (AgNPs) are very famous for killing bacteria. These silver-based nanoparticles (AgNPs) release their charged silver ions that act on bacterial membranes, cut their connection to the outside cell environment, which is essential for life, and become the cause of death of bacteria. Similarly, these silver ions change the structures of the bacteria's protein; due to this, bacteria cannot perfect their functions for the continuity of life. Also, these silver nanoparticles (AgNPs) release reactive oxygen molecules, and bacteria cannot detoxify them, and this ultimately causes the death of bacteria due to oxidative stress (Mukherji et al., 2019). Due to these properties, these silver nanoparticles (AgNPs) are used in medical products like bandages or wound dressings to prevent and control infections. The gold-based nanoparticles (AuNPs) are effective in killing bacteria when used with other antibiotics or antimicrobial peptides. Zinc oxide (ZnO) nanoparticles kill bacteria by releasing harmful reactive oxygen species (ROS). Zinc oxide (ZnO) nanoparticles are used for skin applications to prevent and control infections. Copper-based nanoparticles (CuNPs) also kill bacteria by releasing harmful reactive oxygen molecules. Bacteria form biofilm biotic and abiotic surfaces for their survival. Copper oxide nanoparticles (CuNPs) are specially used in medical instruments to prevent bacterial growth. Both copper and zinc oxide release reactive oxygen molecules, which prevent the formation of bacterial protective coats against microbial agents called biofilm (Applerot et al., 2010; Mousa, 2013).

Lipid based Nanoparticles

The nanoparticles made up of lipids are known as lipid nanoparticles. These lipid-based nanoparticles provide a very efficient drug delivery system into the body. These lipid nanoparticles are highly versatile because all water and fat-soluble drugs can be used with these particles (Yousefi et al., 2019). Famous lipid nanoparticles are liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs) (Khalifa et al., 2022). These nanoparticles are biocompatible with the tissues of the body and have an efficient drug release controlled system (Devrim & Bozkar, 2017). Liposomes have two layers, one for water soluble and other for fat soluble drugs. Similarly, solid lipid nanoparticles and nanostructured lipid carriers provide protective structures for drugs that are released by a controlled mechanism. These nanoparticles also increase solubility and bioavailability means they make drugs available and absorbed by the body to its maximum concentration to a specific site to prevent and control infection. Moreover, another benefit of these nanoparticles is that their structures can also be changed according to the infection for reaching that specific site of infection. Lipid nanoparticles have a versatile nature. These can be used as intravenous treatments, as topical ointments, and in specific areas for effective treatment to prevent and control infections (Md et al., 2017).

Polymeric Nanoparticles

The nanoparticles that are made up of polymers are known as polymeric nanoparticles. The polymer-based nanoparticles are compatible with the tissues of the body and are biodegradable, meaning they easily break down in the body and are removed by the body. So, these types of nanoparticles are very helpful for the transportation of antimicrobials into the body (Agnihotri et al., 2012). These polymer-based nanoparticles also offer a targeted approach and controlled drug release mechanism for antimicrobials to combat specific infection. Polymeric micelles are a type of polymer based nanoparticles which are small structures through which water insoluble drugs can be delivered into the body easily. Dendrimers are another type, which are loaded with many branches that help them incorporate many drugs at a time. Therefore, at a time, these nanoparticles are effective at multiple infection sites. And its unique, highly branched structure makes them able to penetrate and degrade biofilm, which is a protective barrier of bacteria against many antimicrobials (Vassallo et al., 2020). Chitosan nanoparticles are also polymer-based. Chitosan is a polysaccharide made up of chitin from the exoskeleton of crustaceans. These nanoparticles are positively charged, which attach to the negatively charged membrane of bacteria and cause damage by disturbing its arrangement of molecules, leading to the death of the bacteria cell. This property of Chitosan is from inheritance. Due to their unique structure and properties, these nanoparticles are most commonly used for healing purposes and controlled and targeted drug delivery into the body (Ansari-Asl et al., 2022).

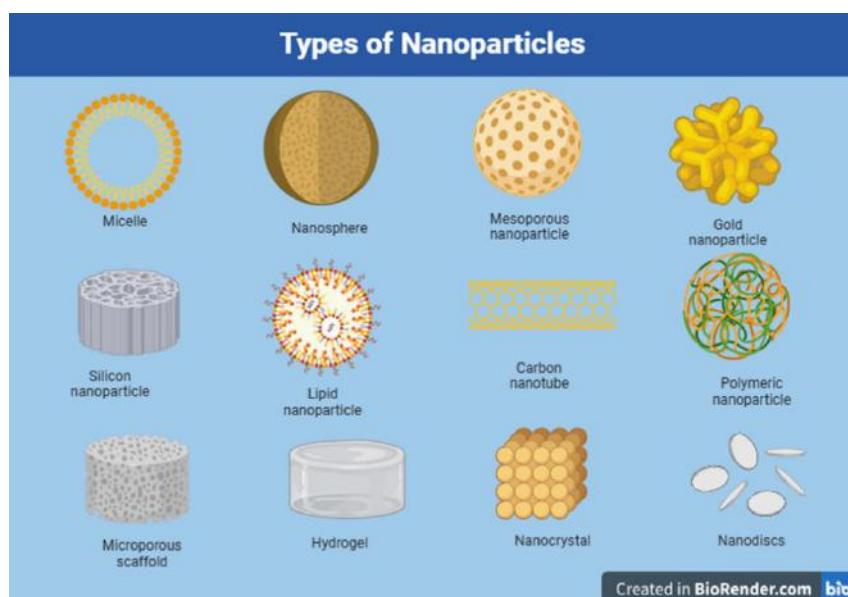


Fig. 3: Different types of Nanoparticles.

Carbon based Nanoparticles

Carbon also used for the manufacturing of NPs such as graphene nanotubes and carbon quantum dots are made up of carbon. These NPs have shown significant antibacterial activity. The carbon NPs cause minimum chemical and physical harm which is not avoidable as they perform their bactericidal activity. The exact mechanism of action of carbon NPs is not confirmed yet but some studies show that carbon nanotubes (multi-walled) helps to destruct the formation of biofilms by different bacteria such as *Klebsiella oxytoca*, *Pseudomonas aeruginosa* and *Staphylococcus epidermidis* (Prestinaci et al., 2015; Jit et al., 2024).

Conclusion

Infections caused by bacteria, virus, and fungi are common and increase at a high speed which also causes the issue of AMR, a major challenge for public health. AMR is the result of misuse of antimicrobial drugs, overuse of antibiotics and this situation demands novel strategies to handle these crises. Nanotechnology is the answer to all these crises as the success rate of treatment with nanotechnology is high as compared to conventional treatment. Decreasing the use of antibiotics, enhancement of drug release, change the target of antibiotics, and modification of enzymes in pathogens, are the various methods to stop the development of AMR. All the functions are performed by nanoparticles as the nanotechnology rises up as a beacon of hope and it provides a large number of solutions against the complexities of AMR. Nanotechnology as a weapon against AMR serves as a leverage for the researchers to explore nanoparticles as an innovative approach against AMR. There is a need of comprehensive understanding of potential of these nanoparticles such as metals, lipids, and polymers to address the challenge of AMR. This will empower the development of understanding of nanotechnology having great advantages to be used as a significant treatment against bacterial infections and AMR.

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The Role of Genome Editing in Targeted Therapy; Advances and Prospective Developments in Human Health

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Abstract

The explosion of research that has come from the bacterial or synthetic nucleases has meant that nearly all eukaryotic organisms can have specific genomic regions targeted and modified provided that the accurate cell animal models of pathological events can be created. Moreover, in recent years only the genome editing has revealed great potential in many different areas starting from the basic research and finishing with the applied biotechnology together with the biomedical research. Newer commercially available nucleases like the zinc finger nuclease (ZFNs), transcription activator like effector nuclease (TALEN) and CRISPR – Cas associated nuclease has ensured a transition from idea to implementation. New modifications of three basic genome editing methods [TALENs, CRISPR/Cas9, ZFNs] and the use of derived products as actual tools for gene editing in a broad range of human pathologies and potential future treatments are examined, with special emphasis on the influence of the eukaryotic system and relevant animal models. Last, we briefly discuss clinical applications of the genome editing platforms for disease regimens and potential issues with the application of this technology.

Keywords: Genome Editing Tools, Mechanisms, Zinc finger nuclease, TALENs, CRISPR/Cas9, Disease modeling

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Introduction

New technologies in genome editing have improved how human genome study so that researchers are now in a position to determine how a particular product of a gene affects an organism's affliction. The advance of genetic engineering in the 1970s when it became possible to change DNA or RNA created a new field of genome editing (Rothstein, 1983). The awareness and application of B or S nucleases that have rapidly developed in the last decade have emerged into several aspects of basic and complex biomedical research and applied biotechnology (Cornu et al., 2017). Through the provision of genome editing infrastructure, it could be carried out both in vitro and in vivo since the infrastructure is delivered in situ. This process in effect means that it generates, reduces and 'edits' genes (Gaj et al., 2013; Ghosh et al., 2019). Pointed DNA modifications begin with nuclease induced double strand breaks (DSBs) and this initiated highly efficient cellular DNA recombination in mammals (Rouet et al., 1994; Kosicki et al., 2018). DNA generated by nucleases Double-strand breaks (DSBs) are repaired by nearly all cell types and species utilizing one of two main mechanisms: either nonhomologous end-joining (NHEJ) or homology-directed repair (HDR), which results in targeted integration or gene disruption (O'Driscoll & Jeggo, 2006).

Since fully matched DNA segments act as homologous templates, HR has mainly been employed to mediate gene targeting, such as gene knock-in or gene knock-out. Thus, its value is rather limited because HR does not function efficiently in non-model species and mammalian cells. An additional strategy to improve HDR-mediated genome editing's performance was to apply targeted nucleases because it was previously shown that DSB could increase the HDR frequency by orders of magnitude. The HDR though may use a template of foreign DNA that mimics the termination region sequence for damage repair once a specific DSB has been generated (Kaniecki et al., 2018).

This technique may be also used for targeted alterations initiated site specifically to fix mutations or to embed new sequences; in this case, the correctly constructed repair template is delivered directly to targeted cells (Kim & Kim, 2014; Verma & Greenberg, 2016). However, while NHEJ-mediated repair beget gene insertions or deletions (indels) of incalculable extent at the DSB site in NHEJ endogenous genes, which finally contribute to gene inactivation, it generally causes errors (Chang et al., 2017). Indications in coding sequence cause frameshift alterations that results in mRNA to degrade & nonsense mediated decay to form nonfunctional truncated protein (Lieber et al., 2010). This procedure is expected computationally to be easier than HR-based approaches as (a) no requirement for the repair matrix (b) type of cell seems to have minimal influence on the efficacy of change. Therefore, like RNAi, NHEJ may be used to apply gene-knock down in immortalized cell lines, but it might bring about 'knock out' mutations that are permanent and un reversing (Delacôte & Lopez, 2008).

To produce the required DSBs at the different DNA target sites, developments in early genome editing have involved the creation of individualized zinc-finger nuclease (ZFN) and mega nucleases (Urnov et al., 2010). Since the desired proteins had to be generated as synthetic molecules with specifically encoded sequence recognition domains coupled with nonspecific nucleases to facilitate targeted DNA scission, these nuclease systems that we had developed entailed special skills to create targeted DNA cutting opportunities hitherto unimaginable with genetic manipulation tools (Cathomen & Joung, 2008; Silva et al., 2011).

The recently identified and highly effective gene editing technology called (CRISPR)-associated (Cas9) nuclease originates from bacterial immune response. Because this technique is capable to be well coded to alter the DNA sequence of integrated eukaryotic cells using an RNA guided DNA cutting module, this method outcompeted the ZFNs and TALENs to bring about preferred genetic changes. Since its first application in mammalian cells in 2013 for gene editing applications, the CRISPR/Cas9 system has quickly been adapted for gene expression regulation. This encompasses treatments as transcriptional or epigenetic changes, DNA repair or modification of any other aspect of the genome (Al-Attar et al., 2011; Cong et al., 2013).

Programmable nucleases have made the development of gene editing tools faster from discovery through clinical application and offered researchers precise control over most if not all genes across a broad spectrum of organisms and cell lines. Today's ongoing preclinical genomic editing is majorly related to developing T cell-based anticancer immunotherapy, hemophilia, muscular diseases, primary immune system defects, metabolic conditions, CVDs, viruses, and muscular diseases. Beyond preclinical research, some of these methods are presently undertaking phase I/II clinical trials. TALENs, CRISPR/Cas9, and ZFN are the three main genome editing technologies. Here, we look at their most recent developments and discuss how their corresponding reagents may be employed as tools for modifying genes for a variety of human illnesses and in exciting new treatments.

2. Structure and Mechanism of Genome Editing Tools

DNA interaction and ZFN structure are composed by fusing nonspecific cleavage domain to DNA target-recruiting domain, bound to zinc finger (Kim et al., 1996). Primarily discovered in 1985, the zinc-finger protein is a part of transcription factor IIIa in *Xenopus* oocytes; the factor is capable of binding to DNA at a definite locus (Diakun et al., 1986). A collection of Cys2His2 zinc fingers, which result from exceptionally stable interactions in their zinc-finger regions with corresponding DNA sequences, are employed to realize the essential specificity of the required zinc finger. About thirty amino acids and two anti-parallel β -sheets facing an α -helix make up the structural motif of the Cys2His2 zinc finger (Beerli & Barbas III, 2002).

The adaptive DNA recognition domain, Cys2-His2-ZF, is now believed to be the most common Genome-binding pattern in eukaryotic transcription factors, despite considerable uncertainty around the specificity of its DNA recognition mode. Each zinc-finger unit's selectivity may identify three base pairs in the DNA and establish base-specific connections by making direct contact with the main groove of the DNA through the finger's α -helical residues (Buck-Koehntop et al., 2012). In eukaryotic cells, the targeted DNA cleavage by ZFN generates DSBs on a specific site of the genome, which the body alters subsequent endogenous NHEJ / HDR repair pathways as required (Smith et al., 2000).

Three main factors impact ZFNs' sequence-based target identification and specificity:

- each finger of amino acid sequence
- How many fingers
- the interaction of the nuclease realm; Because ZFNs are modular, scientists can alter the catalytic and DNA-binding domains independently, even though each ZFN is made up of both. With this knowledge, scientists can create new modules that are both specific and attractive enough to manipulate a genome.

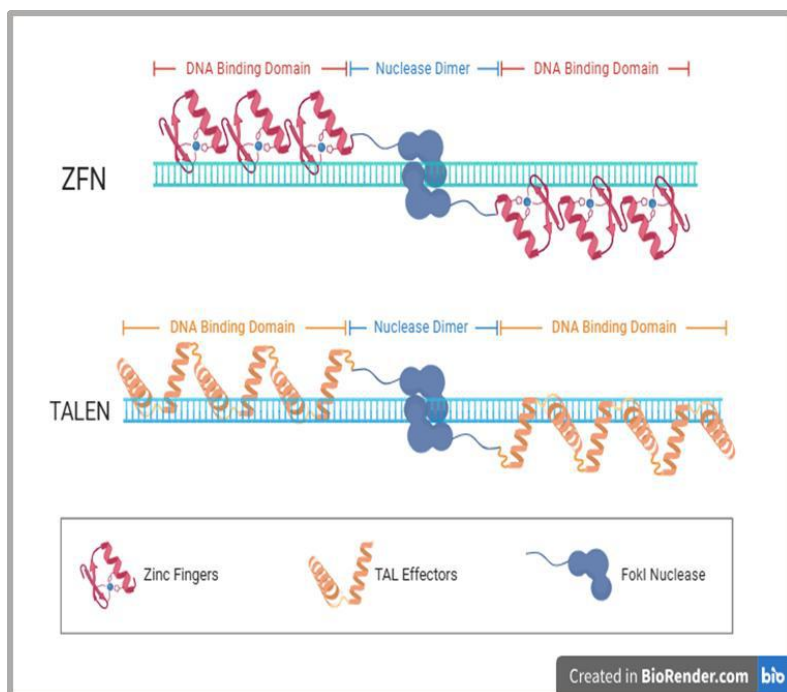


Fig. 1: Transcriptional Activator-Like Effector Nucleases and Zinc-Finger Nucleases attach to DNA using arrays designed to identify a target sequence

2.1. TALENs (a protein-based DNA targeting system)

TALENs are engineered nucleases, which performs in terms of functionality and specificity compared with ZFNs. Like ZFNs, TALENs use general DNA cleavage domain and domain specific for a certain DNA sequence in order to form DSBs. The repetitive sequence from transcription activator-like effector (TALE), a protein first discovered in phytopathogenic *Xanthomonas* bacteria that alters gene transcription in host plant cells on its own, forms this DNA-binding domain (Paschon et al., 2019). The C-terminal core domain of TALE, which is a member of the 33–35 aa sequence motif, interacts with DNA. The two hypervariable amino acids, or repeat variable di-residues (RVDs), at positions 12 and 13 make up the very similar but distinct amino acid sequence inside each repetition. Only C nucleotides are bound by ND, only A/G nucleotides by HN, only G nucleotides by NH, and all nucleotides by NP. RVDs mediate the specificity and severality of DNA binding (Moscou & Bogdanove, 2009; Bogdanove & Voytas, 2011).

2.2 CRISPR/Cas9 (a versatile tool for genome editing)

First reported in *E. coli* in early 1987, CRISPRs have been identified in many more bacteria. The function of short repeat sequences stayed obscure for many years. Until 2005, works showed that the sequences resembled phage DNA. Subsequent investigations showed that these sequences also protect bacteria and archaea from extraneous DNA by using RNA-guided DNA cleavage to provide an adaptive immune response. The CRISPR-Cas systems are often described according to the structural diversity of the Cas genes, as well as their arrangement (Liu et al., 2017).

It is now known that there are six classes for CRISPR-Cas, and at least 29 subtypes for each class, and the number is expanding rapidly. For instance, class 2 CRISPR-Cas systems contain only a single effector protein, while class 1 systems possess multiple-subunit effector complex. CRISPR-Cas systems were limited to class 2 systems that contained a single effector protein. Among them the most frequent subtype is type II CRISPR/Cas9 system that looks rather perspective as the gene editing because the method uses only one Cas protein (SpCas9) that targets certain DNA sequences. The means by which this system functions is constituted of a cas9 nuclease along with single-stranded guide RNA, ultimately abbreviated as the sgRNA (Hillary & Caesar, 2023).

Three popular methods for CRISPR/Cas9 platform to modify genomes have been developed (Janik et al., 2020):

- (1) The plasmid-based CRISPR / Cas9 method simultaneously combines Cas9 genes and sgRNA for extraction in inactive vitro, without multiple transfections and with increased Cas9 and sgRNA half-life.
- (2) disadvantage of direct delivery of Cas9 mRNA & sgRNA into cells is the instable nature of mRNA used for Cas9 mRNA-based techniques leading to transient mRNA expression and temporary gene change.
- (3) The Cas9 protein and sgRNA are directly introduced within the cell, which offers such advantages as immediate action, increased resistance to degradation and low immunogenicity.

Genetic information is permanently and irrevocably altered via DNA editing, which therefore raises inevitable ethical and security concerns. Additionally, gene therapy for nervous system illnesses is limited for some cell types since it is difficult to modify some cells, such neurons, utilizing CRISPR/Cas9-mediated editing. Thus, researchers have also proposed genome editing methods that just modify and change RNA (Asmamaw & Zawdie, 2021; Hillary & Caesar, 2023). After the DNA encodes the essential information into a molecule known as RNA, then RNA basically controls the synthesis of protein. CRISPR technology can treat many diseases by repairing protein function in almost all cells and stop transformation by briefly changing RNA mutations (Asmamaw & Zawdie, 2021). The second approach is to of facing change in genetic variations is through the use of stem cell transplantation with CRISPR/Cas9 technology (Liu et al., 2020; Zhu et al., 2024).

3. Genome Editing for Gene Therapy and Disease Modeling

More realistically, the functions of genes and proper cellular behavior and function can be manipulated by modifying the targeted genes with chimeric tools as ZFNs, TALENs, and CRISPR/Cas9. Through animal model genetic changes, these genome editing techniques have made it easy to examine origin or causes of many diseases and come across molecular avenues that can be used to improve potent treatment approaches (Maeder & Gersbach, 2016).

3.1. Cancer Research

High potential is offered by oncogenes and mutated tumor suppressor genes for application of gene modifying methods. With its early successful genome editing demonstrations in eukaryotic cells to the recent applications in developing the tumor targeted T lymphocytes and hematopoietic stem cells (HSCs), several targeted cleavage events have been reported in diverse important research. It has also invested in a promising area of cancer research and come up with original concepts for gene editing (Shankar et al., 2018).

While a three-finger protein has been designed to selectively inhibit the synthesis of human oncogene that has been transduced into mouse cell line, the ZFN-mediated targeting – a prototype platform for the programmed DNA scission and its applications – was unmasked in 1994 and used to modify genes in human and model organisms cells (Aveson & Barry, 2014). Through the provided DSB error repair, it is possible to access the telomeric area of the combined lineage leukemia (MLL) gene break points cluster region and examine chromosomal rearrangements linked to MLL leukemogenesis, a specially tailored ZFN was next used on a human lymphoblast line of cells from CML patients. Although different to the initial targeted regulation, successful regulation was also achieved at this locus employing ZFNs specifically designed to disrupt the β - and α -chain genes of the endogenous T cell receptor (TCR). Both CD3-TCR surface expression and cell viability of the ZFN-treated cells were significantly reduced to 0% whereas, the cell population showed an increase in the expression of interleukin. ZFN, a new therapy aimed at LTR promoter region of HTLV-1 (Tanaka et al., 2013; Aghamiri et al., 2020).

3.2. Cardiovascular Disease

CVD accounts for the highest mortality and increased risks are reported in many developed nations. Many forms of CVD are often linked to one gene alteration or to a set of several rare familial dominant mutations (Li et al., 2015). In fact, therapeutic cures are concerned more

with the prevention of the manifestation of sickness than with possible hereditary issues. This paper introduced and established the *in vivo* CVD model based on gene editing technology, as well as the survey of damaging genes and the molecular processes, enabling the evaluation of the therapeutic effect of gene therapy in controlling the expression of certain genes and enhancing gene functions. There are many research models of cardiovascular disease including the use of genome editing techniques (German et al., 2019).

Furthermore, CRISPR/Cas9 effectively knocked out MHCII in normal human endothelial cells by simultaneous knockout. To form vessels these cells do not need the stimulation of allogeneic CD4⁺ T lymphocytes. The effectiveness of this technique when it used in STEM- cell bioengineering of allografts: improving heart transplants has been helpful (Musunuru, 2017; Wu et al., 2024).

There has also been much interest in possible therapeutic strategies to reverse disease-causing mutations or to inactivate specific genes that, because of the advance of genome editing technology (Li et al., 2023). For instance, Long QT syndrome (LQTS) is a congenital disease of the heart electrical conduction system and this disease is dominant. It can be seen that LQTS can arise from hybrid mutations in several genes. Some of these genes have obviously identifiable mutations in distinct sites with known biological function. For example, mutations in the alpha protein's hERG gene that codes for potassium voltage-gated channels and creates holes. A mutation in the hERG gene is likely to result in a life-threatening ventricular arrhythmia because its production and activation occurs mainly in smooth muscles and the myocardial tissues. Of course, the potential of such LQTS is that, one day, humans would fix mutations in hERG genes in cardiomyocytes using CRISPR technology (Zhou et al., 2021).

3.3. Metabolic Diseases

Metabolic illness is the term used to depict the pathological status of protein lipid and carbohydrate in the body hence metabolically disturbed. The term metabolic diseases may refer to a range of condition, which may be attributed to the individual's inherited background, as well as the external environment. Gene editing technologies might be used for genetics treatment, functional gene assay as well as for genetic model construction of metabolic diseases such as diabetes, obesity and hypertension. By interacting with delivery system receptor called LepR, the hormone leptin (Lep) was produced by the white fat tissue influencing the hypothalamus metabolic regulation center. Some uses of this natural herb include the following; it can control blood sugar levels and control or influence neuroendocrine functions. Besides, it has advantages of reducing caloric intake and stopping the formation of fat and decreasing appetite (Coppari & Bjørbaek, 2012).

On the basis of the present study, animal model of diabetes is valuable as an experimental tool for drug screening assays, preclinical investigation and pathophysiological observation (Hu et al., 2020). For Ins1 (insulin gene) recombinase Cre insertion was targeted at the stop codon and promoter (Naylor et al., 2016). Morphologically, PCR analysis indicated that the progeny F1 mice had cre-loxP recombination, and other organs although they stained negatively for the gene, all the islets with insulin positive cells were positive for this gene. However, these mice were similarly insensitive to glucose ingestion to that exhibited by wild type mice. Taking advantage of the experimental approaches then, one can use CRISPR/Cas9 system to knock down some of the genes that are implicated in diabetes in human iPSCs (Vethe et al., 2017).

3.4. Neurodegenerative Diseases

The foregoing neurodegenerative diseases progressively strip afflicted individual of the ability to reason, move, and exist autonomously. These illnesses result from Neuronal degeneration and death and Neurons are the cells in the body that keep our bodies and minds functioning. Every ailment has unique causes of its own: Huntington's is due to a toxic protein from a mutated HTT gene; Parkinson's leads to the death of dopamine producing cells caused by aggregation of the α -synuclein protein; Alzheimer's has amyloid- β plaques and toxic tau tangles in the brain; and ALS comes from mutation in genes such as SOD1 or C9orf72 which leads to the degeneration of motor neuron (Fan et al., 2018; Raikwar et al., 2019).

Base editing reduces the likelihood of off-target issues by editing single letter changes in DNA while not wholly deleting a strand of DNA. In addition, there are other forms of RNA therapy, this include RNA interference (RNAi), and antisense oligonucleotides (ASOs) which help to lessen the production of toxic proteins (Nojadeh et al., 2023).

3.5. Viral Diseases

Organic diseases such as the colds, HIV/AIDS, hepatitis B among many others have remained a formidable force in the competitive and ever shrinking world. While traditional therapies often only cure those manifestations of the disease, genome editing technologies, and especially systems based on the CRISPR-Cas, open new horizons for targeted and effective treatment (Kim & Lee, 2022).

To prevent the virus from replicating, the genetic makeup has been modified and through use of CRISPR-Cas9 the DNA of the HIV virus was extracted from AIDS affected cells. The second approach relies on the protection of the immune cells from HIV by changing certain gene signaling known as CCR5. Hepatitis B may yet have a treatment since genome editing may pinpoint and reduce the virus's DNA within liver cells. By making the use of CRISPR-Cas9, the researchers have succeeded in knocking out the HSV DNA that has been known to cause recurring outbreaks in nerve cells. CRISPR-Cas13 attacks the RNA of RNA chain viruses, which include SARS-CoV-2, to reduce their ability to replicate (De Silva Felixge et al., 2018; Kim & Lee, 2022).

However, issues such as effective delivery and hence minimizing off-target effects have remained as existing problems even as these other developments continue apace. For the treatment of viral diseases, genome editing may simply remain a theory but as it is advanced genome editing may be one of the most important tools to unlock permanent and powerful cures.

3.6. Hereditary Eye Diseases

Due to progress in the gene-sequencing technology, conditions such as congenital corneal dystrophy, Leber congenital amaurosis (LCA), congenital glaucoma, congenital cataract, retinitis pigmentosa (RP), Usher syndrome, retinoblastoma (RB), and many other hereditary eye ailments can now be diagnosed genetically more comfortably (Hung et al., 2016).

Animal models of RP have previously been produced using CRISPR/Cas9. Named after the receptor enhancer protein that aids in the development of the endoplasmic reticulum, REEP6 is a newest member of the human REEP/Yop1 protein family. The potential for using AAV and iPSCs to treat associated eye illnesses is increased when CRISPR/Cas9 technology is combined with other methods. It has been demonstrated that CRISPR/Cas9 may fix pathogenic mutations in the retinal pigmentosa GTPase regulator (RPGF) that cause X-linked RP in patient-specific iPSCs. This implies that a tethered iPSC transplantation strategy for different retinal degenerations may involve combining CRISPR with self-directed iPSCs (Benati et al., 2020). According to patient-specific imaging and physiological characterization of three RP individuals carrying frameshift variations in RPGR gene, photoreceptors from RP patients exhibit aberrant shape, location, and electrical activity in iPSC-derived retinal organoids. As a result, CRISPR/Cas9 is the fixed mutation of RPGR that can reverse ciliopathy and stop photoreceptor loss as a mutant repair method (Gallego et al., 2020).

3.7. Other Hereditary Diseases

The most prevalent kind of muscular dystrophy linked to a malfunction in the DMD gene is Duchenne muscular dystrophy. It has been discovered that not all aspects of human disease can be modeled in mice with X-linked muscular dystrophy (mdx). Their diminutive stature, low levels of long-term muscular deterioration and weakening thus hinders research and study of illness. As a result, larger species such as rat rabbit, or pigs are more useful in preclinical researches (Olson, 2021).

More of monkey dystrophin gene was disrupted through CRISPR/Cas9 where it introduced mutations that are characteristic of DMD. Further, the relative targeted rate detection indicates that mosaic mutations resulting from CRISPR/Cas9 may be present in 87 % of the potential dystrophin genotypes in monkey muscle (Ousterout et al., 2015). Notably, three research groups recently reported finding they had erased variations in dystrophin gene that encodes for DMD gene and affects the production of proteins. The researchers employed CRISPR/Cas9 Gene editing to delete altered DMD region from the mdx animal model to generate shorter isoform of dystrophin protein in muscle fibers and to optimize the muscular activity to a certain degree. This gave a possible means of helping to rectify disease causing mutations in peoples muscular tissue (Mani, 2021; Kan & Doudna, 2022).

Patients suffering from primary immunodeficiencies, direct consequences – immunologic defect, or absence of any component of the immune system, can undergo allogeneic HSC transplantation. This might be a dangerous surgery if individuals seeking leukocyte antigen-matched donors are incompatible for tissue matching. Gene therapy is another tempting way of dealing with a patient's own HSCs. Auxiliary HSCs can be applied in situ for regeneration of the deficient cells and for creating animal or cell models that will manifest the adverse impact of mutations inherent in immunocompromised individuals. One of the worst known immunodeficiencies – SCID – results from a gene mutation that opens for IL2RG. This leads to T cell line development arrest and augmented primary or secondary damage to the main B cells (Ameratunga et al., 2024).

4. Conclusions and Future Perspectives

The CRISPR/Cas9 system has shown a remarkable ability to directly interfere with target gene loci or to generate versatile platforms, as well as the astonishing capacity, if the evidence gathered so far is considered, to address diseases influencing human existence through employing genome editing systems for therapeutic intervention. With the present understanding of the genetic and epigenetic characteristics of cancer cell lines, future studies can use pooled CRISPR screening to uncover different synthetic lethal links in the genome and discover new targets for therapeutic intervention. Moreover, noncoding sections of the cancer genome can be reduced by the use of the CRISPR/Cas9 method in cancer research; this advances functional analysis of uncharacterized genotypes. In particular, cell visualization; epigenetic modification; gene expression regulation; medicinal drug development; operational genome screening; gene diagnostics benefited from gene editing techniques. More complexed new genome editing machineries and much more targeted nano structured transports have enhanced transport capacity and reduced toxicity, bringing the genome editing technology at the clinical interfaces though in its collective use; the off-target effects are yet to be minimized.

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Role of Gold and Silver Nanoparticles as Cancer Therapeutic Agents

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Abstract

Nanotechnology has shown promising advancements in the field of cancer therapy, which further provides innovative strategies, particularly for diagnosis and treatment purposes. Due to the unique properties and range of applications of nanoparticles, nanoparticle (NP)-based techniques have created an emerging interest in the field of cancer. Among all, silver and gold nanoparticles (AgNPs and AuNPs) are of more importance and interest to use due to some of their important properties, including size, shape, and biocompatibility. Therefore, this chapter provides an overview of the most recent innovations and advancements in using silver and gold nanoparticles in the field of cancer therapy, along with their application in imaging and diagnosis. The chapter also provides an understanding related to various manufacturing techniques, which are mainly used to make the nanoparticles, along with the understanding of how they work against the cancerous cells, which mainly involve targeting necessary cellular pathways and ultimately stimulating apoptosis, a programmed cell death. The difficulties and potential outcomes in bringing NP-based tactics from the bench to the patient's bedside, highlighting the significance of interdisciplinary teamwork and legal issues, were also discussed. All things considered, this chapter offers insightful information about the potential of AgNPs and AuNPs as promising agents for cancer therapy and diagnosis, opening up new possibilities for the creation of efficient and individualized treatment plans.

Keywords: Nanoparticle, Cancer, Silver, Gold, Synergistic, Biomedical application

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Introduction

According to the International Public Health Concern, cancer is still considered as one of the leading causes of death, with 10.0 million deaths predicted from the disease in 2020. Moreover, the World Health Organization (WHO) projects that it will have tripled by the end of 2040 (Taha, 2022). A group of illnesses collectively referred to as cancer is defined by invasiveness and unchecked, random cell division. An unhealthy lifestyle, including smoking, drinking tobacco, eating an unbalanced diet, and experiencing stress, is an important influence on the estimation of cancer risk. It has been difficult to determine how many onco-gene related mutations, and tumor gene expression, along with DNA, which helps in repairing genes, are involved. Hereditary factors are only associated with 5–10% of cancer cases. Growing older is another significant concern (Gavas et al., 2021).

Because of its high level of effectiveness, chemotherapy is today one of the most widely used anti-cancer treatments. Practical restrictions have been brought about by its poor selectivity for tumor cells and difficulties delivering drugs to the tumor location effectively. Multi-drug resistance is yet an additional challenge to effective treatment. New drug delivery techniques have been developed in response to these problems (Sun et al., 2023). A promising multidisciplinary field of study, nanotechnology offers materials at the nanoscale that may find application in a number of scientific fields. It exhibits a large surface area to volume ratio as well as new and improved properties due to the quantum size effect. This is the primary characteristic that has led to the extensive application of nanomaterials (Kabir et al., 2023).

Silver Nanoparticles (AgNPs)

Silver nanoparticles (AgNPs) are attracting more attention in cancer research, which further demonstrates an innate anti-proliferative effect (Takáč et al., 2023). These properties of nanoparticles may impact how they are absorbed by cells to give a beneficial effect (Mahmud et al.). AgNPs are being understood to develop new cancer-related tools for diagnostic and therapeutic applications. Notably, silver is considered a noble metal, along with antibacterial and antifungal activity (Takáč et al., 2023).

There are various methods that have been used for the many synthesis processes. For the synthesis of AgNPs, there is a method known as

a green chemical method has been used potentially (Zhang et al., 2016). Moreover, the green-generated AgNPs provide a number of biological properties, such as anticancer and antibacterial activity (Kabir et al., 2023).

There are various analytical methods that have been employed to evaluate the synthesized nanomaterial. The common example of the method used is microscopy. There are many kinds of microscopy which can be used such as atomic force microscopy (AFM), scanning electron microscopy (SEM), transmission electron microscopy (TEM), dynamic light scattering (DLS), X-ray photoelectron spectroscopy (XPS), X-ray diffractometry (XRD), and Fourier transform infrared spectroscopy (FTIR) (Zhang et al., 2016). The biological activity of nanoparticles is influenced by their size, shape, dissolving rate, efficiency of ion release, surface chemistry, and cell type (Iqbal et al., 2025). During the synthesis of AgNPs, many types of reducing agents are also used, and they play an important role in determining cytotoxicity. However, it is crucial to create nanoparticles, particularly those AgNPs with specialized structures, which are mainly distributed equally in size, shape, and action, to use for different biological applications (Luqman et al., 2023).

Green AgNPs may prove to be advantageous theragnostic agents in the pursuit of additional biological application discoveries. Nowadays, the creation of several toxicity studies pertaining to nanoparticles periodically results in a negative view of their application (Sajid et al., 2025). However, since toxicity has a lethal effect that cancer cells find undesirable, it may be useful in cancer therapy. Numerous studies indicate that adding AgNPs to cancer treatments has shown favorable outcomes (Yesilot & Aydin, 2019).

Anticancer Activity of AgNPs

Frequent *in vitro* investigations have demonstrated that AgNPs can enter cells through endocytosis, and their location within the cell can be identified as the end lysosomal compartment and the cytoplasm's perinuclear area. Furthermore, by interfering with cell respiration, AgNPs have the ability to penetrate the mitochondria and release reactive oxygen species (Yesilot & Aydin, 2019). ROS, which include superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radical ($HO^\bullet$), are byproducts of biological oxygen metabolism (Gohar et al., 2024). It is important in signaling pathways. AgNPs exposure raises ROS levels, which in turn causes cytotoxicity, reduces cell survival and growth rates, leading to damage of organelles, ultimately leading to cell death. Since tumor cells are more prone to oxidative stress-induced damage than healthy cells and produce larger quantities of ROS, ROS inducers are particularly interesting for controlling the progression of cancer (KhokharVoytas et al., 2023). AgNPs may cause ROS production, which in turn may lead to cell death, but they may also affect the amounts and antioxidant compounds' action within the cells (Miranda et al., 2022).

Cancer cells may experience mitochondrial damage, oxidative stress, DNA damage, or induction of apoptosis as a result of AgNPs' harmful processes. Additionally, investigations have shown that Ag-NPs modify the way that vascular endothelial growth factor (VEGF) functions. It is sometimes referred to as vascular permeability factor and is essential to tumor angiogenesis (Yesilot & Aydin, 2019). These findings are demonstrated in Figure 1.

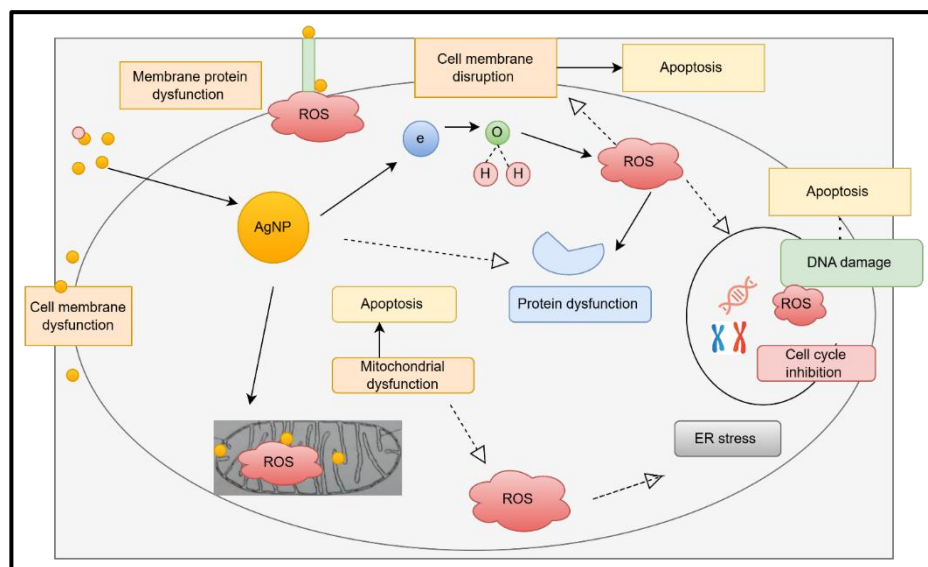


Fig. 1: AgNPs disturb both the structural and functional integrity of cellular membranes, macromolecules, and organelles and raise the rate of apoptosis.

Gold Nanoparticles (AuNPs)

A great interest has been shown to the latest innovations and breakthroughs with gold nanoparticles (AuNP) in the fields of theragnostic and medicine. They have received a recent upsurge in therapies and are utilized in diagnosis. AuNP has a close relationship to chemistry and was utilized as art embellishments as early as the Roman era (735 BC). Research has shown that gold nanoparticles are employed in several scientific domains, including treatment and diagnosis (Sakthi Devi et al., 2022).

For a number of reasons, the usage of AuNPs is becoming more and more common in various fields of study. First off, related to the very toxic Cd and AgNPs, AuNPs are thought to be comparatively biologically non-reactive and thus appropriate for *in vivo* applications, but other groups are contesting this theory (Asif et al., 2025). The strong optical characteristics of AgNPs resulting from localized surface Plasmon resonance (LSPR), readily adjustable surface chemistry, which permits easy control over the size and form of the particles during production, and finally, the versatility in adding surface functional groups. Since AuNPs can combine easily into a single molecular package, which can further be regarded as multifunctional (Abbas et al., 2025). There are many studies which describe the applications of magnetic nanoparticles

and functionalized fullerene-based nanomaterials with quantum dots for the detection and treatment of human diseases provide instances of other nanomaterials for biomedical applications (Bhattacharyya et al., 2011; Lim et al., 2011).

According to a recent study, AuNPs specifically target cancer cells (Lin, 2015). AuNPs are widely used in drug administration, in conjunction with a therapeutic molecule, or alone with genes to offer significantly enhanced anti-tumor toxicity. Photo thermal therapy uses GNP as a probe due to their significant near-infrared surface Plasmon resonance (SPR) absorption. In this process, the target is heated and exposed to non-ionizing light sources, like lasers (Khan et al., 2023). When a laser is used on gold nanoparticles, the SPR band is converted to heat, which eventually results in cell necrosis and hyperthermia. For an individual to survive, necrosis is essential. Deadly illnesses have been linked to uncontrolled cell death. Powerful controls on unchecked cell death are therefore essential for the treatment of illness. AuNPs are well-liked due to their durability and simplicity in decorating. In Nano medicine and disease treatment, AuNPs are frequently utilized, especially in photothermal therapy and drug delivery (Chugh et al., 2018).

Anticancer Activity of AuNPs

The study indicates that AuNPs have also been observed to cause a number of types of cell death, mostly caused by internal processes such as mitochondrial instability, as shown in Figure 2, ER stress, and the production of ROS (Chugh et al., 2018). Once inside the cells, tumor suppressor genes and oncogenes are targeted by AuNPs, which causes cancer. Cells perish in a process known as apoptosis. In a different study, it was discovered that AuNPs localized to the nucleus improved apoptosis, cytokinesis inhibition, and cell-cycle arrest (Tiloke et al., 2016).

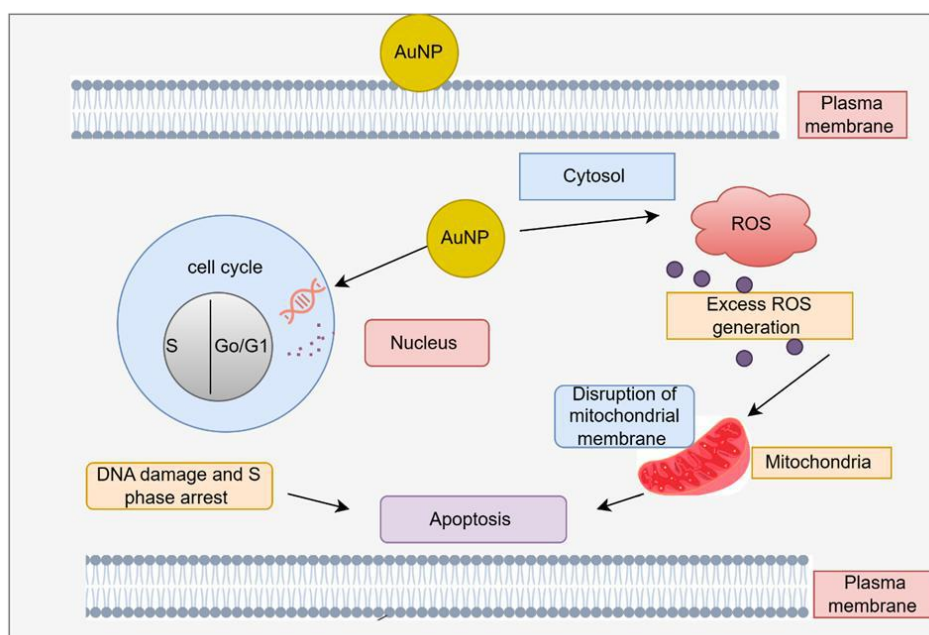


Fig. 2: Diagrammatic illustration of the suggested process for the human cervical cancer cell line (Helga) AuNPs synthesized from PLE to induce cell death

Because of their unique photo-optical characteristics, AuNPs have been effectively used in photothermal and photodynamic therapy. Because of their significant surface Plasmon resonance absorption in near-infrared areas, which produces warming effects when exposed to non-ionizing radiation such as lasers, AuNPs are employed as an enhancer in PTT (Khan et al., 2023). When a laser is applied to GNPs, heat is generated in the SPR band, which finally results in bursting and necrosis of the cells. Photodynamic treatment is the consequence of a photosensitizer, such as 5-aminolevulinic acid (5-ALA), interacting with molecular targets when exposed to light. Reactive oxygen species (ROS) are created when oxygen is present in a cell, and this can damage cells. Proteins, lipids, DNA, and other substances, resulting in necrosis or apoptosis (cell death). Gold nanoparticles have been used in the distribution of these photosensitive materials. tumor cell-specific sensitizers (Chugh et al., 2018).

Synthesis of Nanoparticles

Numerous methods have been employed for the synthesis process. Conventional physical and chemical techniques are often thought to be highly risky and costly. It's noteworthy that NPs created biologically have upright solubility, constancy, and yield. Biological methods appear to be the most basic, fast, safe, reliable, and eco-friendly among the various synthetic procedures for nanoparticles (NPs) as shown in Figure 3. They can yield definite size and shape in optimal conditions for relevant studies (Zhang et al., 2016).

Physical Method

The two methods for creating metallic nanoparticles including laser ablation and evaporation. For this, a tube furnace is used in the gas phase to process the evaporation-condensation to create nanoparticles. The furnace, which is a crucible containing the metal source material evaporated into the carrier gas for amalgamation, is located in the middle of the tube. The quantity, volume, and form of the final nanoparticles formed using this method are controlled by changes made to the reactor system (Chugh et al., 2018). AgNPs were created using standard

physical techniques like pyrolysis and spark discharge (Zhang et al., 2016). Additionally, AgNPs have been effectively produced in substantial quantities by using a ceramic heater in place of a tube furnace, which overcomes several drawbacks related to tube furnaces. Laser ablation is the process of removing a solid target material by irradiating it in that area with a laser (Nadeem et al., 2025). There are many factors that can affect metal nanoparticles, which include laser fluency, target solid, and liquid media (Chugh et al., 2018).

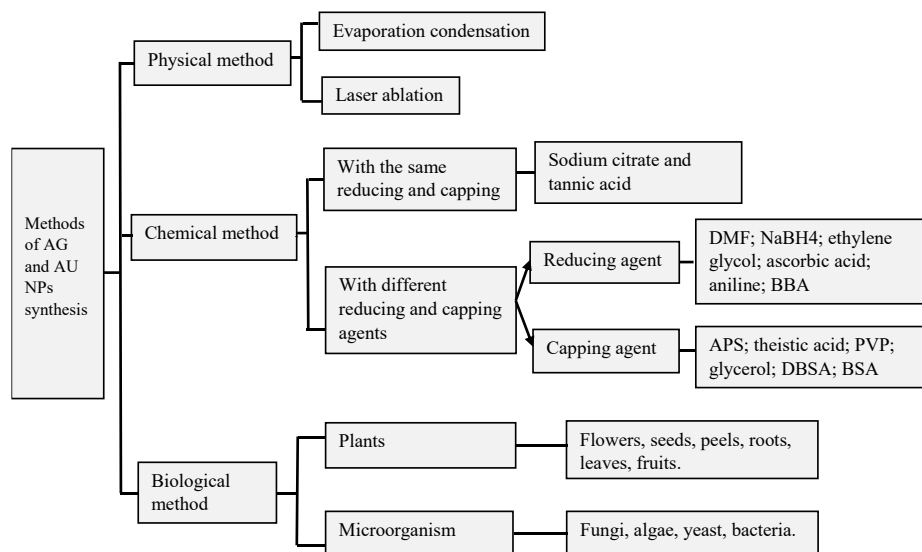


Fig. 3: Illustrates the three main techniques for producing AgNPs and AuNPs.

Table 1: AgNPs' possible therapeutic options for various cancer types.

AgNPs synthesis route	Size of AgNPs	Dose of AgNPs	Targeted cancer cells	Comments	Reference
Polydopamine (PDA)-coated Au-AgNPs	96.7 ± 6.1 nm	20–80 µg/mL	Human papillary thyroid cancer TPC-1	p53, LC3-A/B, DHODH, autophagosomes, and autolysosomes development during S phase cell cycle arrest	(Wang et al., 2019)
Aqueous extract of <i>Zingiber officinale</i> and <i>Curcuma longa</i> rhizome	20–51 nm	25 to 500 mg/mL	Human colon carcinoma (HT-29)	AgNPs produced may have anti-cancer properties.	(Venkatadri et al., 2020)
Shrimp shell extracted chitin	17 to 49 nm	57 ± 1.5 µg/mL	Human hepatocarcinoma (HepG2) cells	The potential of AgNPs is associated with the increased Bax, cytochrome-c, caspase-3, and caspase-9.	(Vijayakumar et al., 2020)
<i>Ginkgo biloba</i> leaves aqueous extract	40.2 ± 1.2 nm	3/6 µg/mL	Human cervical cancer (HeLa, SiHa)	Apoptosis induction and suppression of proliferation, all are mediated by SOD, GSH-Px, mitochondrial cytochrome c, Bcl-2, cytosolic cytochrome c, Bax, and cleaved caspase-3, -9.	(Xu et al., 2020)
Aqueous extract of <i>Satureja rechingeri</i>	62 ± 1 nm	Dose-dependent pattern	AGS gastric cancer cell line.	AgNPs decreased the appearance of the cyclin D1 and cyclin E genes while increasing the expression of the pro-apoptotic genes caspase-3, caspase-9, and Bax.	(Shiripoure et al., 2021)
Aqueous extract of <i>Zingiber officinale</i>	18.93 nm	172 mg/mL	Human pancreatic cancer cell lines	AgNPs demonstrated dose-dependent anti-cancer effects against AsPC-1 and extremely low cell survival.	(Wang et al., 2021)
<i>Annona muricata</i> Extract	6–31 nm	17.34 µM	Human breast cancer THP-1, AMJ-13	Apoptosis induction and colony formation inhibition ↑ by MMP ↑ p53, LC3-I/L.	(Jabir et al., 2021)
Aqueous extract of <i>Malva sylvestris</i>	74.4 nm	10–200 nm	Ovarian cancer cell lines OVCAR-3 and SK-OV-3.	The viability of ovarian cancer cells was eliminated by synthesized AgNPs primarily through upregulating caspase 3 and caspase 8, as well as by increasing the Bax/Bcl-2 ratio.	(Abbasi et al., 2022)
Fruit extract of <i>Dovyalis caffra</i>	12–53 nm	150 mg/mL	Prostate Cancer cell lines (PC-3)	It is thought to be a safe and promising source for Ag-NPs with anticancer action.	(Al-Rajhi et al., 2022)
Leaf extract of <i>Allium saralicum</i>	13.9–55.2 nm	208, 250, 200, and 188 µg/ml	Breast cancer cell lines i.e., SK-BR-3, MDA-MB-231, AU565 [AU-565], and Hs 281	The inclusion of AgNPs decreased the viability of cancer cells.	(Xu et al., 2023)

Chemical Method

Metal nanoparticles can be created chemically by reducing their metal salts. Thus, to get any NPs, metallic salts, such as Ag, Au, or others, can be reduced. To reduce this, various chemical agents, including oxalic acid, sugar citrate, and sodium borohydride, can be used. When a reducing material transfers electrons to a silver ion in a liquid phase, the silver ion's valence changes from positive to zero. (Preethi et al., 2016; Chugh et al., 2018). Sodium borohydride (NaBH₄) and dodecethiol can then be used to reduce the complex and provide stability. The scientists found that even little changes in a variable can have a significant impact on the structure, average size, size distribution, stability, and self-assembly tendencies of nanoparticles (Sehgal & Kumar, 2022).

Although diazonium gold (III) salt can also be utilized, gold (III) chloride or chloroauric acid is often the precursor in the synthesis of AuNPs. The latter can be reduced with 9-BBN (9-borabicyclonane) and coated with bovine serum albumin (BSA) to produce stable spherical AuNPs with a mean diameter of about 7 nm. This reduction can be made overnight at room temperature. Chloroauric acid's Au³⁺ can be reduced to Au using sodium borohydride, and then the resulting spherical NPs with a mean diameter of around 9 nm can be coated with cystamine (Preethi et al., 2016).

Trisodium citrate is the most utilized reducing and capping agent. It performs best at neutral pH, high temperatures (about 100 °C), and average reaction times (about 20 minutes). When the reaction conditions are changed, spherical AuNPs with tunable dimensions of roughly 9nm, 14nm, or 40nm are produced (Ujica et al., 2020).

Biological Method

There are two main methods for synthesizing NPs, including top-down and bottom-up. The top-down method of nanoparticles synthesis involves lithographic procedures and laser ablation, etc. While the bottom-up technique synthesizes nanoparticles from simpler compounds (Taha, 2022). These techniques have given rise to the green synthesis of metallic nanoparticles by using plant resources (Jabeen et al., 2021).

Plants produce many types of nanoparticles with different sizes and other characteristics, as shown in Table 1 (Sehgal & Kumar, 2022).

Characterization of Ag and Au Nanoparticles

For the synthesis, silver and gold nanoparticles must be characterized on the basis of some of their characteristics, including size, shape, and other details (Ujica et al., 2020). These may be dependent on using various techniques, some are also mentioned in Table 2, like scanning electron microscopy (SEM) and transmission electron microscopy (TEM) (Parthiban et al., 2019).

Table 2: Characterization of silver (AgNPs) and Gold (AuNPs)

Method name	Characteristics	References
Dynamic light scattering	Studies on zeta potential, size, and size distribution	(Ahmad et al., 2017)
Scanning and transmission electron microscopy	Dimensions, dispersion of sizes, and form	(Ranoszek-Soliwoda et al., 2017)
Ultraviolet-visible spectroscopy	Represents the existence of nanoparticles	(Nanda et al., 2018)
High resolution transmission electron microscopy	NPs' morphology, structure, and form	(Choudhary et al., 2018)
Atomic force microscopy	Dimensions, morphology, and grouping	(Daphedar & Taranath, 2018)
Scanning electron microscopy	Characteristics of surfaces	(Zhang et al., 2019)
Fourier-transform infrared spectroscopy	Spectrum or substances that are found on the surface	(Rajkumar et al., 2019)
X-ray diffraction	Crystal structure	(Gopinath et al., 2019)
X-ray photoelectron Spectroscopy	The elements' empirical formula, elemental makeup, chemical and electronic states, as well as the other elements to which they are connected	(Rolim et al., 2019)
Transmission electron microscopy	Morphology and size distribution	(Sunderam et al., 2019)

Conclusion

Currently, cancer is still a common cause of death worldwide, but using silver and gold nanoparticles in the field of cancer has provided a promising advancement and benefits in treating this illness. These NPs are important and beneficial in the case of therapeutic treatments due to some of their important properties, including their electrical and chemical properties. Their adaptability in the field of cancer is evaluated by their ability to target specific cancerous cells without any damage to healthy cells and tissues. Further research on the application of NPs, along with the interest in the "green" technique for nanoparticles in cancer therapy, is now emerging because they are environmentally friendly and beneficial to use. Silver and gold nanoparticles can be synthesized using the green chemistry synthetic method. To completely comprehend their safety profile, maximize their effectiveness, and handle issues like possible toxicity and long-term stability, more research is necessary. Au and AgNPs offer hope for more efficient and customized cancer treatments for patients everywhere, marking a promising new chapter in the field.

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Introduction to Biosafety and Biosecurity in the Context of Biorisk Assessment and Management in Biomedical and Clinical Laboratory Settings

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Abstract

These days, biosafety and biosecurity in clinical and academic research facilities are major worldwide concerns. It is the primary duty of governments worldwide to increase their awareness and readiness for detecting and containing hazardous biological agents; this duty includes not only providing a biologically safe environment for laboratory workers but also the biosafety of others in the institution and community. Given the high rate of biological harm caused by evolving infectious diseases and bioterrorism, we are all equally responsible for Biosafety and Biosecurity at work. The successful execution of laboratory tests depends on safe and efficient laboratory operations and pathogen handling, which also affects the safety of the laboratory environment, pathogens, and laboratory personnel. This chapter discusses the fundamental concepts of laboratory Biorisk assessment and management, laboratory biosafety, and laboratory biosecurity. Furthermore, research that is carried out for legal purposes and yields knowledge, information, technology, or products that have both positive and negative impacts is known as dual-use research of concern. Laboratory policy guides ought to provide biosafety and biosecurity protocols for the benefit of laboratory staff.

Keywords: Biosafety, Biosecurity, Biorisk, Estimation, Clinical laboratories

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Introduction

Biomedical and clinical laboratories are pivotal in advancing healthcare, yet they handle biological agents that pose inherent risks. Effective management of these risks through biosafety and biosecurity is critical to safeguarding personnel, the public, and the environment (Cornish et al., 2021). Research in life sciences that uses biological agents may pose harmful effects. It is because clinical laboratories commonly handle unknown idiopathic specimens and specimens that may be infected with several illnesses, the hazards associated with the safety of laboratory personnel in a clinical laboratory setting differ from those in a research or teaching laboratory. Most public and animal health clinical laboratories adopt biosafety methods, engineering, and buildings that meet Biosafety Level 2 (BSL-2). The infectious agent or other hazards in the specimens they handle and process may be unknown to the clinical diagnostic laboratory employees (Meehan & Potts, 2020). These hazards might include adverse outcomes of the injuries resulting from unexpected and unintentional exposure to risks (biosafety) and their potential misuse (biosecurity risks) that cause others to induce harmful effects either directly or indirectly. These hazards are collectively termed as biorisks. The term biorisk management (BRM) is used to assess, identify, evaluate, and mitigate these associated biorisks (Greene et al., 2023).

Biosafety and biosecurity guidelines are the collection of rules, regulations, and laboratory practices essential for the laboratory personnel who are working with potential pathogens such as viruses, bacteria, parasites, and fungi. These guidelines are the key factors to guarantee the proper maintenance and monitoring of biosafety and biosecurity policies and procedures at all levels of laboratory management (Kalam et al., 2021). Laboratory-acquired infections (LAIs) are extremely prevalent worldwide. According to preliminary data from the early 20th century, about 4,000 LAIs happened worldwide between 1930 and 1978 (Muneer et al., 2021). Globally, laboratories encounter biosafety and biosecurity-related challenges that need to be addressed in accordance with appropriate biorisk management guidelines for lab personnel.

According to the World Health Organization, laboratory biosafety is defined as “The containment principles, technologies, and practices that are implemented to prevent unintentional exposure to pathogens, their toxins, and or their accidental release”. Based on these traits, innate variables, and the mode of transmission, the World Health Organization (WHO) has suggested a system of classification for laboratory use that classifies biorisk agents into four risk groups. The risks to the community and laboratory personnel are covered by the four groups (Zaki, 2010). Laboratory biosafety comprises four basic controls that include personal protective equipment (PPEs), engineering controls, Standard operating procedures (SOPs), and administrative controls. The World Health Organization defines biosecurity as the procedures, technology, and containment methods used to stop the intentional misuse or release of microbes. It is predicated on four main controls: information, material, personal, and physical (World Health, 2004).

These two terms complement each other to form the term laboratory bio-risk management (BRM), which describes the proactive control of hazards and the formulation of strategies to reduce the occurrence of incidents when working with toxins and infectious agents. Risk assessment, risk management, risk communication, and hazard identification are the primary elements of bio-risk management (Muneer et al., 2021). This chapter is based on biorisk assessment and biorisk management with underlying principles of biosafety and biosecurity, focusing on their integration in clinical laboratory settings in order to address threats associated with accidental and intentional damage (Ameneiros, 2024). The biosafety and biosecurity risk assessment is illustrated in Figure 1.

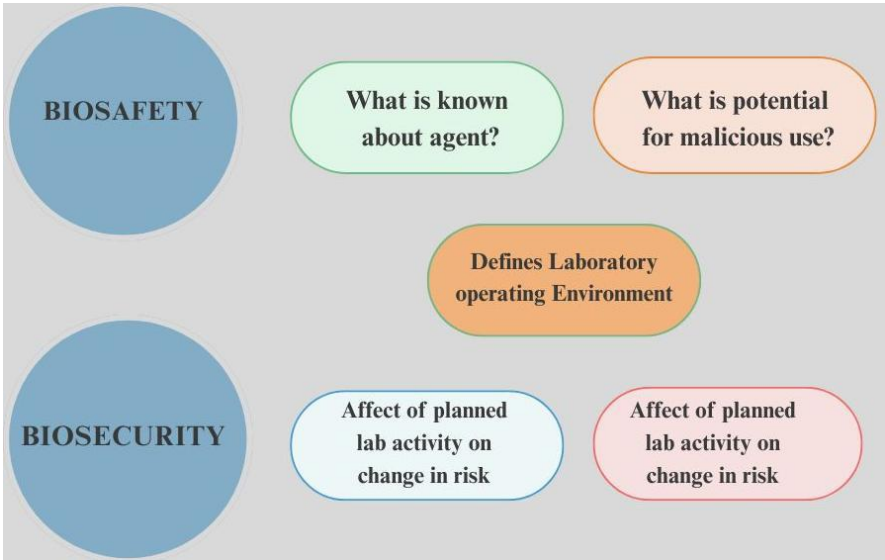


Fig. 1: Biosafety and Biosecurity Risk Assessment (canva.com)

Biosafety Risk Assessment Process

To detect and control the biorisks existing in a biological laboratory, a laboratory risk assessment should be a methodical procedure. Every facet of the workplace is examined in a risk assessment, including the site, planned tasks, staff, storage, sample transportation and transfer, destruction, access, and security, among other things (Astuto-Gribble & Caskey, 2014). A biosafety risk assessment ought to follow a methodical and reproducible procedure, such as the five-step technical approach outlined and demonstrated in Table 1.

Table 1: Summary of the procedure of Biorisk Assessment

	Step 1	Step 2	Step 3	References
Situation	Identify the hazard. For this, a list of biological agents used should be made.	Consider the host, such as lab staff, the human community, and the animal community.	Consider work activities and environment, such as location, etc.	(Peng et al., 2018b)
Risk	Consider that all risks could be more than one risks.	-	-	(Montibeller et al., 2020)
Characterize risk	Check the likelihood of infection with the agent.	Check the likelihood of infection on the host.	Check the likelihood of infection in terms of the environment.	(Astuto-Gribble & Caskey, 2014)

Biosecurity Risk Assessment

There are a few significant distinctions between biosecurity and biosafety assessments. A biosecurity evaluation entails identifying the facility's vulnerabilities, threats, and laboratory assets in addition to the current biosecurity program that is in place to reduce biosecurity risks. A biosecurity risk assessment will be used to determine the consequences of potential theft or destruction of the designated assets. Finding potential security risks based on these factors is the first step in putting a biosecurity program into action (Astuto-Gribble & Caskey, 2014). The biosecurity risk assessment procedure is summarized in Table 2.

Biorisk Management

Laboratory biosafety and biosecurity are crucial in controlling infectious disease outbreaks. This can be accomplished by designing the procedures in such a way that proves to be protective for the laboratory workers and the working environment from potential pathogens and

other biohazard risks associated with them (Cornish et al., 2021). Laboratory acquired infections (LAIs) were first acknowledged in the late 19th and early 20th century which was marked as the evolutionary period of the initiation of the history of biosafety and biosecurity.

Table 2: Summary of biosecurity risk assessment process and steps

	Step 1	Step 2	Step 3	References
Define situation	Identify the assets, such as it is a pathogen, a toxin, or an animal.	Identify the threat, such as it is an outsider or an insider, etc.	Identify the lab environment for personnel and physical security.	(Montibeller et al., 2020)
Define risk	Creating potential scenarios to - consider various assets.	-	-	(Astuto-Gribble & Caskey, 2014)
Characterizing risk	Asset assessment, such as a result of the use of a malicious agent.	Assessment by impact on laboratory personnel.	Facility assessment to determine the environmental condition.	(Burnette & Tobin, 2021)

The spread of *Corynebacterium diphtheria* by mouth pipetting in 1898 highlighted the demand for the development of safe and effective laboratory procedures and practices. A number of containment facilities and procedures were introduced with the increasing risk of the spread of pathogenic micro-organisms in the laboratory. These practices included from the use of personal protective equipments (PPEs) to the proper handling and disposal of biological waste material (Qasmi & Khan, 2019). The upgradation of the laboratories with high containment laboratory facilities was introduced for the safe handling of dangerous pathogens of contagious nature. This includes the introduction of laboratories with different biosafety levels (BSL). This step proved to be a significant turning point in the history of biosafety laboratories.

The environmental biosecurity of the laboratory was addressed after the use of pathogens and their spores as biological weapons during Cold War. These stringent measures came into practice in the mid-1900s. The environmental biosecurity was ensured with the equipment of a laboratory with best containment facilities like controlled access, HEPA filter-based ventilation, and closed rooms (Yeh et al., 2021). Outbreaks like Ebola, SARS, and avian influenza virus H5N1 highlighted the need for environmental biosecurity (Mphande-Nyasulu et al., 2024). Low and middle-income countries (LMICs) are far behind in establishing uniform standards, thus lack well-equipped laboratories with high containment facilities due to difference in the availability of resources (Cornish et al., 2021). The selection criteria for biosafety level depend on the pathogen to be handled. BSL can also be adjusted according to the potential of pathogen with the adoption of necessary measures such as SARS-Cov-2 can be diagnosed in BSL-2 with the adoption of necessary measures needed in BSL-3 (Sherin, 2024). The BSL framework ensures the safe and effective operation of laboratories by minimizing risks to humans and the environment.

Principles of Biosafety in Clinical Laboratories

Laboratory biosafety principles focus on the use of different approaches for the minimization of the risk originating from the mishandling of pathogens and biological hazards. Biosafety levels are classified as biosafety level 1, biosafety level 2, biosafety level 3, and biosafety level 4 based on their containment facilities and pathogenicity of the pathogen to be addressed. All biosafety levels highlight the use of special laboratory frameworks and standards of working in the laboratory, such as safety gear, safe laboratory practices and procedures, building design, working environment, and safety of working laboratory personnel and public (Gallandat & Lantagne, 2017). BSL-4 is the highest level of biosafety, handles the pathogenic micro-organisms found to cause fatal diseases such as Ebola virus, whereas BSL-1 handles from no to moderately low pathogenicity microorganisms such as *E. coli* (K-12) and *B. subtilis* (Brass et al., 2017).

Standard microbiological practices should be ensured. Eatables and beverages should not be allowed in laboratories. Standard microbiological practices like availability of sink, frequent hand washing, safe waste management techniques, and cleaning of the work surface with proper disinfectant after the completion of work should be adopted (Roy, 2009).

In addition to this, BSL-2 addresses the handling of pathogens of moderate to severe pathogenicity. These include *S. aureus*, *Salmonella* spp., and hepatitis B virus.

Moderately dangerous pathogens responsible for causing low-potential diseases are studied in a BSL-2 laboratory, such as *Staphylococcus aureus*, *Salmonella* spp., and hepatitis B virus. Use of personal protective equipment such as overalls, gloves, mask, eye protection, and a suitable biosafety cabinet (BSC) is recommended at this level. There are restrictions on access to BSL-2 labs, and staff members need to receive pathogen management training. Sharps handling is kept to a minimum to lower the danger of needle stick injuries, and decontamination procedures for waste and surfaces are more stringent than at BSL-1 (Barkham, 2004). BSL-3 is intended for use with substances including *Mycobacterium tuberculosis*, SARS-CoV-2, and anthrax that can cause serious or even fatal illnesses when inhaled. With sealed windows, regulated airflow to maintain negative pressure, and specialized ventilation systems with HEPA filtration, laboratories are designed to stop the spread of germs. Employees must use PPE suitable for the pathogen and wear respiratory protection. Aerosol-producing processes are carried out in approved BSCs. Only authorized workers are allowed inside, and labs need to have an anteroom where PPE can be put on and taken off. To make sure safety procedures are followed, risk assessments are carried out on a regular basis (Caskey et al., 2010).

The highest biosafety level, BSL-4, is only used for studies on substances like the Marburg and Ebola viruses that have no known cure and a high risk of aerosol-transmitted diseases. These labs are frequently remote establishments with stringent safety regulations and access restrictions. Employees must operate in Class III biosafety cabinets or specially created labs with high-containment features while wearing fully encapsulated, positive-pressure suits. All exhausted air is filtered and cleaned before it is exhausted. Laboratories are equipped with safer disposal techniques, chemical showers, and installation of airlock systems. For employees operating at this level, supervision and training are essential to guaranteeing strict adherence to procedures (Bressler & Hawley, 2017).

Personal protective equipment (PPE) are the key factor to ensure laboratory biosafety. PPEs considerably pose lower exposure risks for the lab worker by ensuring safety physical barrier between biohazard substances and the working laboratory personnel. Gloves, lab coats, face shields, and respiratory protection are examples of common PPE that are suited to the particular biosafety level and laboratory protocols. BSL-

1 require basic facilities like wearing of lab coats and gloves whereas, BSL-3 required HEPA filtered based ventilation and completely closed rooms and sealed protective suits (Roy, 2009). PPE must be used and maintained properly to be effective because incorrect handling might counteract its protective effects (Noble, 2011). Because aerosols may include pathogenic pathogens in high containment laboratories (BSL-3 and BSL-4), respiratory protection is especially important. Employees frequently wear positive-pressure suits or powered air-purifying respirators at these levels to avoid breathing in germs. This equipment is essential for handling substances like the Ebola virus and *Mycobacterium tuberculosis*, which can cause serious or fatal illnesses when inhaled (Bressler & Hawley, 2017). The most widely used PPE is gloves, which act as a barrier to prevent direct contact with infectious substances. When handling sharp objects, they are especially crucial because unintentional punctures might allow viruses to enter the body. For an extra degree of protection in high-risk scenarios, double gloves are advised. For gloves to be effective, though, they must be used in concert with other strategies, like practicing good hand hygiene (Noble, 2011). Goggles and face shields defend the eyes and mucous membranes from splashes and aerosols. These are necessary when working with liquid cultures or when performing droplet-generating processes like centrifugation. Most labs handling biohazardous materials need properly fitting goggles and shields because they greatly lower the danger of exposure to hazardous fluids (Noble, 2011). PPE needs to be utilized in conjunction with engineering controls, administrative controls, and appropriate laboratory techniques as part of a larger biosafety plan. Special training programmes and workshops need to be conducted in order to ensure the safe use of personal protective equipment, such as how to put it on and take it off, and it's safer disposal. The possibility of contamination of PPEs can be mitigated by their proper handling and use (Sa & Ikram, 2020). Finally, maintaining a safety culture in clinical laboratories needs the development of administrative controls. These controls include developing and executing standard operating procedures (SOPs), carrying out regular risk assessment tasks, and ensuring comprehensive training of the laboratory personnel through different workshop sessions and seminars etc. Ensuring the appointment of regular biosafety officers and other necessary administrative staff in the laboratory, executing emergency response plans, and maintaining incident reporting systems are further administrative actions that need to be taken in the clinical laboratory (Caskey et al., 2010). This framework provides the safe and consistent operation of a biosafety laboratory. Integration of administrative controls, all BSLs, and PPE makes up the biosafety standards of the laboratory. They provide a high degree of protection, including prevention of laboratory-acquired infections (LAIs) (Barkham, 2004).

Biosafety Measures and Controls

Different collaborative approaches and policies have been in use to prevent the dissemination of pathogens and their spores/toxins to the environment. These are termed as biosecurity. In order to ensure the safety and security of the public, it is necessary to control the progression of the disease outbreak (Renault et al., 2021). Collaborative efforts are required for the implementation of these policies nationally and internationally to control pandemics and calamities, as it happened in the case of COVID-19.

Implementation of these strategies and policies at the international level needs collaborative efforts from the global communities, with special focus on the biosafety and biosecurity of the laboratory personnel, health care professionals, such as paramedical staff who are dealing with infectious agents (Maehira & Spencer, 2019; Orelle et al., 2022). Cross-contamination should be prevented in order to ensure the safety of the workers. Implementing the above policies and biosecurity and biosafety strategies and protocols will minimize the risk of accidental release of the pathogens (World Health, 2024).

For biorisk management, it is essential to overcome LAIs. Micro-organisms responsible for causing LAIs include *Salmonella* spp., *M. tuberculosis* and *Brucella* spp. Adoption of good microbiology practices can help mitigate these risks. Training of the laboratory staff is essential to regulate the use of PPE, engineering controls and administrative procedures (Peng et al., 2018a). A number of administrative and control measures were adopted during the COVID-19 pandemic to break the chain of the spread of the disease outbreak (Cheng et al., 2021). Risk assessment is done at the pre-operational and operational stages of the biomedical laboratory. Other good microbiological practices include the use of proper disinfectants to clean the work surface, such as sodium hypochlorite or 70% alcohol, waste management, SOPs for the use of biosafety cabinets, and the proper handling of pathogens are required (Bhat et al., 2020). Strict adherence to the SOPs is recommended to handle the dangerous viruses in the laboratory for personal and public health safety. Low and middle-income countries have to face severe challenges of the scarcity of standard operating laboratories and poor lab infrastructure due to a lack of enough resources. In order to meet the standards of biomedical and clinical laboratories, laboratory practices are adopted in compliance with the International Standard No. ISO 3500:2019. This will help laboratory staff meet administrative deficiencies and will help better performance and evaluation of the different laboratory techniques and conducive work environment (Maehira & Spencer, 2019; Orelle et al., 2022).

Training of the workers for the proper bio waste management and handling of the potential pathogens is required (El Magrahi, 2017). Further training programmes and the supply of PPEs, BSCs, and other necessary materials should be ensured in the clinical laboratory. Laboratory infrastructure should also be addressed as per SOPs. These shortcomings can be addressed by updating training programmes and laboratory practices from time to time (Ogaro et al., 2018).

Innovation in Biosafety and Biosecurity in Clinical Laboratories

These covered risk group classification and biosafety containment levels, the efficacy of various risk mitigation strategies, the proper use of biosafety cabinets (BSC), regulations, and the roles and duties of staff in implementing biorisk management (BRM). Other risk control measures include the use of PPE, a suitable BSC in order to deal with infectious agents, maintenance of BSCs, labeling and segregation of the samples, waste handling, spill kits and availability of trained staff, fire extinguisher, and smoke detectors (Sarwar & Vijayan, 2021). The updation in the infrastructure of the laboratory has also ensured improved biosafety practices and policies, legal framework, and collaborative approaches from international communities to mitigate the risk associated with the spread of LAIs and handling of biological hazardous material (Astuto-Gribble & Caskey, 2014).

Furthermore, the development of International Standard Operating Number ISO 35001:2019 for biorisk management in compliance with

laboratory biosafety and biosecurity (Lestari et al., 2021). WHO laboratory biosafety manual focuses on the use of strategies for the biorisk management, which emphasizes that laboratories to adopt policies related to personal safety (Ficociello et al., 2023).

Training and Monitoring System

Laboratory monitoring with the help of digital devices, such Internet of Things (IoT), should be implemented. This system consistently monitors parameters such as temperature, humidity, air flow, and other factors in order to ensure biosafety in the clinical laboratory. Apart from this, security locks and security alarms linked to electronic devices also ensure safety and help take immediate action in case of emergency (Samonte et al., 2021). To handle high-risk risk, virtual reality can be used to avoid exposure to the potentially dangerous pathogens and toxins, such as in BSL-3. VR provides the expertise on laboratory biosafety protocols (Kaltsidis et al., 2021). Furthermore, a conducive work environment can be assured by following the guidelines of the immersion learning module (Cardoso et al., 2021).

International Collaboration

Collaborative international efforts and co-operations are required for the proper compliance with the biosafety measures in the laboratory. The globalization of different practices and procedures related to biosafety and biosecurity relies on two initiatives, such as the Global Health Security Agenda (GHSA) and the WHO laboratory Biosafety manual. These address the capacity building. Low and middle-income countries, due to low resources, are not able to build such well-equipped laboratories of international standards with proper containment facilities, so they halt the compliance process (Maehira & Spencer, 2019). Coordinated approaches focus on the localized action plan in terms of workforce development that is best suited to the laboratory biosafety requirements (Safdar et al., 2023). The US has established the National Biosafety and Biosecurity Agency (NBBA) to handle the pathogens responsible for global pandemics such as COVID-19 in order to meet the current requirements of biological research (Gillum et al., 2024).

Furthermore, the legislation body in East Africa has adopted the legislation protocols named Cartagena Protocol to strengthen the legislation on biosafety and biosecurity (Nahs et al., 2024). A conducive work environment can be created following coordinated approaches such as exchange of information, technical assistance, and biosafety standards (Maehira & Spencer, 2019).

Conclusion

Different training programmes on biorisk management and risk assessment should be conducted routinely. Comprehensive and long lasting impacts of such trainings can be achieved if followed properly. In order to ensure BRM in the laboratory, training programmes should be conducted as per the requirements of the institution, the concerned laboratory and their proficiency levels. Biorisk assessment ensures personal safety, environmental safety and public health safety, whereas biorisk management helps identify the risk, mitigate it and ensure the adoption of coordinated approaches and policies for the continuous evaluation and improvements of effective BRM. These goals could be approached with strict compliance to different surveillance programmes such as GHSA and WHO, legislation, laboratory workers training nationally and internationally particularly in low resource countries such as Pakistan.

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Advances in Medicinal Chemistry: Metal-Based Compounds as Innovative Therapeutic Agents

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Abstract

The field of medicinal chemistry owes much of its progress to organometallic compounds since they are known to be important for their therapeutic and bioactive effects. In medicine, they are applied to help cure cancer, different bacteria, and problems linked to swelling and the brain. Many compounds made using organometallic chemistry are effective in treating cancer since they only focus on cancer tissue and not on healthy tissues. The development of drugs using organometallic compounds has the potential to assist in handling drug-resistant bacteria and aid the treatment of Alzheimer's and similar diseases. Since they are able to act on redox reactions, DNA, and the immune system, they are essential for finding new breakthroughs in medicine. This chapter covers how organometallic compounds can play a part in medicine and how they could enable the creation of novel treatments.

Keywords: Metals, Compounds, Medicine, Therapeutics, Health

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Introduction

Since these materials are carbon and other metals, their atoms attaching to one another is made possible by a chemical bond (Gasser et al., 2011). A combination of natural and man-made portions in the molecules ensures that the metal and carbon blend easily in the liquid. Just like ions and covalent molecules, they can strengthen their bonds, which becomes beneficial in many circumstances. The importance of these structures for living things and the world is clear from all kinds of living things (Aziz et al., 2024). Metals have been found to benefit medicine because they ease illnesses and maintain the normal functioning of the body. Iron-based medicines are used by doctors in chemical treatment for various medical concerns, while special metals are applied to find different objects inside the body (Ong et al., 2020). Scientists use them to produce drugs because they interact with body components, exist in several forms, and can be slightly modified. Medical organometallic chemistry focuses on producing some compounds that could benefit medicine and discovering how they are processed in the body (Brown et al., 2015). Ferrocene was the first organometallic chemical to be looked at for its medical use after its anti-cancer properties were discovered. Consequently, more research was done on using organometallic chemicals to treat cancer (Koepf-Maier et al., 1987). The first studies on organometallic compounds resulted in them being used as medicines for several health issues. Iridium, ruthenium, and rhodium from the platinum-group metals can be used to make organometallic compounds that could help treat parasite diseases, for example, malaria. Discovering that ferroquine, a metal-carbon-based medicine, works on malaria shows that such drugs differ in how they interact with enzymes (Mbaba et al., 2020). Using real-world instances, we can show how organometallic compounds are used in medicine. In chemotherapy, cisplatin is used to bind with DNA in testicular, ovarian, and lung cancer patients, preventing the cells from reproducing. It has been found that ferrocene-based drugs may prevent HIV from replicating, which brings new opportunities for developing antiviral medicines (Ong et al., 2020). They point out how organometallic compounds can overcome the resistance to traditional medicines and suggest that they will be significant in future medical breakthroughs.

Medical Uses of Organometallic Compounds

During the last couple of years, organometallic compounds have been valuable in medicine due to the effectiveness they show in treating various illnesses. It connects the research on plant or herbal remedies for the treatment of cancer, various viral diseases, inflammation, and cases of Alzheimer's (Brown et al., 2015). The table that follows discusses the agents used in therapy and explains how they can be helpful, but also points out their limitations. Various benefits are given in the Table 1.

A lot of metal complexes are now used to treat illnesses, as they are able to help the body in their own special ways. As shown in Figure 1 below, several metals like titanium, calcium, sodium, iron, copper, and even a few more are used to address a range of diseases. A good example is titanium, which is used in joint replacement, and strontium is used as a medicine for people affected by bone cancer (Diao et al., 2024). Often, sodium and iron compounds are added to medicines to address conditions such as heartburn and high blood pressure, while copper compounds are used to address Menkes disease (Zhang et al., 2022). It is also important to note that mixing silver and zinc can slow down the growth of harmful bacteria, so these chemicals are often found in treatment for burns and infections. Some other metal complexes, for example, those from vanadium and lithium, are under investigation to see if they can help control blood sugar in diabetes and improve emotional well-being in other patients (Matai et al., 2020). The versatility of metal complexes extends to their roles in cancer therapy, neurodegenerative diseases, and infectious diseases, highlighting their significance as therapeutic agents. Ongoing research continues to expand their applications, emphasizing the importance of organometallic compounds in enhancing efficacy and selectivity for specific medical conditions.

Table 1: Benefits of organometallic compounds and their health risks

Therapeutic Agents	Uses	Limitations	References
Iridium (III) complexes	ROS-mediated apoptosis and mitochondrial malfunction as remedies for cancer.	Potential toxicity to normal cells and the need for further research on their mechanisms and long-term effects.	(Lo et al., 2012)
UiO-66-NH ₂ (MOF based on zirconium)	Bone regeneration and the treatment of bone tumors.	Need for further studies on long-term safety and potential side effects in clinical applications	(Yuan et al., 2023)
Complexes based on gold(I) and including SERD and TrxR inhibitors	Treatment of ER-positive breast cancer by producing ROS and degrading estrogen receptors.	While gold complexes exhibit potent activity, their safety profiles and potential side effects require thorough investigation to ensure clinical viability.	(Lu et al., 2023)
Ru (II) complexes	half-sandwich Therapy of melanoma through immune response modulation and ICD induction.	Need for further research on its mechanisms and potential side effects in clinical applications.	(Xu et al., 2023)
Nanoparticles of taxifolin ruthenium-p-cymene (Tax Ru-NPs)	Treatment of lung cancer by preventing metastasis and triggering apoptosis.	The path to clinical use is complicated by stringent regulatory requirements for nanoparticle-based therapies, which may delay their availability.	(Matai et al., 2020)
Gentamicin-loaded Gm@UiO-66-MA	MOF, Overcomes bacterial resistance and increases the effectiveness of antibiotics.	MOFs can be sensitive to environmental conditions, which may affect their stability and drug release profiles.	(Sun et al., 2013)
Zinc phthalocyanine (ZnPc)	Mycobacterial infections can be treated with antimicrobial photodynamic treatment (aPDT).	ZnPc's hydrophobic nature limits its systemic administration, necessitating complex formulations to enhance solubility.	(Keyal et al., 2018)
Heptamethine-based compounds	Staphylococcus epidermidis antibacterial treatment using photoactivation.	Poor water solubility, low singlet oxygen production, and non-targetability, which hinder their effectiveness in photodynamic therapy and clinical applications.	(Zhang et al., 2022)
Organo-osmium (II) half-sandwich complexes	Redox processes are used to treat drug-resistant Mycobacterium TB.	Lack of selectivity between Mtb and human cells, raising concerns about potential toxicity.	(Coverdale et al., 2021)
Copper-based metallo-surfactants	Photodynamic treatment for Staphylococcus aureus that is resistant to many drugs.	Need for innovative approaches to accelerate wound healing.	(Diao et al., 2024)
CO-releasing nanocomposites	MRSA antibacterial therapy and biofilm targeting using ROS production.	Antibiotic resistance leading to challenging infections.	(Tirkey et al., 2022)
Copper-thiosemicarbazone complex	They have potential applications in anti-cancer chemotherapy and as non-tissue selective blood perfusion tracers.	Careful interpretation of percentage uptake measurements is crucial, and active transport mechanisms need further investigation.	(Dearling et al., 2002)

Applications in Anticancer Therapies

One of the biggest ailments endangering human health today is cancer. The mortality rate is still high, and its incidence is growing gradually (Kerru et al., 2017). By offering replacements for traditional platinum-based treatments like cisplatin, which are effective but usually hampered by major side effects and drug resistance, organometallic compounds have drastically transformed the way that cancer is treated. More recently, iridium (III) compounds with improved anticancer effects have been discovered. These compounds demonstrate cytotoxicity for tumor cells while preserving the health of the kidneys, liver, and heart. In addition, they prove effective in restraining tumor growth. The mechanisms simultaneously induce DNA damage, disrupt mitochondrial workings, and trigger apoptosis by means of ROS to prevent cancer cell growth. In vivo testing has confirmed that some of these complexes show stronger inhibitory effects against cancerous growth than cisplatin (Du et al., 2019). Bone repair and tumor therapy benefit from metal-organic frameworks and their related materials when treating bone tumors. These materials have been shown to both treat cancer and facilitate new bone growth. Both bone regeneration and faster healing after surgery are promoted by these materials. As a result, these materials can serve as precursors for designing novel medicines that work well in treating bone tumors (Yuan et al., 2023). A range of strategies suggests that organometallic materials are highly promising for the therapy of ER-positive breast cancer. By simultaneously integrating both a SERD and an inhibitor for TrxR, it's possible to both reduce estrogen receptor expression and disrupt the cell's redox balance at once. This ROS production can both stop the growth of cancer and boost the immune system.

The recent advances in multifunctional compound development now allow for more precise treatments of breast cancer (Lu et al., 2023). Derivatives of Cu, Zn, and Co transition metal complexes with a heterocyclic connection to benzene exhibited superior anticancer death properties against a wide range of tumor types, notably esophageal cancer. It is important to mention that the Cu-based compound was the most effective in fighting cancer. It caused DNA damage, changed mitochondria, and increased ROS inside the cells to lead to apoptosis. Such complexes may be useful for further development as anticancer drugs since they can stop cell division and damage the mitochondria. Just as organometallics have been used to attack breast cancer by targeting two areas, using organometallics in cancer therapy is now being considered as they also target both redox balance and cancer cell metabolism (Zhi et al., 2019). Ruthenium-based organometallic compounds could be used to fight cancer since they can induce ICD, which activates the immune system's response. A Ru (II) half-sandwich molecule promotes ICD by activating four important markers, such as calreticulin (CRT), high mobility group box 1 (HMGB1), heat shock protein 70 (Hsp70), and also by releasing more ATP. The complex helps the immune system fight melanoma cells and prevent their spread while enhancing the immune system's attack on tumors. Ru-containing complexes suppress melanoma by damaging mitochondria and causing ER stress to trigger both an attack on the tumor and the activation of an immune response (Xu et al., 2023). TaxRu-NPs may be useful in the treatment of cancer. Taxifolin ruthenium-p-cymene nanoparticle (TaxRu-NPs) are beneficial for chemotherapy since they promote apoptosis, inhibit clumping and prevent the proliferation of cancer cells. It was found that TaxRu-NPs promote wound healing and block cell proliferation. TaxRu-NPs also decrease the levels of important immune cells and control the amount of two proteins involved in the promotion of tumor growth, VEGF and β -catenin. Inhibition of the VEGF/ β -catenin pathway via TaxRu-NPs decreases the chances of metastasis and angiogenesis in late-stage lung cancer. we've learned how available data can guide the creation of therapies for advanced cancers of the lung (Das et al., 2024).

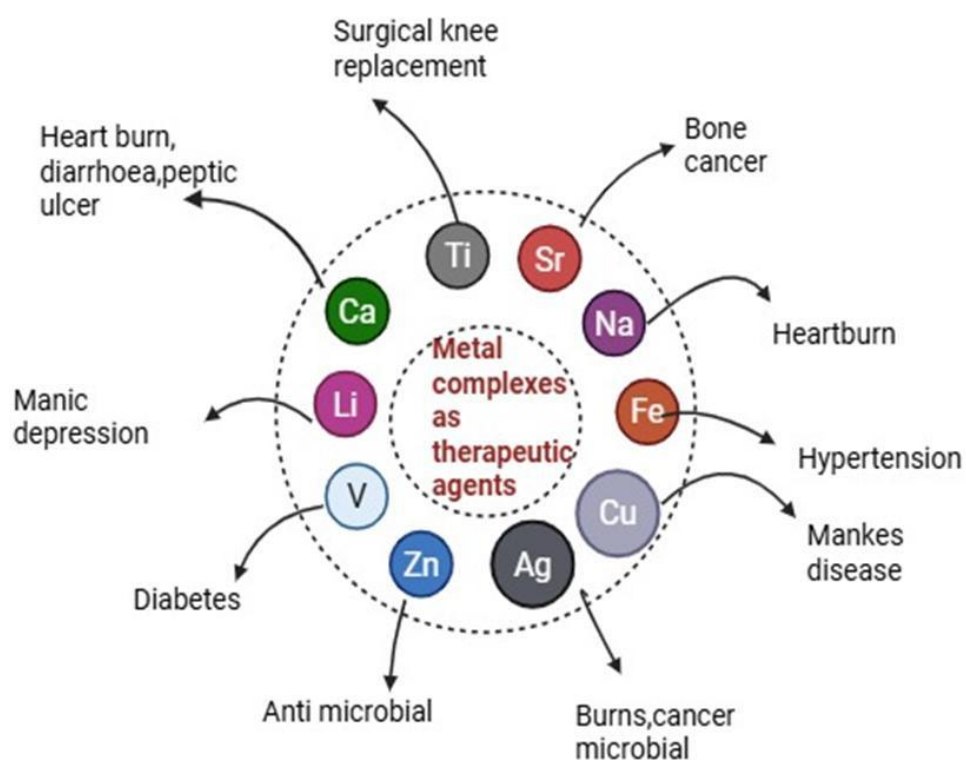


Fig. 1: Therapeutic applications of various metal complexes in the treatment of diverse diseases

Applications in Antibacterial Therapies

Interest in using metal-based medicines to improve outcomes in antibacterial treatment continues to grow (Maqsood et al., 2024). Gm@UiO-66-MA was created by combining gentamicin with a specially prepared material produced through the reaction between UiO-66-NH₂ and maleic anhydride. This process has the ability to remove bacterial H₂S, which plays a role in developing resistance to some antibiotics. Gm@UiO-66-MA can reduce biofilm strength and improve the potency of gentamicin against antibiotic-resistant *Escherichia coli*. Clinical trials showed that this novel therapy helps prevent infection and promotes faster healing of challenging bacterial wounds (Huo et al., 2023). Resistant to most antibiotics and capable of developing biofilms, *M. chelonae* and *M. fortuitum* cause difficult infections. The photosensitizing qualities of phthalocyanines have proved that the antimicrobial photodynamic treatment works effectively. These compounds do not work well in solutions that contain water. Putting ZnNPs into liposomes elevates the photodynamic effect and the stability and accuracy of the solution used to target *M. fortuitum* (Miretti et al., 2022). Compounds that contain heptamethine and sulfonamide are special for treating infections, especially those caused by *Staphylococcus epidermidis*. After being exposed to certain wavelengths, the compounds show greater antibacterial action and also prevent bacterial carbonic anhydrases (CAs). Antimicrobial resistance is considered a significant problem in health care by organizations across the world. It is necessary to bring new ideas into healthcare to uncover antibiotics that have different ways of working. These half-sandwich organo-osmium (II) complexes have a strong effect against drug-resistant *Mycobacterium tuberculosis* (Mtb) since their minimum inhibitory concentrations (MIC) are very low, ranging between 1.25-2.5 μ M. They are able to pass quickly into bacterial cells through thiol-based redox reactions inside the cell. Their ability to

fight tuberculosis is increased by their effectiveness and distinctive method of working (Coverdale et al., 2021). Vesicles made from copper-based metallosurfactants and anionic surfactants are very suitable for carrying photosensitizers such as methylene blue (MB) and Rose Bengal (RB). The presence of these vesicles makes it possible for PDT to produce singlet oxygen, which then kills *Staphylococcus aureus*, a bacterium that does not respond to many antibiotics. Besides, they contain dark toxicity and help damage the DNA of bacteria, as confirmed by spectroscopic and comet experiments. Because they can be used in two ways and are easy to produce, they appear to be promising for use as new antibacterial PDT agents (Sharma et al., 2020). OMeTBP@FeCONPs, which make use of photoresponsive CO, are a new approach to treating *S. aureus* and MRSA, as they target biofilms while minimizing the harm to nearby tissues by generating ROS only when exposed to light (Cao et al., 2023). Based on the issue of antimicrobial resistance, a new complex of copper and thiosemicarbazone could be useful against bacteria, as it significantly reduces the growth of two important bacteria. Since it is stable and water-soluble in the body, this complex could make it possible to use safer and better antibacterial drugs (Fabra et al., 2024). The most effective ruthenium-based complex has an antibacterial action against *S. aureus* at a MIC value of 6.25 µg/mL. Only one of the investigated Ruthenium-based complexes displays antimicrobial activity against *S. aureus* with a MIC of 6.25 µg/mL. The substance produces ROS, which damages the membranes of bacteria and hampers the formation of biofilms while simultaneously enhancing the actions of ordinary antibiotics on the microorganisms. Research in living systems has shown that the compound is effective in battling *S. aureus*. There is a chance that these complexes could help in treating infections caused by drug-resistant bacteria (Wang et al., 2023). The research suggests that incorporating organometallics in therapy could help manage infections and tackle the issue of increased bacterial resistance.

Applications in Anti-Inflammatory Therapies

Delivering small interfering RNA using zinc-based polyplexes improves the treatment of lung tissue harmed by acute lung injury. The use of polyplexes improves the delivery of siRNA to macrophages when compared to other methods. Integrating zinc dipicolylamine and carboxylated mannan into gene delivery leads to better results in managing persistent inflammation within the lungs. It offers an alternative approach for delivering siRNA to treat varied inflammatory disorders (Zhang et al., 2024). It has been established that, since zinc pyrithione (ZPT) has a metal component, it plays a part in colitis treatment by managing TRP and Ca²⁺ pathways in the intestinal wall cells. Because ZPT can reduce inflammation and help mend the inner lining of the digestive system, it could be useful for treating diseases of the GI tract, as other metals are being explored for their anti-inflammatory activities in different parts of the body (Zhang et al., 2024). The study shows that systems containing organometallics could be applied to treat inflammatory conditions. Using UiO-66-NH₂ MOF, scientists coated the surface of macrophages to develop a new system for emodin, which can treat inflammation. By using this technology, doctors achieve better results when treating patients with AP due to the long-term medication they can supply. Some scientists believe these treatments can play a key role in addressing inflammatory illnesses (Yang et al., 2024). Doctors are testing polaprezinc (Pol) because it is made from zinc and is believed to reduce inflammation in the brain, improving treatment for diseases such as Alzheimer's. It manages to reduce the production of waste in microglial cells by blocking the NF-κB pathway, mainly stopping the creation of NO, ROS, and cytokines. Therefore, zinc helps reduce neuroinflammation, suggesting that it can contribute to the treatment of neurodegenerative illnesses. Together with Asp G, there is evidence that Pol works better for treating neuroinflammatory diseases (Ban et al., 2024).

Table 2: Applications of metal-based compounds in treating various infectious diseases

Therapies	Applications	References
Anticancer Therapies	The integration of nonsteroidal anti-inflammatory drugs (NSAIDs) with organometallic complexes has shown enhanced anticancer properties, demonstrating the potential for hybrid therapeutic strategies. Treatment for rheumatoid arthritis with gold-based compounds. Enhancing efficacy and improving safety in cancer therapies.	(Paunescu et al., 2016) (Casini et al., 2018) (Chen et al., 2017)
Antibacterial Therapies	Compounds made from metals usually disrupt the cell membrane or the metabolism of bacteria, while existing antibiotics are not likely to do the same. Acting as catalytically active sites and photosensitizers and killing bacteria by releasing metal ions and micro-molecules. Act as photocatalytic agents for indoor air pollutant control.	(Evans et al., 2021) (Han et al., 2022) (Biegański et al., 2021)
Anti-inflammatory Therapies	Treatment of inflammatory bowel diseases (IBD) and diagnosis and treatment of colorectal cancer (CRC). Immobilized metal-organic compounds have shown promise in treating purulent-inflammatory diseases of the skin, improving healing processes. Metal complexes of nonsteroidal anti-inflammatory drugs (NSAIDs) like tenoxicam have demonstrated superior anti-inflammatory effects compared to their parent compounds.	(Szczepaniak et al., 2019) (Кадомцева et al., 2021) (Muslu et al., 2021)
Anti-neurodegenerative Therapies	The efficacy of bis(thiosemicarbazone) metal complexes in treating animal models of Alzheimer's and Parkinson's diseases. Metal chelation to slow neurodegenerative disease progression and redistributing metal ions to alleviate cellular deficiencies. Protection of neuronal cells from inflammation and from oxidative stress in neurodegenerative diseases.	(Mckenzie-Nickson et al., 2016) (C Badrick et al., 2011) (Rapposelli et al., 2021)

Therapies for Neurodegenerative Diseases

While Alzheimer's disease (AD) cannot be cured, it is one of the leading neurodegenerative diseases that may cause a person to die. Dementia due to Alzheimer's disease is the leading cause of mental decline, memory issues, and issues with language use (Wan et al., 2020; Dubois et al., 2021). Practically, zinc-based amide carboxylates are used to manage Alzheimer's disease in a way that is not done with other compounds. They are expected to be helpful in treating Alzheimer's, as they bring down phosphodiesterase IV, which in turn improves learning and memory in animals. They may help alleviate oxidative stress by turning on enzymes that help reduce it, and by regulating the work of acetylcholinesterase. Using zinc scaffolds might help to alter important biochemical factors like neurotransmitters, tau proteins, and amyloid- β , which hints at their potential as a therapy for AD (Waseem et al., 2022). Triphenylphosphoranylidene derivatives are part of a group of chemicals called organometallic compounds, and they can stop two important things related to Alzheimer's disease: the breakdown of acetylcholine and the grouping together of sticky protein fragments called beta amyloid. This means they might be useful for treating Alzheimer's disease. The compounds were found to be safe to use with cells, and they worked well when tested in real living things, also passing easily through the barrier that separates blood from the brain. This shows that these oils can help solve some of the reasons why Alzheimer's happens in the first place (El-Hussieny et al., 2023). Substances made from zinc and amide carboxylates have been found to help animals learn and remember better, and there's hope they might also work the same way in people with Alzheimer's. They help to lower the effect of damaging molecules in the brain and affect important brain chemicals such as acetylcholinesterase and amyloid- β , which makes some people think that these drugs could be useful in treating Alzheimer's disease. Different doses of zinc scaffolds suggest that they might help with treating diseases where the brain and nerves break down, like dementia or Parkinson's (Waseem et al., 2022). Cationic methylated Zinc phthalocyanines (called *cZnPc* for short) work well in blocking amyloid beta peptide from clumping together, which can help slow down or prevent Alzheimer's disease. Because (*cZnPc*) helps to stop the damage caused by sticky Alzheimer's proteins and keeps nerve cells healthy, this discovery could lead people to look into using zinc-based compounds to treat the disease.. This ability to go through the blood-brain barrier increases the significance of drugs for treating neurodegenerative diseases (Sheikh et al., 2024). Various applications of metal-based compounds are shown in Table 2.

Conclusion

The chapter talks about how organometallic compounds are becoming more important in medicine and highlights their possible application as drugs. For example, organometallics, with metal-carbon bonds, have proved helpful in the treatment of cancer, infections, and diseases of the brain. Platinum drugs, such as cisplatin, have been applied for a long time in cancer treatment, and the use of ruthenium, iridium, and similar metals in new medications is being tested for resistance to antibiotics and Alzheimer's. Ways in which these chemicals do their work, including their effects on DNA, redox reactions, and the immune system, are also discussed. The chapter notes that organometallics are constantly being studied since they introduce new methods to tackle illnesses that do not respond to typical therapy.

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Role of Nanoparticles in the Treatment of Lung Cancer

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Abstract

Among cancer-related fatalities, lung cancer continues to rank with a high mortality rate and few accessible therapies. With the advancements in nanotechnology, more acceptable drug delivery methods, focused therapies, and early detection are possible. Nanoparticles (NPs) have special properties, including small size, large surface area, and the ability to be functionalized, which gives them more potential to enhance the effectiveness and reduce the harmful effects of indigenous therapies. In this chapter, the application of nanoparticles in different aspects of gene therapy, drug delivery, and diagnostics is reviewed, along with their collaboration in pulmonary cancer treatment. Observing different types of nanoparticles like dendrimers, liposomes, metal-based nanoparticles, and polymeric nanoparticles and highlighting the features that how they can permit and regulate the medications, improve drug solubility with early and fast detection. The chapter concludes by emphasizing how nanoparticles open different ways to treat lung cancer with their physicochemical characteristics.

Keywords: Lung cancer, Nanoparticles, Gene therapy, Medication

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Introduction

Lung cancer is one of the main causes of cancer-related fatalities. It is divided into two primary types: small cell lung cancer (SCLC), which is more aggressive, and non-small cell lung cancer (NSCLC), which is the most prevalent. Although smoking is a major risk factor for lung cancer, other variables like genetic mutations, environmental exposure, and air pollution can also cause illness to develop in non-smokers (Ambrose et al., 2025). Shortness of breath, weight loss, chest pain, and a persistent cough are common symptoms, though they might not show up until the illness has advanced. Although many cases are discovered at an advanced stage, early detection is essential for improving results (Aggarwal et al., 2016).

Lung cancer is currently treated with immunotherapy, targeted treatments, radiation therapy, chemotherapy, and surgery. While chemotherapy and radiation are frequently used to reduce tumors and manage symptoms in advanced stages, surgical excision is an option for early-stage non-small cell lung cancer. Immunotherapy uses the body's immune system to combat the cancer, whereas targeted therapies try to stop particular molecular alterations that fuel the growth of the disease (Cardarella et al., 2012). The cancer kind, stage, and genetic makeup of the tumor all influence the therapy option, and personalized medicine is becoming a more and more important component of management. Lung cancer is still challenging to treat despite advancements in care, and research is constantly being conducted to increase patient survival and quality of life (Sethi, 2002).

Nanotechnology: Basics and Principles

The science and engineering discipline of nanotechnology is concerned with the manipulation of matter at the atomic or molecular scale, usually between 1 and 100 nanometers. Materials' physical, chemical, and biological characteristics can vary greatly at this size compared to a larger one. The enhanced surface area-to-volume ratio at the nanoscale and quantum processes are the causes of this unusual behavior (Polanski et al., 2016). The development, production, and application of systems, technologies, and structures with new properties or functions emerging at the nanoscale are referred to as nanotechnology (Iqbal et al., 2025).

Even as there is a lot of potential in nanotechnology, safety, environmental, and ethical issues also arise. Nanoparticles would prove to be especially unstable and toxic to mankind as well as the environment, owing to their minute size (Sajid et al., 2025). Accordingly, extensive studies have to be undertaken in understanding and controlling any potential risks that nanotechnology poses so that its benefits can be reaped without causing harm (Romaszko & Doboszyńska, 2018). The main aim of nanotechnology is to utilize materials with specific attributes at the

nanoscale to stimulate innovation and creativity. It has the potential to transform electronics, health, and environmental sustainability, but needs prudent development with consideration of risks and ethics (Travis et al., 2015).

Nanoparticles: Types and Properties Relevant to Cancer Therapy

The materials with typical sizes between 1-100 nm are referred to as nanoparticles or engineered materials. Nanoparticles exhibit a range of properties owing to their minute dimensions, which provide them with unique properties, such as NPs utilized in the treatment of cancer. NPs can be employed to attack cancers, reduce the toxic impacts of conventional therapies, improve the drug delivery system because of their tiny dimensions, surface charge, shape as well and surface chemistry (Travis et al., 2015). The most common nanoparticle types applied in treating cancer are polymeric nanoparticles, metallic nanoparticles, liposomes, dendrimers, and micelles, respectively (Fatima et al., 2025). Lipid nanoparticles called liposomes are able to encapsulate hydrophobic drugs to avoid degradation and permit controlled release at the target location. Dendrimers are highly branched, tree-like polymers that could be altered for drug delivery. They have several sites for drug attachment and surface modifications that make targeting easier (Franceschi & Bidoli, 1999).

Polymeric nanoparticles, which are made of biodegradable polymers that offer controlled drug release and minimal toxicity, boost the bioavailability of drugs at the tumor site. The metallic nanoparticles, such as gold and silver, have special optical properties that can be used for therapeutic and imaging drug delivery, as depicted in Figure 1. Micelles are small aggregates of amphipathic molecules that can solubilize hydrophobic drugs and release them in a controlled manner (Carrasco-Esteban et al., 2021). One of the properties of nanoparticles that makes them useful for treating cancer is the enhanced permeability and retention (EPR) effect. It permits the particles to gather at the sites of tumors. NPs are able to penetrate into arteries that are often leaked because of the tumor and more easily accumulate in the tumor tissues due to their minute size, thereby increasing the efficacy of the treatment. Moreover, by rendering nanoparticles biodegradable and friendly, the chances for side effects can be minimized (Chandolu & Dass, 2013).

Surface modification is crucial for enhancing the selectivity of nanoparticles for cancer cells. Targeting ligands, including peptides or antibodies, can be designed to bind to the surface of nanoparticles and specifically bind to receptors on cancer cells, enhancing the specificity of drug delivery. Healthy tissues can be prevented, and the target effect minimized through the support of this method (Babu et al., 2013). For drug delivery, nanoparticles are designed to deliver their load silently without resistance in a delayed or controlled manner. For example, multiple nanoparticles can release their drugs when there is a change in the environment of tumor cells, such as the presence or absence of specific enzymes, pH, and temperature (Babu et al., 2013).

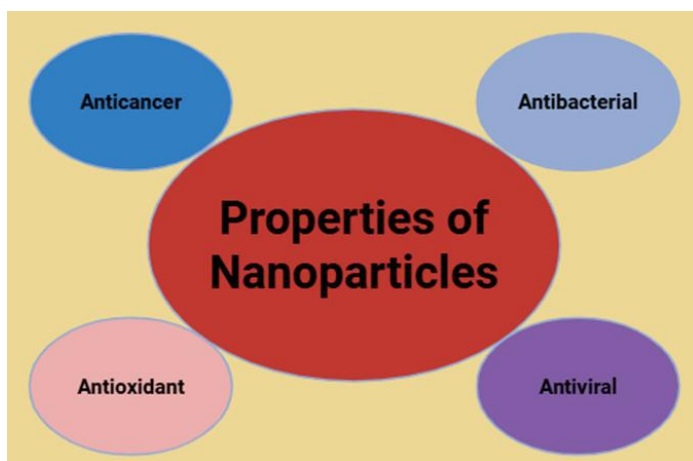


Fig. 1: Various properties of nanoparticles

Apart from that, nanoscale diagnostics and disease imaging are also feasible using nanoparticles. In imaging order, the metal nanoparticles, such as gold and silver, are specifically used because these have the ability to enhance the contrast in various imaging techniques like MRI, CT scan, and X-rays. For instance, the growth of tumor cells can be ceased in photothermal and photodynamic therapies by light absorption and then release of light in the form of reactive oxygen species (ROS) or heat via metallic nanoparticles. In some conditions, as mentioned in Table 1, nanoparticles may likely exhibit curative effects (Mottaghitalab et al., 2019). But there are still some obstacles that should be resolved for the proper efficacy of nanoparticles. Problems such as the possible damage of nanoparticles, their long-term stability, and problems related to their growing size should be taken into account initially prior to the synthesis of nanoparticles. Despite these difficulties, the innocuousness and effectiveness of drugs that are encapsulated within nanoparticles are currently enhanced by sophisticated development and discovery, leading to the revolutionary project

for cancer treatment (Lee et al., 2015).

Mechanisms of Nanoparticle Action in Cancer Treatment

NPs possess a variety of therapeutic applications for the treatment of cancer by leveraging their special characteristics to improve the delivery, efficacy of anticancer drugs, and tumor eradication techniques (Ahmed et al., 2025). As a result of vasculature leakages, poor lymph flow, the enhanced retention (EPR), and selective penetrating capability allow nanoparticles to target cancer cells. The toxicity decrease and increasing drug concentration enable the nanoparticles to directly target cancer cells (Ahmad et al., 2015). Furthermore, putting drugs in NPs not only improves their safety in the body, but also ensures they only release drugs at the target memory cell (Roa et al., 2011). Giving drugs a nanoparticle coating results in a larger mechanism of action and an increase in their bioactivity. Using a technique called smart drug delivery to send medicine to patients is considered valuable. Certain molecules, including micro molecules, amino acids, and antibodies, might bond to NPs and direct them to the sites of tumors where the receptors they are attached to look for matching molecules. Because treatment reaches the tumor directly, it improves how well treatment works and limits harm to nearby healthy tissue. Additionally, targeted nanoparticles can aid in intracellular delivery, allowing medications to enter cancer cells and exert their therapeutic effects there (Lu et al., 2014).

Table 1: Nanoparticles used to treat several types of cancer, their mode of action, and advantages

Nanoparticle Type	Size (nm)	Mechanism of action	Target	Advantages	References
Magnetic nanoparticles	50-100	Hyperthermia and	Targeted tumor imaging	Dual therapeutic and diagnostic potential (theragnostic)	Chen et al., 2021
PLDA nanoparticles	100-300	Sustained release of cisplatin	Tumor microenvironment	Biodegradable FDA approved	Kumar et al., 2019
Selenium nanoparticles	100-150	Induction of apoptosis and Inhibition of proliferation	Lung cancer cell lines	Antioxidant Properties, Low toxicity	Huang et al., 2023
Lipid-based nanoparticles	80-200	Encapsulation of Chemotherapeutics (e.g., paclitaxel)	Lung Tumor cells	Controlled drug release, reduced toxicity	Singh et al., 2020
Gold nanoparticles (AuNPs)	10-50	Photothermal therapy and drug delivery	EGFR-Overexpressing cells	High biocompatibility, surface modification	Zhang et al., 2021
Silver nanoparticles	20-100	ROS generation and apoptosis	Cancer stem cells	Strong cytotoxic effect, easy synthesis	Ali et al., 2022

Through direct physical and chemical impacts, nanoparticles can aid in the treatment of cancer in addition to delivering drugs. When subjected to light, heat, or electromagnetic fields, some nanoparticles, especially metallic ones like gold or silver, display special characteristics. In photothermal therapy, for instance, nanoparticles have the ability to absorb light, including near-infrared, and transform it into heat. This process kills cancer cells near the nanoparticles. Similar to this, in photodynamic therapy, when light activates nanoparticles, they can produce reactive oxygen species as shown in Figure 2, which causes oxidative stress and cancer cell death (Long et al., 2014). Additionally, nanoparticles can be employed in combination with therapeutic approaches, including immunotherapy and chemotherapy. For example, nanoparticles laden with chemicals that stimulate the immune system can also transport chemotherapeutic drugs. Through the direct destruction of cancer cells and the indirect stimulation of immune responses to target remaining cancer cells, these combination therapies improve the body's capacity to combat the tumor. Additionally, by preventing angiogenesis (the growth of new blood vessels) or boosting oxygen delivery to tumors, nanoparticles can be engineered to disturb the tumor microenvironment and increase the efficacy of other treatments (Kim et al., 2015). Nanoparticles are considered a workable and feasible treatment because they have the ability to penetrate biological obstacles such as blood blood-brain barrier. This characteristic is particularly helpful for cancers that have historically been challenging to cure with conventional therapy because it is challenging to distribute drugs via protective barriers (Woodman et al., 2021).

Nanoparticle-Based Drug Delivery Systems for Lung Cancer

Technologies based on nanoparticles based on drug delivery can enhance solubility, antitumor drug targeting, and efficacy, as well as minimize side effects. But lungs have a large surface area, nearly adjacent to air pathways, and a huge blood supply, which is why lungs show great potential and hurdles for medication. Modifying nanoparticles can suppress these barriers and reach towards tumor site more effectively (Sarkar et al., 2017). A major strength of nanoparticles to enhance drug solubility is an important benefit to utilize them for the treatment of lung cancer. Drugs that treat lung cancer from the family of therapeutic drugs such as paclitaxel and cisplatin, may fail to work properly or be given in adequate amounts because they have a limited ability to mix with water.

One of the best ways to make anticancer drugs work better is to capture them within nanoparticles for easier distribution within the body (Kumari et al., 2023). Many nanoparticles in the treatment of pulmonary cancer lies in their ability for targeted delivery of drugs. When we make the receptors focus outside the tumor cell, we are able to limit the harmful effects, help healthy cells, and use drugs correctly (Ambrose et al., 2025). When the binder is matched to folate or EGFR receptors on the surface of pleural cancer cells, the nanoparticles become more effective. Using this strategy can support drug efficiency and protect important organs by making more drugs collect at the cancer site (Bandyopadhyay et al., 2015).

Drug-receptor delivery is helpful, but the main alternative technique is using nanoparticles for their strong high EPR and porous properties. Because tumor blood vessels are not ordered, NPs build up more easily within cancer cells than in normal cells. When the passive targeting approach boosts how many drugs reach cancer cells and improves the therapy's results (Garbuzenko et al., 2014). Finding the best delivery spot and timing for the drug is possible now. Directing the release of medicine like this means the amount in the bloodstream stays appropriate for a longer time, and doses can be further apart to prevent many side effects. Offering this, nanoparticles can react when pH levels, temperature or the surroundings inside a tumor differ (KhokharVoytas et al., 2023).

When NPs meet malignant cells, their substances are released which improves their focus and stops serious deterioration (Azarmi et al., 2008). Genes and the body's immune system can be supported in their cancer-related therapy by using nanoparticles. With this approach, tumors can be prevented because chemotherapy-resistant genes are shut down by placing small interfering RNA and plasmid DNA into nanoparticles. Immunomodulators such as checkpoint inhibitors and cytokines are sometimes given as nanoparticles to improve the body's response to cancer (Lee et al., 2015).

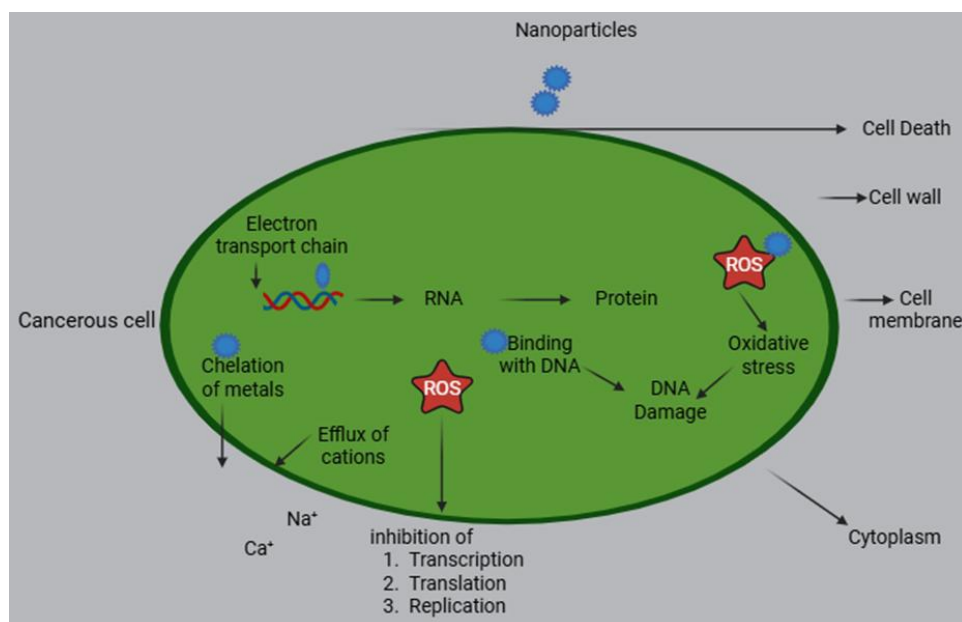


Fig. 2: Mechanism of action of nanoparticles towards cancerous cells

NPs are applied to benefit from rising imaging and diagnostic approaches in the care of patients with pulmonary cancer. When used, metallic nanoparticles made from gold or silica improve the capabilities of MRI, CT, and PET imaging methods. By watching the movement of treatment chemicals, these NPs report in real time on the progress of the treatment (Zheng et al., 2018). There are a number of benefits to using nanoparticles, but certain difficulties remain with using them for lung cancer. A main problem is that nanoparticles might be removed rapidly by the immune system and delivered to organs that you don't want them to go to. Stress is placed on two key points: nanoparticles must be biocompatible and stable for a long period (Aghebati-Maleki et al., 2020). Developing nanoparticle technology, custom targeting, and equipping them with functions is why nanotechnology is used to fight lung cancer (Menon et al., 2017).

Nanoparticles in Chemotherapy for Lung Cancer

Applying nanoparticles to systemic anti-cancer therapy in lung cancer can both reduce serious problems and make chemotherapy more effective. Lung cancer, which causes many cancer deaths, is managed with a treatment called chemotherapy. Sometimes, chemotherapy is not as effective because it may fail for patients, become difficult to make a solution from, and result in side effects for normal body cells. NPs help medications get past these barriers by supplying drugs as needed, releasing them under control, and targeting them to merge cancer treatment and lung tumor recovery (Liu et al., 2023). NPs stabilize and dissolve both hydrophobic and hydrophilic drugs at the treatment site in the body. The availability and usefulness of key chemotherapy drugs such as paclitaxel and cisplatin might become limited because they dissolve little in water. Wrapping drugs in nanoparticles increases the amount that reaches a tumor and reduces the body's exposure to them (Sharma et al., 2019).

NPs used in chemotherapy for lung cancer are good at attacking tumor cells while reducing the harm done to normal tissues. Generally, more than one type of receptor or surface antigen is found on tumor cells than on normal cells (Ambrose et al., 2025). Attaching antibodies, peptides, and such molecules to nanoparticles allows them to bind to exactly those receptors found on lung cancer cells. Making drugs more effective at the tumor, with nanoparticles, reduces the impacts of chemotherapy on normal cells (Kim et al., 2023). Other than active targeting, nanoparticles may be aided in cancers by the enhanced permeability and retention (EPR) effect. The irregular, porous nature of tumor blood vessels means that nanoparticles accumulate inside tumors faster than they accumulate inside normal tissues. Thanks to having the drug at a higher level in the tumor and safeguarding normal tissues, this passive targeting method can ensure that drugs arrive accurately at the cancer location (Feng et al., 2024).

Controlled and regulated drug release is also an important feature of NPs in chemotherapy. In conventional chemotherapy, repeated administration of medication is usually required, which is the reason for drug concentration peaks and troughs, which can be responsible for the higher chances of complications and lower therapeutic efficacy (Abbas et al., 2025). It is possible to design nanoparticles that release their pharmacological load in a controlled fashion, ensuring that the drug level remains constant over time. NPs are capable of being designed to release their content when multiple stimuli, including enzymes or pH specific to a particular tumor cell, take place in the tumor microenvironment. This targeted and controlled release optimizes efficiency while reducing toxicity by making certain that the drug is active at the site of cancer for a longer duration of time (Lee et al., 2016). NPs can prevent suppression of the prime hurdle in the treatment of lung cancer, i.e., chemotherapy resistance.

A number of mechanisms can lead to cancer cells developing resistance against chemotherapy drugs, including the formation of altered drug targets or efflux pumps that remove drugs from the cells. NPs are able to acquire some of these mechanisms of resistance by facilitating entry of the drug into the tumor cells through various processes such as endocytosis. Besides, NPs are also designed to transport multiple drugs at a time by targeting cancer cells through various mechanisms (Mohtar et al., 2021). Moreover, nanoparticles are also used to apply multimodal therapies to lung cancer. For instance, by combining chemotherapeutic drugs with other therapeutic modalities like immunotherapies or targeted therapies, nanoparticles can offer a diversified treatment strategy (Abbas et al., 2025).

These various methods aid in the delivery of drugs to the tumor site, resulting in decreased resistance, improving outcomes, and boosting the efficiency of treatment (Zheng et al., 2023). NPs are under consideration for radiology requisition of lung cancer despite medication portage. The performance of radiology methods such as CT scans, MRI applied for other diseases can be improved further by applying gold or silver metallic NPs. The primary uses of such nanoparticles are to govern the curing process, manage the medication treatment, and provide streaming reports regarding therapeutic response (Sristi et al., 2023).

Nanoparticles-based Photothermal and Photodynamic Therapy

Both photodynamic and photothermal therapies are typically based on nanoparticles that are mainly used to assassinate the cancer cells by light, which can further enhance the effectiveness of conventional therapies. The nanoparticles have the potential to directly connect with light, and absorbing light can be used to give remedial effects, while sound tissues can also be prevented from being damaged in these therapies (Zhou et al., 2021). Nanoparticles are made to absorb light in photothermal therapy, frequently giving off their spectrum in the near infrared region (NIR) and transforming the light in the form of heat. Due to the release of heat, the temperature increases in a controlled manner called hyperthermia, which surrounds the nanoparticles. Apoptosis or necrosis may result from the heat generated by this light absorption, which raises the tumor cells' temperature to a degree where they are harmed or killed (He et al., 2016). The main pros of photothermal therapy are its potential to only target the malignant site while preventing the nearby healthy tissues and resisting damage to the surrounding areas (Khullar et al., 2009).

Materials such as silica, gold, carbon-based nanoparticles, or copper-based compounds are used to produce nanoparticles that can be further utilized in photothermal therapy due to their high photothermal transformation efficiency. These nanoparticles become more functionalized when bind with ligands or antibodies to target cancer cells, only resulting in increasing selectivity and efficiency of therapy (Tian et al., 2020). In spite of that, photosensitizers can be used in photodynamic treatment (PDT), which becomes only activated on exposure to light in the visible or ultraviolet region. Because of the activation of photosensitizers, reactive oxygen species are produced, particularly singlet oxygen, that can damage the inner cell environment, including proteins, lipids, and DNA. Reactive oxygen species (ROS) can cause oxidative stress in tumor cells, resulting in shrinkage and death of the tumor mass. But PDT is useful for cancer that is near the surface because light penetration is limited only to a few millimeters into tissues (Vanza et al., 2020). Nanoparticles work as transporters for photosensitizers to enhance stability, solubility, and bio accessibility in photothermal therapy. Nanoparticles are engineered to react with particular stimuli in a malignant, tiny environment, like levels of enzymes, pH, to release or free the photosensitizer at the right place and at the right time into the tumor site to protect the healthy cells. This controlled release can improve the therapeutic effectiveness of PDT by ensuring that greater amounts of the photosensitizer reach the tumor and increasing the generation of ROS (Essa et al., 2020).

Conclusion

Treatment for lung cancer is changing quickly, and the therapies based on nanoparticles will be important in determining the course of treatment in the future. Nanoparticles have now become a game-changing technology, giving creative strategies for health care, protection and maintenance, diagnostics, and treatment in lung cancer therapy. Targeted drug delivery using nanoparticles is one of the most exciting new developments. The targeting and destruction of tumor cells without harming nearby healthy cells are also possible by combining nanoparticles with advanced medical therapies such as photodynamic and photothermal therapy. By overcoming the shortcomings of existing therapeutic techniques, nanotechnology holds the potential to completely transform the way lung cancer is identified, treated, and controlled. However, the advancements gained so far give optimism for the future of cancer treatment because nanoparticles have the potential to completely transform the way the cancer is treated by increasing patient outcomes, reducing side effects, and boosting precision.

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The Bridge between Nanotechnology and Biotechnology: and its Targeted Drug Delivery Perspective

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Abstract

Particularly in the field of targeted drug delivery, the combination of nanotechnology with biotechnology has produced a paradigm shift in contemporary research. Precision control over physical and chemical interactions is made possible by nanotechnology, which manipulates matter at the nanoscale. Nanobiotechnology, a multidisciplinary discipline that leverages the strengths of both sciences to overcome the constraints of conventional drug delivery technologies, is the result of two fields working together. This chapter discusses procedures of targeted drug delivery, emphasizing active targeting, which improves therapeutic specificity and efficacy by using molecular recognition, and passive targeting, which takes use of the distinct microenvironment of sick tissues. It investigates how nanotechnology can reduce toxicity and adverse effects while increasing drug solubility, bioavailability, and therapeutic index. The chapter also covers advanced uses, including vaccine delivery platforms that boost immune responses, protein delivery systems that shield therapeutic proteins from enzymatic degradation, and gene therapy for genetic illnesses using nanoparticles. Nanobiotechnology has transformed the course of medicine by tackling issues including poor drug targeting, low efficacy, and quick excretion. These two fields have the potential to totally transform healthcare by providing novel approaches to the prevention and treatment of illness.

Keywords: Nanobiotechnology, Pharmacogenomics Integration, Nanoscale Manipulation

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Introduction

What is Nanotechnology?

Nanotechnology is the term for technology that is implemented at the nanoscale and can be used in the real world. The term refers to controlling or restructuring matter at the atomic and molecular levels within the range of 1 to 100 nanometers (Shanmugam, 2019). Nanoscience is an acronym utilised to describe the underlying science. Matter's attributes at the nanoscale differ from those at the larger scale (Borisenko & Ossicini, 2013). A material's qualities initially stay the same when its dimensions are lowered from a big size, but eventually minor modifications take place. Lastly, there may be significant changes in characteristics as the size falls below 100 nm (Raoux et al., 2008). Applications of physical, chemical, and biological systems at scales ranging from individual atoms or molecules to submicron dimensions, as well as the incorporation of the resultant nanostructures into larger systems, are all included in nanotechnology (Nasrollahzadeh et al., 2019).

What is Biotechnology?

"Biotechnology" describes the application of living things or their byproducts to alter human surroundings and health. Karl Ereky, a Hungarian engineer, first used the phrase "biotechnology" in 1919 (Gupta et al., 2017). According to biotechnology, biotechnology is the process of manipulating DNA, such as transferring genes from one organism to another, or it is the application of relatively new technologies whose effects are unknown and should be handled carefully. For instance in the application of gene therapy, stem cells, and genetically engineered creatures (Glick & Patten, 2022).

What is Nanobiotechnology?

Nanobiotechnology is a highly interdisciplinary field due to its ability to combine physical principles, chemical properties, and biological characteristics (Rai & Saraswat, 2022). A new and groundbreaking class of multifunctional devices and systems with better functionality, sensitivity, and specificity can be created by combining physical sciences and biological technology. For the past thirty years, physical scientists

have worked to reduce the physical size of device components in order to create faster and more effective physical devices. Through the use of deep UV-lithography, they have achieved a typical size of about 20 nm. This area of study is founded on the idea that biology can benefit from new tools that nanotechnology can provide, and that biological principles can direct nanotechnology to create new, highly complex functioning nanosystems, such as cell organelles (Wong et al., 2013). At the intersection of these two areas of study is nanobiotechnology. It analyzes and creates a nanobiosystem to satisfy a wide range of specialized applications by utilizing nanotechnology and biotechnology (Logothetidis, 2012).

Importance of Targeted Drug Delivery?

Addressing drug development concerns pertaining to the delivery of certain medications to their site of action in therapeutically acceptable concentrations has grown in importance in this intricate and constantly changing field of medicine (Hillery et al., 2002). The pharmaceutical industry has undoubtedly seen the discovery of numerous novel drug molecules as a result of the development of pharmaceutical sciences, ranging from small molecule medications to macromolecules like proteins and peptides. Drug delivery systems (DDS) are used to address these issues. These systems can be devices or formulations that make it easier to administer a medication to the body while enhancing its pharmacokinetic and biodistribution properties as well as the overall treatment's efficacy and safety (Liu et al., 2016). Targeting the medicines entails enhancing the system's specificity toward the body's pharmacologically significant target. This comprise giving the patient the DDS, delivering it to the diseased target site, releasing the active components in and around the target, and preventing nonspecific toxicity in healthy cells (Jain, 2020).

Role of Nanotechnology in Drug Delivery

Nanotechnology is the engineering of functional systems at the molecular scale. It is a promising approach for efficient delivery of drugs inside the body (Singh, 2010). The nanotechnology as a drug delivery tool has many advantages over conventional drug delivery methods. It basically deals with development of nanostructures of 5-200nm in size (Lata et al., 2017). This method dissolves and disables pharmaceuticals into compostable nanoparticles, which actually aids in drug adsorption and shields them from chemical and physical deterioration. Several biodegradable nanostructures are being developed at the moment for this use (Jyothika et al., 2024). The use of nanoparticles to deliver medications to certain cells has been made possible by nanotechnology (Figure 1). The goal of targeted medication administration is to lessen drug side effects while also lowering drug use and treatment costs. The primary focus of drug delivery is on boosting biological availability at specific locations inside the body as well as over a period of time (Tibbitt et al., 2016).

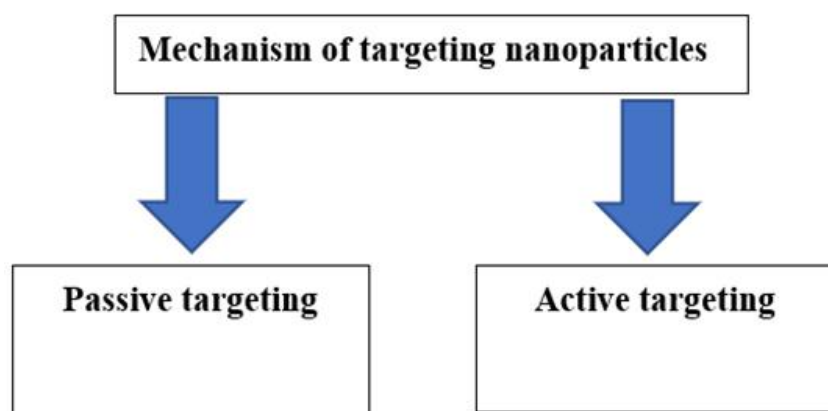


Fig. 1: The type of mechanisms of target nanoparticles

Passive Targeting

Increased permeability and retention time: Nanoparticles that meet the aforementioned criteria, such as having a higher probability of reaching the intended tumor tissues and the capacity to circulate in the bloodstream for extended periods of time. Nanoparticles can accumulate in tumor tissues due to the special properties of tumor cells (Moghimi et al., 2001).

Microenvironment of Tumor vessels: An additional feature of passive targeting is the distinct environment that surrounds tumor cells, which differs from that of healthy cells. Furthermore, certain enzymes such as matrix metalloproteinases are released by cancer cells and are linked to their survival strategies (Danhier et al., 2010). Matrix metalloproteinase-2 was found to specifically cleave an albumin-bound version of doxorubicin that contained an octapeptide sequence between the drug and the carrier that was specific to the enzyme in an *in-vitro* investigation (Iaccarino et al., 2019).

Active Targeting

As the passive targeting faces the different sort of limitations so to overcome this situation. An earlier attempt was made to directly conjugate an antibody to a medication (Garrett, 2001). However, such early antibody-drug conjugates have not demonstrated the anticipated outcomes in clinical studies when used as an effective cancer treatment method.

Antigen expression: A number of characteristics that make cell-surface antigens and receptors especially appropriate tumor-specific targets should ideally be present (Carter et al., 2004). They should, first and foremost, only be expressed on tumor cells and not on healthy ones. Secondly, all targeted tumor cells should display them uniformly. Finally, it is not advisable to release cell-surface antigens and receptors into the bloodstream (Zhao et al., 2013).

Internalization of targeted conjugates: One crucial factor in choosing the right targeting ligands is whether the targeted conjugates can be

absorbed after attaching to the target cells (Forssen & Willis, 1998). Internalization typically happens through endocytosis mediated by receptors. Using the folate receptor as an example, an endosome is created when a conjugate that is targeted for folate binds to the cell surface and is encased by the invaginating plasma membrane. Target organelles get newly produced endosomes (Vyas et al., 2001). If the drug has the right physico-chemical characteristics to pass through the endosomal membrane, it is released from the conjugate and enters the cytoplasm when the pH level in the endosome's interior becomes acidic and lysozymes are activated (Çağdaş et al., 2014). Depending on the medication, released substances are subsequently transported by their intended organelle. In the meantime, the conjugate's released folate receptor goes back to the cell membrane to bind and initiate a second round of transport (Deng & Bae, 2020).

This is how the limitations of the passive targeting should be overcome by active targeting

The Convergence of Nanotechnology and Biotechnology

The convergence of nanotechnology and biotechnology represents a transformative frontier at the intersection of two dynamic fields, offering innovative solutions to some of the most pressing challenges facing humanity (Hassan & Fathi, 2024). From healthcare to energy production, nanotechnology the manipulation of matter at the nanoscale and biotechnology the use of biological systems and processes to create products and technologies have each transformed a number of industries (Saxena, 2023). In recent years, the union of nanotechnology with biotechnology has led to amazing improvements across several sectors, including medical, energy, and environmental sustainability. This convergence is centered on the capacity to build materials and electronics at the nanoscale, where special features appear that allow for unprecedented control over physical and chemical events as well as precise interactions with biological systems (Roco et al., 2013). Improved imaging methods, less invasive procedures, and the direct administration of medicinal drugs to diseased cells with the fewest possible negative effects are all made possible by this precision (Licha & Olbrich, 2005). Furthermore, the convergence of nanotechnology and biotechnology has a great deal of potential to address the global energy challenge. Nanostructured materials possess exceptional qualities that can be utilized to enhance the efficiency of energy production, storage, and conversion processes (Zhang et al., 2016). As illustrated in the figure below, the combination of nanotechnology with biotechnology has resulted in the development of a new field known as nanobiotechnology by utilizing

the fundamental control of chemical, physical, and biological processes in a synergistic manner (Figure 2).

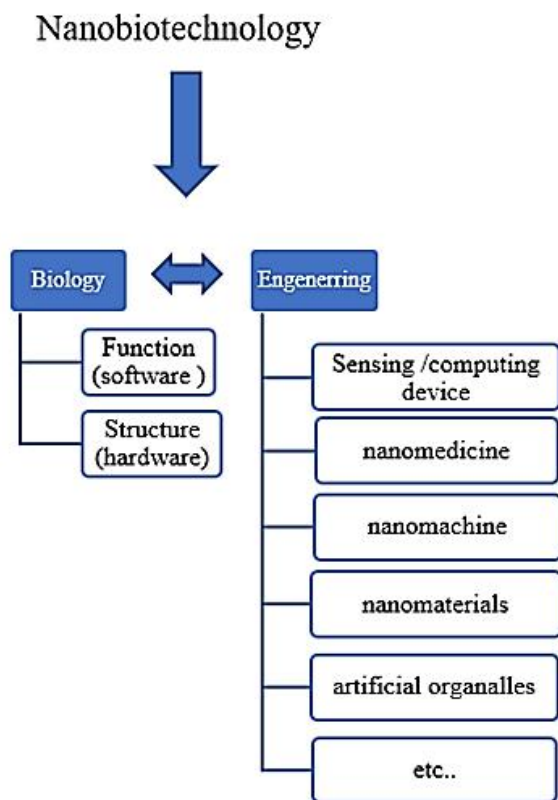


Fig. 2: Factors on which nanobiotechnology depends

as the medication molecule's affinity (Overington et al., 2006). A low drug affinity for the target molecule will result in a smaller maximal response. One of the main issues with medication molecules that causes treatment of serious diseases to take longer is low efficacy (Manzari et al., 2021).

Fast Excretion: The process by which drugs are eliminated from the body by excretory organs such as the kidneys is known as excretion or elimination. Rapid drug molecule excretion reduces the medicine's effectiveness because the target organs do not receive the appropriate quantity of the drug molecule (Kok-Yong et al., 2015).

Fraction of drug required zone is not persists: For optimal treatment, a certain amount of medicine must accumulate in a certain area of

Challenges and Problems Associated with Drug Development and Delivery

Oral ingestion or intravascular injection are two methods used in conventional or traditional drug development and delivery systems (Jain, 2020). The distribution of drugs within the body is the responsibility of the systemic blood circulation. As a result, only a tiny percentage of the active medication ingredients reach the organs (Benet et al., 1996). Occasionally, drugs can also have negative effects on organs that are not their intended target. Additionally, creating novel pharmacological molecules is a costly and time-consuming procedure (Ramsay et al., 2018). Pharmaceutical businesses are now dealing with the following issues and difficulties related to drug development and delivery

Low Solubility: One of the main issues that arises during the creation of a particular medication formulation is low water solubility. The bioavailability of the drug is hampered by poor solubility. As a result, it is the main obstacle for novel chemical entities that industry and scientists find (Ramsay et al., 2018).

Low Bioavailability: The portion of a pharmacological dose that is available for systemic circulation is known as bioavailability. It is among the drug's primary pharmacokinetic characteristics. When a medication is given intravenously, its bioavailability is 100%; however, when it is given orally or through other methods, its bioavailability declines because of partial absorption. Therefore, when administering the medication other than intravenously, bioavailability needs to be taken into account (Benet et al., 1996).

Low Efficacy: Efficacy is the highest reaction that a medication dose can produce. A medicine must have a high affinity for the target in order to connect tightly with it and be considered highly efficient. This is referred to

the organ, such as tumor cells, where the drug concentration must be higher than in normal cells. Chemotherapeutic drugs used to treat cancer are linked to suboptimal drug accumulation (Lammers et al., 2012).

Nanobiotechnology Applications

Innovative drug delivery systems are crucial strategic instruments that the pharmaceutical industry employs to grow its drug markets. Basic biology and the creation of novel biological technologies, such as imaging probes, biocompatible drug delivery systems, or nanodevices, can both benefit from the successful use of nanotechnology (Crommelin & Florence, 2013). It is generally accepted that achieving a desirable kinetic profile can be facilitated by precisely controlling the drug carrier, which in turn can help modulate drug release. Therefore, the size of the medication's or drug carrier's particles directly affects how well the drug is delivered to different sections of the body (Pillai et al., 2023). The common applications are described as following:

Gene therapy: Since the human genome has been sequenced, gene therapy is increasingly concentrating on DNA or gene delivery. Since exogenous DNA plasmids regulate gene structure, regulation, and function, their delivery into cells is a potent tool in the treatment of genetic illnesses (Yin et al., 2017). Although the nucleus is thought to be the final location for DNA delivery, mitochondrial DNA delivery is equally crucial. Coupling chemicals like transferrin, asialoorosomucoid, folate, a tibody (CD3, CD34), or calcium phosphate to the DNA polyplexes can increase the transfection effectiveness of DNA (Kean, 2006). Moreover, nuclear localization sequence (NLS) tags can be affixed to the delivery mechanism or directly to the DNA molecule to improve the efficiency of DNA uptake into the nucleus via the nuclear pore complex (NPC). In order to process and target these macromolecules in the intracellular compartment more effectively, future research should concentrate on comprehending the mechanism of the carrier-DNA complex absorption (Jiang et al., 2019).

Protein delivery: However, renal filtration, proteolytic breakdown, receptor-mediated clearance, and storage in nonspecific organs and tissues quickly remove the majority of proteins and peptides from the bloodstream (Bourquin et al., 2018). Protein medications are being used to treat a variety of illnesses as a result of developments in the field of molecular biology. These formulations, however, call for a delivery mechanism that can both deliver the medication to the intended location and shield protein and peptide medications from enzymatic breakdown (Brown et al., 2020). Numerous strategies have been investigated to address these issues. By decreasing glomerular filtration, conjugating proteins and peptides with nanodelivery systems like liposomes or nanoparticles increases their blood circulation duration. These systems encapsulate or attach the protein medication to a polymeric or liposomal matrix, which then undergoes hydrolysis or enzymatic digestion to release the protein in a controlled manner (Yetisgin et al., 2020). Optimized pharmacokinetics, reduced dosage frequency, improved efficacy, bioavailability, solubility, and stability are further benefits.

Vaccine delivery: A theoretically perfect vaccination will never be effective unless it is properly developed and administered. Adjuvants and other formulation methods are now being tested to deliver vaccinations in a safe and efficient way (Cunningham et al., 2016). Adjuvants can be employed as vaccine delivery methods that target antigen-presenting cells or as immunostimulatory agents that activate the innate immune system. The ability of mucosal or topical adjuvants to stimulate the innate immune system, along with the benefits of easier administration and improved patient compliance, is attracting interest even though the mechanism of action of the majority of these adjuvants is only partially understood (Wang et al., 2019). Modified cholera toxin and *E. coli* heat labile enterotoxin are the most commonly utilized adjuvants for mucosal administration (Holmgren et al., 2006). According to reports, the mean immunological response resulting from this combination was similar to that of two alum injections given separately. Nanoparticles may be employed as vaccine adjuvants, according to these investigations; nevertheless, more investigation is needed to confirm these systems (Filipić et al., 2023).

Nanobiotechnology for the Combination of Drug Design and Drug Delivery

Many drugs discovered in the past could not be used in patients because a suitable method of drug delivery was lacking. Calando Pharmaceuticals (Duarte, CA, USA) is one example of a company that uses nanoparticle delivery to create short interfering RNAs (siRNAs) as anticancer drugs (Zhou et al., 2013). Sequence selection and the creation of efficient siRNA molecules that attach to (and self-assemble with) the siRNA to produce homogeneous colloidal-sized particles with a diameter of around 50nm are employed in proprietary technology (Jain, 2005). Larger particles cannot escape the bloodstream and enter the tumor since they are delivered intravenously. Drug particles are swiftly eliminated by the kidneys if they are less than 10nm in size (Sun et al., 2021).

Nanobiotechnology and Drug Discovery for Personalized Medicine

Simply said, customized medicine refers to the recommendation of particular therapies and treatments that are most appropriate for a given person (Ginsburg & Willard, 2009). The foundation of personalized medicine is the notion that a patient's genotype should be used to determine their treatment options, however other characteristics are also taken into account. Nanobiotechnologies are already being employed in molecular diagnostics, which is a crucial aspect of customized treatment (Ginsburg & Willard, 2009). While pharmacogenomics and pharmacogenetics are now being used to match existing medications to the appropriate people for maximum efficacy and safety, pharmacoproteomics may be used in the future to find and create customized medications for particular patient groups. In addition to simplifying the integration of diagnostics and therapies, nanobiotechnology has potential for assisting in the identification of tailored medications (Chawla et al., 2021).

Conclusion

Targeted medication delivery has been revolutionized by the integration of nanotechnology and biotechnology, which has solved important issues with drug solubility, bioavailability, and specificity. Nanobiotechnology makes precise and effective treatments possible by utilizing biological systems and nanoscale manipulation, reducing side effects and improving therapeutic results. Combining the domains of gene therapy, protein delivery, customized medicine, and vaccine development provides creative answers to challenging medical problems. Despite

current challenges, this collaboration has the potential to completely transform healthcare while unlocking the door to future, more customized successful and effective treatments.

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Nanoparticles as a Better Alternative Agent for Effective Drug Delivery System

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Abstract

Nanoparticles present a potential yet effective solution against traditional drug delivery systems which benefit from their small size scale and broad surface area and better drug availability properties alongside targeted and prolonged drug delivery capabilities. The widespread use of conventional drug delivery systems comes with various problems because they lead to low drug uptake and fast degradation and result in drug substances spreading across non-specific areas producing systemic reactions including gastrointestinal distress and pain from injections and tissue damage. Restricted drug distribution leads to both diminished medication effectiveness and heightened resistance in pathogens and raises the number of harmful side effects. Nanoparticles resolve these problems through their fresh mechanism of action which enables them to deliver drugs more specifically and efficiently.

Keywords: Nanoparticles, Alternative methods, Traditional drug delivery agents, Mechanisms, Drug delivery

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Introduction

Nanoparticles are small sized particles that ranges from 1-100nm (Qurashi et al., 2024). Nanoparticles have unique biological, chemical, and physical properties due to their small size (Ahmad et al., 2024). These properties make them enable to be used for multiple fields including material science, medicine, electronics, and many more (Saeed et al., 2025). The small size of nanoparticles allows them to interact with the biological systems more effectively as compared to the other agents which are bigger in size (Yusuf et al., 2023). Effectiveness of the drug can be enhanced by the effective drug delivery systems (Chandrakala et al., 2022). Nanoparticles can be used as an effective system for drug delivery because of the larger surface area, potential for modification, enhanced bioavailability, and ability to encapsulate multiple drugs (Mitchell et al., 2021). In the recent years, nanoparticles have acquired a significant attention of the researchers to make better alternative ways for drug delivery system (Liu et al., 2023). The multiple significant properties of nanoparticles make them ideal carrier for the delivery of drugs in humans and animals (Afzal et al., 2022). The traditional methods for the drug delivery are not very effective because of multiple reasons including rapid degradation, non-specific distribution, and poor solubility (Waheed et al., 2022). These drawbacks of traditional delivery of therapeutic agents can cause multiple other side effects (Sultana et al., 2022). Drug resistance is also increasing day by day because of these poor methods (Qureshi et al., 2023). Plant-based compounds are also under study as an alternative strategy to overcome the resistance issue (Abbas et al., 2025). However, nanoparticles have the ability to enhance the stability of drugs, provide targeted delivery of the drugs, and provide sustained and controlled release of the drug (Bai et al., 2022). Different types of the nanoparticles have been extensively studied for their potential use for the treatment and cure of multiple diseases of humans and animals (Dominguez-Oliva et al., 2023). Most commonly used types of nanoparticles are metallic nanoparticles, polymeric nanoparticles, polymers, and dendrimers (Khan et al., 2022). They can be used to treat multiple diseases, including neurological disorders, infection, and cancer (Rahman et al., 2022). This chapter focuses on the importance of the nanoparticles as better alternative agents for drug delivery system in humans and animals and their mechanisms of action.

1. Drug Delivery Systems

The traditional methods for the drug delivery to cure or treat the disease or infection have several drawbacks (Sultana et al., 2022). The most common routes used for drug delivery include oral drug delivery system, intravenous route, intramuscular route, subcutaneous route,

transdermal and tropical route, pulmonary route, and ophthalmic and nasal route (Gupta et al., 2022; Wiwanitkit, 2024). Detail of these routes, agents used for each route and their drawbacks are given as follows:

1.1. Oral Route

Tablets, solutions, and capsules are used for the oral route of drug delivery (Salunke et al., 2022). Drugs given through the oral route are ingested and absorbed in gastrointestinal tract (Vinarov et al., 2021). The major drawback of using oral route is poor or variable absorption depending on the gastric pH, enzyme degradation, and food intake (Azman et al., 2022). Drugs given through the oral route of administration need to pass the 1st-pass metabolism of the liver, which makes poor bioavailability (Saleem et al., 2024). However, if we need quick onset, oral route for drug administration is not recommended because it has very poor and slow onset of the drugs (Baryakova et al., 2023). Because of these numerous drawbacks of using tablets, syrups/solutions, and capsules, we need to focus on the alternative method for drug delivery (Nangare et al., 2021).

1.2. Intravenous Route

Injectables are given through the intravenous route of administration (Bruno et al., 2022). This method has the fastest onset of the drugs as the drug is directly delivered into the bloodstream of the organisms (Sultana et al., 2022). However, this method has its several side effects. In this method of drug administration, the drug is distributed non-specifically, which may lead to systemic toxicity (Chen et al., 2025). The given drug is released quickly from the body and thus needs frequent doses of drug (Baryakova et al., 2023). However, this method requires more experience and professional administration, and patient's convenience is limited in this method (Hansen & Solbakken, 2024).

1.3. Subcutaneous and Intramuscular Route

In subcutaneous and intramuscular route of drug administration, the drug is given directly under the skin and into the muscle respectively (Dubbelboer & Sjögren, 2022). The given drug is then gradually absorbed in the bloodstream. Like every traditional method of drug delivery, this method also has some drawbacks. When the drug is given through subcutaneous or intramuscular route, there can be pain, irritation, and discomfort at the site of the injection (Davis et al., 2024). Drug efficacy of this method is very variable because of the inconsistent rate of drug absorption in the bloodstream of the organism (Haripriya & Suthindhiran, 2023). However, drug suitability is limited for some drugs that require immediate action.

1.4. Transdermal and Tropical Route

Creams, ointments, and patches are used for tropical and transdermal route of drug administration (Witkowska et al., 2024). In this method, the drugs are applied to the skin for systemic and localized absorption (Gowda et al., 2022). The major drawback of this method is limited and poor absorption of the drug through the skin barrier (Alkilani et al., 2022). There is a high risk of skin allergy and severe irritation of skin (Lee & Goh, 2021). However, this method is only suitable for the fat-soluble (lipophilic) drugs which have very small molecular weight (Umbarkar, 2021).

1.5. Pulmonary Route

Nebulizers and inhalers are used through pulmonary route of drug administration (Heida et al., 2023). In this method, drugs are inhaled through oral-nasal route into the lungs (Sadeghi et al., 2024). This method has a high risk of lungs infection/damage or irritation (Li & Schneider-Futschik, 2023). It requires frequent administration because of the very short duration of drug action (Kienitz et al., 2022).

1.6. Ophthalmic and Nasal Route

Eye drops and nasal sprays are administered through ophthalmic and nasal route respectively (Wirta et al., 2022). The drug is given directly into the eyes and nasal cavity for systemic and local effects (Gupta et al., 2025). Some drugs (mostly hydrophilic) have very limited absorption (Lanier et al., 2021). It can also cause severe irritation, allergic reaction to some drugs, and discomfort (Salapatek et al., 2021). However, eye drops and nasal sprays have very short time of retention because of the fast clearance through mucosal secretions and tears (Račić & Krajišnik, 2023).

2. Importance of Advanced Drug Delivery Agents

Because of so many drawbacks of traditional agents of drug delivery, we need to focus on the alternative ways in order to increase the efficiency of the drugs. Advanced drug delivery agents, mainly nanoparticle plays very important role in improving the many properties of drug delivery (De et al., 2022). The details of each property are given as follows:

2.1. Sustained and Controlled Release

Nanoparticles have the ability for very controlled and sustained release of the drug (Bai et al., 2022). This ensures the constant release of the drug over a longer period of time. Low dosage and less frequent administration of the drug is required because of this ability of nanoparticles (Rahman et al., 2022).

2.2. Targeted Drug Delivery

Nanoparticles are engineered to deliver the drug at a specific desired site (Sharma et al., 2022). Nanoparticles can be directly targeted to the cells and tissues, which can reduce the toxicity that is caused by other drug delivery agents (Unnikrishnan et al., 2023). Targeted drug delivery reduces the off-target effects that enhance the effectiveness of the drug (Riaz et al., 2025).

2.3. Enhanced Bioavailability

Nanoparticles enhance the bioavailability of drugs by improving the stability and solubility of the drugs (Kumari et al., 2023). This ensures the maximum absorption of the drug in the bloodstream of the organism. The drug is released in the sustained manner which aids in a maximum improvement in the health recovery of humans or animals (Yang et al., 2023).

2.4. Reduction in Side Effects

Most common side effects using traditional drug delivery agents include vomiting, diarrhoea, overdosing, pain, discomfort, abscess formation, skin irritation, nervousness, headache, nausea and many more (Phadke & Amin, 2021). These side effects can be reduced by using nanoparticles.

3. Mechanisms of Drug Delivery through Nanoparticles

There are multiple mechanism of actions of the nanoparticles (Abdulmalek et al., 2021). The most significant mechanism of the action of nanoparticles is disruption of the cell membrane. Nanoparticles have the ability to attach at the surface of the bacteria's cell wall or cell membrane. They affix to the bacterial cell wall/membrane and cause severe damage to it (You et al., 2025). Death of the bacteria happens because of the leakage of the important cellular components and material (Elbasuney et al., 2023). However, nanoparticles can also cause instability in the cellular membrane of the bacteria, that leads to disruption in the cellular function and alteration in the cell permeability. Some nanoparticles have the ability to disrupt the function and integrity of the cell by releasing metal ions on the surface of the cell membrane. Another important mechanism of the action of nanoparticles is the production of reaction oxygen species, which leads to the production of oxidative stress. Reactive oxygen species are highly reactive molecules that can damage the cell and its component including proteins, DNA, and lipids (Juan et al., 2021). This will ultimately cause the death of the cells. However, some other mechanisms of the action of nanoparticles include enzyme degradation, protein denaturation, DNA damage, and inhibition of different cell functioning (Figure 1).

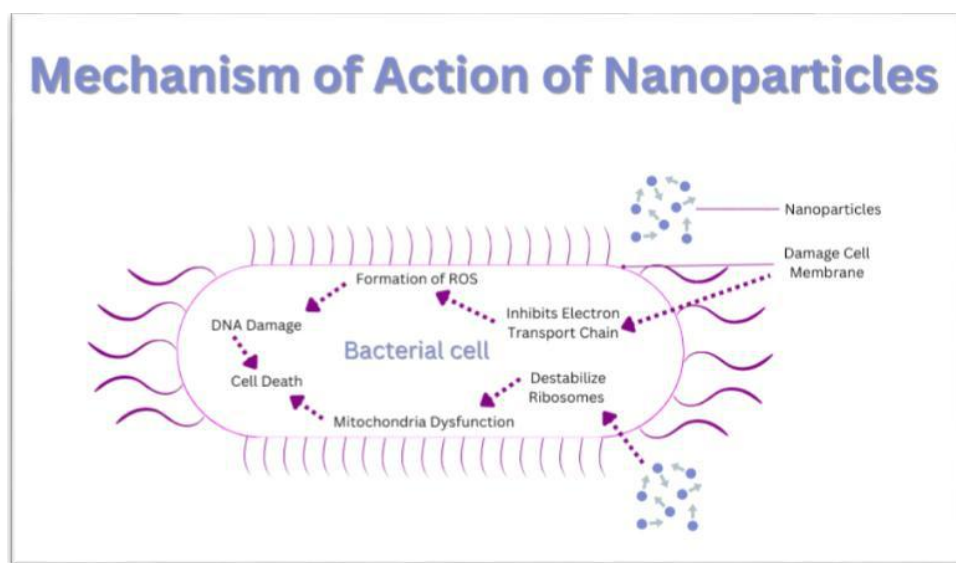


Fig. 1: Mechanism of Action of Nanoparticles

4. Limitations

Nanoparticles have more benefits as compared to any other traditional drug delivery agent (Chandrakala et al., 2022). However, there are some limitations to using nanoparticles as drug delivery agents. Some nanoparticles have toxic effects on the human and animal body, that is why they cannot be used for a longer period of time (Ajdary et al., 2021). Some types of the nanoparticles cause hypersensitivity effects and activate the immune system of the organism. The nanoparticles are hard to manufacture because of their very small size. However, we have limited knowledge about the safety index, toxicity of the nanoparticles, and long-term using effects. Targeted drug delivery and bio-distribution of the drugs with the help of nanoparticles is also another challenging task (Skotland et al., 2022). We need more study and research on these limitations of the nanoparticles so that they can be used as better alternative agents for drug delivery and improve health and life of organisms.

Conclusion

Nanoparticles present a potential yet effective solution against traditional drug delivery systems which benefit from their small size scale and broad surface area and better drug availability properties alongside targeted and prolonged drug delivery capabilities. The widespread use of conventional drug delivery systems comes with various problems because they lead to low drug uptake and fast degradation and result in drug substances spreading across non-specific areas, producing systemic reactions including gastrointestinal distress and pain from injections and tissue damage. Restricted drug distribution leads to both diminished medication effectiveness and heightened resistance in pathogens and raises the number of harmful side effects. Nanoparticles resolve these problems through their fresh mechanism of action which enables them to deliver drugs more specifically and efficiently. Nanocomplexes enable successive and controlled drug delivery, which enables patients to take medications less frequently with lower general drug amounts circulating inside their bodies. Such a feature leads both patients and healthcare providers toward better treatment results. The designed nature of nanoparticles enables precise targeting of specific cells and tissues, which

minimizes adverse effects along with toxicities. The increased bioavailability enables the drug to reach its target location in optimal concentrations, which results in more efficient treatment while reducing recovery times.

The bacterial cell membrane disruption effect together with ROS production and metal ion release by nanoparticles renders them high performing in combating infections including drug-resistant bacteria strains. The range of advantages of nanoparticles does not eliminate their existence of specific drawbacks. Multiple issues persist related to natural nanoparticle toxicity and both sensitivity reactions and immune system reactions as well as problems with large-scale production. Studies regarding long-term effects and bio-distribution of nanoparticles need further investigation because full understanding of these aspects remains incomplete.

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Role of Metallic Nanoparticles as Additives in Poultry

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Abstract

The poultry industry is fulfilling the major requirements of protein for humans. The poultry industry is booming around the globe to compete with chicken meat production. The growth of the poultry sector needs advancements in every field significantly the feed advancements. There is a significant increase in the efficiency of the feed for growing and laying birds with the help of nanoparticles. There are multiple types of nanoparticles that are under study. However, the metallic nanoparticles are the best that enhance the effectiveness of the feed. Metal nanoparticles include zinc, selenium, copper, and silver. Nanoparticles have the ability to offer less toxicity, improved bioavailability, and improved absorption of the feed. Metallic nanoparticles have shown potential results in the improvement of egg production, efficiency of feed, meat texture, growth promotion, and productivity. However, the safety index of the nanoparticles must be evaluated through extensive research. This chapter demonstrates the benefits and limitations of the metallic nanoparticles in the poultry industry and its future implementations.

Keywords: Nanoparticles, Metallic nanoparticles, Poultry, Additives, Alternative

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Introduction

Poultry is a core component of global food systems, providing a scalable and adaptable source of protein for populations worldwide (Ferdous et al., 2023). It fulfills the nutritional requirements of expanding populations, especially in regions with limited access to other protein sources (Kleyn & Ciacciariello, 2021). Poultry sector empowering millions of people worldwide, mainly developing countries (Ahmed et al., 2021). To optimize the performance and quality of products, experts have applied nano-biotechnology, and it proves to be an advancement in the poultry field if followed by farmers properly with precaution and care (Sadr et al., 2023). Nanoparticles (NPs) are characterized by their nanoscale dimensions and tiny particle size and possess a broad spectrum of attributes (Khan et al., 2022). NPs are acquiring widespread acceptance in poultry farming owing to their favorable attributes, such as low toxicity, high bioavailability and significant surface area relative to macro-scale particles, and extended action (Saeed et al., 2025). Implementation of different nano-sized trace element supplements in the poultry industry has been proven to be efficient in the world practice (Nechitailo et al., 2025). It enhances the economic benefits of poultry farming by boosting meat and egg productivity (Naumenko et al., 2023). It enhances digestibility in the gut and their action on specific body tissues (Pramanik et al., 2023). These NPs play a beneficial role in the treatment, diagnosis, and prophylaxis of diseases in poultry (Heshmati et al., 2023).

Nevertheless, metallic NPs like calcium, copper, selenium, iron, gold, silver, zinc, and chromium etc. appear to be effective as mineral supplements compared to inorganic mineral supplements because of their improved absorption (Michalak et al., 2022). These mineral NPs avoid antagonistic effects with other minerals, developmental efficiency, and physiological activities (Alharby et al., 2021; Wohlmuth et al., 2022). They work commendably at notably reduced doses compared to the levels recommended for larger particles (Tripathi et al., 2024). These nanoparticles can be synthesized by different methods, including physical, chemical, green, and biosynthetic methods (Alsaiani et al., 2023). Supplementing diets with mineral NP might be a promising strategy in the future (Bhagat & Singh, 2022). Even with their toxicological limitations to metallic NPs, multiple studies have explored the effects regarding metabolism, productivity, health, and notably antioxidant properties (Wang et al., 2024). The incorporation of metal nanoparticles into poultry production represents a promising area of research (Ahmad et al., 2022). It is targeting the development of nutritional additives, antimicrobial agents, and growth promoters because of their antioxidant, antibacterial, and immune-modulating properties (Ashraf et al., 2024). More detailed research is also necessary on the harmful effects and the strategies to combat it (Solano et al., 2021).

Synthesis and Properties of Nanoparticles

A nanoparticle is a microscopic entity measuring 1 to 100 nanometers (Ahmad et al., 2024; Qurashi et al., 2024). Nanoparticles have

distinct physical and chemical properties because of their miniature size and extensive surface area (Joudeh & Linke, 2022). Nanoparticles can be synthesized in various ways like physical, chemical and biosynthesis (Hachem et al., 2022). These processes are further classified into multiple steps or methods (Table 1).

Table 1: Different Methods of Synthesis of Nanoparticles

Physical Method	Chemical Method	Biological method
- Condensation and Evaporation method - Chemical vapor deposition method - Electric arc discharge method - Laser ablation method - Gas phase synthesis method - Ball milling–annealing method - Physical vapor precipitation method (Jagdeo, 2023)	- Reduction method, this method is further divided into 2 reduction methods: chemical and indirect reduction that is, by extraction of methods. - Inert gas condensation. - Sedimentation method. (alkaline, sol gel, coprecipitation hydrothermal) (Khan et al., 2022)	Green synthesis, plants or microorganisms (algae, virus, fungi, and bacteria) (Pandit et al., 2022)

Use of nanoparticles in poultry farming show evident results by promoting growth rates of birds (Sharif et al., 2021). Best results are because of the effective absorption of these NPs from the gastrointestinal tract, exerting a stronger biological effect on the body (Waheed et al., 2022). NPs improve the nutritional value of products while minimizing the toxicity of the agents used and support high bioavailability of minerals (Arshad et al., 2021; Thangavelu et al., 2024). The integration of nanoparticles to enhance feed efficiency and poultry well-being can effectively reduce the antibiotic resistance and incidence of diseases (Abreu et al., 2023). Nanoparticles can achieve desired effects at lower doses compared to traditional supplements (Abdelnour et al., 2021).

These NPs are useful because of cost-effectiveness, more efficiency, minimum dosage requirements, lower antagonism and enhanced bioavailability of essential nutrients (Raza et al., 2024). Nanoparticles can help maintain a balanced nutrient profile in poultry diets. Nanoparticles can enhance immunity and disease resistance, reduce oxidative stress and heat stress, give antimicrobial effects, promote overall health and well-being. It enhances eggs and meat production and quality and improves meat texture. NPs promote healthy gut microbiomes of birds and results in optimal digestion and nutrient absorption (Qu et al., 2023). Nanoparticles exhibit antimicrobial, antiviral, antiprotozoal, antifungal, and antioxidant properties, demonstrating their potential as therapeutic agents.

Table 2: Benefits of Metallic Nanoparticles

Sr. no.	Metallic Nanoparticles	Benefits or Results
1.	Zinc oxide NPs	Pronounced antioxidant properties, positive effect on productivity, weight gain, feed digestibility, and carcass characteristics and homeostasis of poultry, egg quality, immune status and improve serum enzymes activity during the starter period (Czyżowska & Barbasz, 2022).
2.	Zinc NPs	Improvement of performance, carcass characteristics, humoral immunity, meat quality, antioxidant activity. No deleterious effect on the developing embryo and percentage of hatchability in case of in-Ovo administration (Grasso et al., 2022).
3.	Silver & Gold NPs	potential alternatives to antibiotics and could solve the resistance problem of microorganisms to antibiotics (Toczek et al., 2022).
4.	Copper NPs	Improved percentage of breast and leg muscles, chicken growth
5.	Copper oxide NPs	Antioxidant, improve production, egg quality, and immune status but limited in usage because of their toxicokinetic (Tortella et al., 2024).
6.	Chromium NPs	positively affect sperm survival in turkeys, increase the resistance of the broiler chickens' body to heat stress and normalizing the metabolism of sex hormones (Majewski et al., 2022).
7.	Silver, copper, Zinc NPs	Alternative to antibiotics against the main pathogens of poultry infectious diseases, such as <i>Salmonella</i> and <i>Campylobacter</i> (Raja et al., 2023).
8.	Iron oxide NPs	Produce safe and high-quality meat, enhance detoxify biological fluids, antimicrobial therapy, and tissue regeneration, solve oxidative stress (Kumar et al., 2024).
9.	Calcium carbonate NPs	Better average feed conversion rate and increased relative eggshell mass and eggshell mass/surface area (Fadia et al., 2021).
10.	Manganese NPs	Added to sperm diluent increased the mitochondrial membrane potential and activity of the plasma membrane. As a result, all spermatozoa showed good motility during the storage period (Haque et al., 2021).
11.	Selenium NPs	Improvement of growth performance, increased water holding capacity of meat, mainly improved the oxidation resistance or control oxidative stress (Bano et al., 2021).
12.	Chromium NPs	Improved the weight gain and feed conversion ratio of heat-stressed chicks, enhanced antibody titers of heat-stressed broilers as well as antibody titers against avian influenza and infectious bronchitis (Manzoor et al., 2022).

Use of Metallic Nanoparticles as Poultry Feed Additives

Metal/metal oxide Nanoparticles such as zinc, copper, silver, and selenium, nanoparticles can serve as alternative growth and health enhancing supplements to antibiotics, providing a potential alternative for promoting animal health (Krishnani et al., 2022). These can be given directly to the drinking water or feed, by parenteral injection or by in-Ovo route and can provide the embryos with extra nutrients. It is proposed

that in-Ovo administration of metal-containing nanoparticles enables more efficient use of microelements during embryo development compared to feed supplementation, which could enhance embryo development (Michalak et al., 2022).

Silver, selenium, and zinc nanoparticles are primarily evaluated as antimicrobial agents (Ifijen et al., 2022). The most studied are silver nanoparticles, which display a wide range of antimicrobial properties (Bamal et al., 2021). It proves effective against multiple bacteria like *Salmonella typhimurium*, *Salmonella pullorum*, *Pseudomonas*, *Escherichia coli*, *Staphylococcus aureus* and *Klebsiella* (Abou Elez et al., 2021).

Current research suggests that metal NPs in poultry feed additives require immediate scientific attention and more comprehensive investigation related to their safe doses and toxicity issues (Wang et al., 2024). The main elements of the positive effects of metal NPs on poultry health include a synergistic combination of antioxidant, antimicrobial, and immune-modulating effects (Abd El-Hack et al., 2023). Here are the results of the research on the use of metal nanoparticles in poultry and their possible potential listed in Table 2.

Limitations to the use of Nanoparticles

Besides the advantages of the use of NPs, it is essential to consider their potential negative outcomes (Adams et al., 2022). There is a possibility of potential deposition of nanomaterials in the ecosystem through excretion and development of new forms of environmental contamination (Malakar et al., 2021). They may contaminate air, soil and water sources, affecting plant and aquatic life (Bhardwaj et al., 2023). If these NPs accumulate in birds, it leads to bio-magnification in the food chain and directly harms consumers (Uddin et al., 2021). NPs mainly cause harm if not used in the right quantity or dose. So, always take great care of the dose given to the birds (Bhardwaj et al., 2023). This can also be solved by conducting further detailed research to ensure the exact quantity of NPs necessary for beneficial outcome. It is mandatory to assess the potential risks associated with nanomaterials used to ensure safety (Committee et al., 2021). Addition of nanoparticles to the animal diet can cause pathological alterations in animal tissues, including pancreas, kidney, liver, adrenal glands, small intestine and brain. There is a continuous need for research and development to understand the potential impacts of nanomaterials (Gottardo et al., 2021). Proper precautionary measures can help prevent potential harm to humans and the environment (Dhama et al., 2021).

Conclusion

Poultry provides a fundamental and flexible nutritional supply that continues to grow in global demand for protein. Progressive alternatives based on metallic nanoparticles, which include zinc and silver and copper and selenium, and chromium, can enhance both efficiency and productivity and quality of the product while boosting immunity. These nanoparticles benefit from their dimensions at the nanometer level because they increase nutrient absorption while minimizing interactions between different nutrients and produce better overall biological function at lower concentration levels. NPs demonstrate antioxidants along with antimicrobial and anti-viral and antifungal and immune-modulatory characteristics which produce significant benefits for improving egg and meat quality along with gut health and disease resistance and stress tolerance. The poultry sector benefits from nanoparticles synthesized using physical, chemical and green methods which demonstrate the agents' versatility. The in-Ovo administration of NPs represents a novel technique for embryonic development improvement as well as enhanced nutrient utilization. The multitude of advantages derived from nanoparticles should be acknowledged, but environmental plus toxicological risks surrounding their use demand continued investigation. The application of improper dosage levels might cause tissue accumulation issues in birds as well as chain-based bio-magnification effects which thereby risk both human consumers and ecosystem health. Researchers have yet to unravel all possible effects which nanoparticle exposure has on poultry organs and general health outcomes. The application of metallic nanoparticles should be handled with care even though they stand as groundbreaking technological developments with considerable promise. The successful implementation of nanoparticles in poultry farming depends on maintaining proper drug concentrations and ongoing testing and complete toxicological study for risk reduction. Future developments in nanotechnology sustainability together with strict scientific examination will lead to safe nanoparticle applications in poultry farming which boost animal well-being and secures food supplies and protect the environment.

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Nanoparticles in Targeted Drug Delivery: Role in Early Diagnosis and Drug Discovery

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Abstract

Numerous significant advancements in our understanding of the biological mechanisms underlying the genesis of cancer have occurred in recent years. These developments have enabled the identification of promising new targets for the treatment of cancer. Oncology has been transformed by nanotechnology, which has made site-specific cancer treatments and tailored oncomedicine possible. Nanomedicines increase the effectiveness of treatment by focusing on cancer cells in the tumor microenvironment. Both organic and inorganic nanoparticles are essential for delivering drugs to tumor locations, overcoming delivery obstacles, and improving nanocarriers. By boosting medicine concentration at particular sites and reducing negative effects, targeted drug delivery improves treatment. Targeted therapies are improved, drug-NP interactions are predicted, and biomarker detection is enhanced when artificial intelligence (AI) and nanomedicines are combined. Drug delivery and cancer detection are two applications for nanomaterials like dendrimers and quantum dots. Notwithstanding developments, further study is required to improve medicine delivery and diagnostics with AI and nanoparticles. This chapter highlights the available Nano-formulated therapy in cancer treatment.

Keywords: Cancer, Nanoparticles, Artificial intelligence, Drug delivery system

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Introduction

The global burden of cancer extends beyond health implications, significantly impacting economies and vulnerable populations. In 2022, the United States alone reported 1.9 million new cancer cases, resulting in 609,360 deaths (Siegel et al., 2022). Cancer, a term encompassing a variety of diseases characterized by the transformation of normal cells into malignant ones, remains a leading global health concern, with millions of new cases annually. Its complexity, driven by factors like resistance to apoptosis, angiogenesis, and metastasis, makes it difficult to detect early, with symptoms often manifesting only after metastasis has occurred (Sethi & Kang, 2018). Although chemotherapy, radiation, and surgery are still often used to treat cancer, they have several drawbacks, such as serious side effects and the emergence of drug resistance. For example, systemic toxicity from chemotherapy can impact both diseased and non-cancerous cells, resulting in issues that are frequently permanent if not identified in time (Raghavakaimal et al., 2022).

Conventional cancer treatments, such as radiation, chemotherapy, and surgery, have significant disadvantages, especially in advanced stages. These include low bioavailability and medication toxicity (Olusanya et al., 2018). Chemotherapy often fails due to non-specific targeting and inadequate drug concentration at tumor sites. Research is being done on combination drugs with lower toxicity and synergistic effects to fight multidrug resistance. Targeted treatment still faces challenges with inefficient drug delivery to tumors, which leads to cancer cell resistance and recurrence. These difficulties underscore the need for cutting-edge cancer technology. These problems can be solved by nanotechnology, which does drug delivery, early diagnosis, and treatment by nanoparticles application (Ambrose et al., 2025).

PLGA-PEG/NR7 (for oral squamous cell carcinoma) and Ferumoxtran-10 (for MRI imaging) are two nanoparticles that have been giving increased drug entrance and target delivery. In Europe, lung, breast, and colorectal cancer cases are highly recorded (25% of all types of cancer cases) worldwide (Hofmarcher et al., 2018). Lung cancer is a major cause of cancer-related deaths in poorly developed countries globally. There are various factors that can increase cancer risks like, lack of exercise, not eating properly and smoking (Wang et al., 2015). Scientists have been developing quantum and gold dots that can diagnose and treat cancer in a more accurate and precise way (Adir et al., 2020).

Combination of nanotechnology and artificial intelligence (AI), new, precise, and cost-effective ways are opening for the treatment of cancer. Because AI brings revolution by increasing drug target delivery and synergies, quick data analysis, optimizing material characteristics, and simplifying difficult activities (Adir et al., 2020). While, in the case of nanotechnology, Ag-based and magnetic metallic NPs are treating cancer, by preventing them from growing, and enhancing their appearance during diagnosis (Mirza & Siddiqui, 2014). The fact is that due to some problems like, how NPs can stay in the body for long time, deal with various types of tumors, and reach their specific target tumor site, there is still need for further studies in order to obtain better results in cancer treatment (Mitchell et al., 2017). In order to overcome these problems, there is a need for the experts to work together, successfully link laboratory findings with practical applications, and need of innovative studies. As a result, this chapter examines the significant role that NPs play in cancer treatment, focusing especially on their potential as a targeted delivery system for tumor treatment.

Typical Cancer Treatments: Assessing Progress and Unmet Promises

The particular physiology of the diseased organ determines the choice of traditional cancer treatments, such as surgery, chemotherapy, and radiation therapy. Despite clinical success, many treatments continue to have serious limitations that restrict their efficacy (Atlihan-Gundogdu et al., 2020). There are more than 200 forms of cancer, which are categorized either by the type of cell or tissue impacted or by the site of origin, such as the breast, lung, skin, colon, or liver (Carbone, 2020). Sarcoma (from connective tissues like bone, cartilage, or muscle), leukemia (from blood cells), lymphoma and myeloma (from immune cells), carcinoma (from skin or epithelial tissues lining organs), and brain and spinal cord tumors are a few examples. The tumor stage has a major impact on the therapeutic selection, and survival results are greatly impacted by early identification. Cancer at advanced stage IV is usually treatable but incurable (Chidambaram et al., 2011).

One important feature of cancer cells is their fast division, which is the focus of conventional chemotherapy. But a lot of good cells, such as those in the digestive system, bone marrow, and hair follicles, also divide rapidly, which might have negative, non-specific side effects (Tilsed et al., 2022). Organ failure, hair loss, mucositis, immunosuppression, anemia, and thrombocytopenia are a few of these that frequently call for dose modifications, postponements of treatment, or even stopping altogether. Furthermore, solid tumors where cell development slows down close to the tumor core may respond less well to chemotherapy (Senapati et al., 2018). Chemotherapeutic drugs are quickly removed from circulation and frequently do not reach solid tumor cores, which limits their ability to interact with cancer cells. Their inability to dissolve further impairs their capacity to efficiently pass across cellular membranes (Dallavalle et al., 2020). In chemotherapy, drug resistance occurs when cancer cells create defenses against drug accumulation, such as overexpressing P-glycoprotein (Heming et al., 2022). These difficulties highlight the necessity of precise, focused treatments. The next part examines precision cancer medicine, which goes beyond traditional therapies and seeks to customize care to each patient's own genetic and molecular cancer profile for a more individualized and successful outcome.

Using Nanotechnology for Accurate Cancer Treatment

The concept of "precision medicine," popularized around 2010 and advanced by President Obama's 2015 Precision Medicine Initiative (PMI), aims to deliver tailored treatments based on individual genetic and molecular profiles (Terry, 2015). While often used interchangeably with personalized medicine, subtle differences exist, with precision medicine focusing on disease prediction and targeted prevention. This approach not only tailors treatments but also helps reduce tumor development and progression through personalized risk assessments and proactive management (Delpierre & Lefèvre, 2023). Precision medicine tailors treatments based on an individual's genetics, environment, and lifestyle, while targeted drug delivery optimizes drug distribution to disease sites, reducing off-target effects. Together, they enhance therapeutic outcomes and improve cancer treatment efficacy (Manzari et al., 2021). Table 1 gives some of the important NPs used for cancer therapy.

Targeting Nanoparticles Molecularly and Ligand-Based for Accurate Cancer Treatment

Developments in tumor biology have led to the targeting of cancer-specific proteins, oncogenes, and pathways for targeted drug delivery (Tiwari et al., 2023a). NPs offer ground-breaking approaches to cancer treatment through two targeting strategies: passive targeting, which capitalizes on the enhanced permeability and retention (EPR) effect in tumors, and active targeting, in which ligand-functionalized NPs attach to overexpressed cancer cell receptors (Khan et al., 2023). These techniques enhance receptor-mediated endocytosis, reduce off-target toxicity, and enhance tumor selectivity (Mamnoon et al., 2020). Because of their accessibility, high binding affinity, and specificity, especially in breast cancer, antibodies are frequently utilized in targeted cancer therapy (Sun et al., 2022). Their "Y" structure allows precise antigen binding. Other ligands, like small peptides and proteins, offer advantages such as low molecular weight, reduced immunogenicity, and easy production. Aptamers, synthetic DNA or RNA oligonucleotides, form 3-dimensional structures that tightly bind specific cancer cell markers (Trivedi et al., 2024). Precision medicine has thus advanced therapies targeting tumor-specific antigens, enhancing treatment specificity and effectiveness (Xu & Wang, 2015).

Prostate-specific membrane antigen (PSMA) is highly specific to prostate cancer cells and enables targeted drug delivery. PSMA-targeted nanoparticles like BIND-014, loaded with docetaxel, showed enhanced pharmacokinetics and efficacy in phase I and II trials, selectively targeting tumors with PSMA expression (Wang et al., 2022). In metastatic castration-resistant prostate cancer, BIND-014 improved survival and reduced PSA levels in a subset of patients (Von Hoff et al., 2016). Biomarkers like HER2 in breast cancer enable targeted NPs therapies. MM-302 NPs combined with trastuzumab showed improved safety in early trials but did not increase survival in phase II (HERMIONE trial). Additional targets, such as Tfr and EGFR, enhance drug delivery to breast cancer cells, with promising preclinical results, though clinical trials are pending for some NPs (Kumari et al., 2016).

Integrated Cancer Screening and Treatments Using Nanoparticles

Nanotheranostics integrates nanotechnology for personalized cancer imaging and therapy, improving detection, staging, and treatment monitoring (Murar et al., 2022). NPs target tumor cells, deliver higher drug doses with fewer side effects, and track treatment progress. Silica

NPs (C-dots) labeled with ^{124}I PET and Cy5 optical agents showed safety and rapid renal clearance in metastatic melanoma patients (Phillips et al., 2014). Oncogenic biomarkers, including proteins, carbohydrates, and nucleic acids, help detect cancer, predict relapse, and monitor treatment (Das et al., 2023). Protein biomarkers are found by converting signals utilizing QD-based biosensors and interacting with antibodies or aptamers (Kim & Yoo, 2021). Colorectal, liver, prostate, and ovarian cancers are detected using biomarkers such as CEA, AFP, PSA, and CA-125, and lateral flow procedures are made easier by QD-conjugated aptamers and silica NPs (Gumus et al., 2023).

Table 1: Nanoparticle-Encapsulated Drugs for Targeted Cancer Therapy: Current Systems and Limitations

Sr. No	Drug Name	Nanoparticle Type	Active Drug	Cancer Type	Biological Application	Disadvantage	References
1	Linalool Encapsulated Solid Lipid NPs	Solid NP	Lipid Linalool	Hepatocellular carcinoma (HepG2), lung cancer (A549)	Anti-cancer efficacy	Uncertain gelation, low incorporation due to the crystalline nature	(Misra & Sahoo, 2010)
2	PCL-Tween80 Polymeric NP	Polymeric NP	-	General anti-tumor	Improved anti-tumor efficacy	Lack of in vivo studies	(Ma et al., 2011)
3	C225 Antibody Conjugated AuNP	Gold NP	-	Hepatocellular carcinoma	Noninvasive radiofrequency-based treatment	Limited radiofrequency absorption	(Raoof et al., 2012)
4	CD44 Antibody Targeted Liposomal NP	Liposomal NP	-	Hepatocellular carcinoma	Imaging and therapy	Low specificity and efficacy	(Wang et al., 2012)
5	Mit-Loaded Liposome (Mit-GML)	Liposomal NP	Mitomycin	Breast cancer (MCF-7)	Image-guided targeted therapy	Reduced cytotoxicity vs. free drug	(He et al., 2014)
6	HPTOC-DOX Polymeric Micelle	Polymeric Micelle	DOX	General anti-cancer	Enhanced anti-cancer efficacy	Low uptake, short shelf life	(Nam et al., 2015)
7	PP-SS-DTX/DTX Polymeric Micelle	Polymeric Micelle	Docetaxel	Breast (MCF-7), melanoma (B16F10)	Anti-cancer activity	Delayed release	(Guo et al., 2016)
8	Curcumin Loaded PMMA-PEG/ZnO	Polymeric NP	Curcumin	Gastric cancer	Anti-angiogenic, anti-proliferative	Limited solubility and stability	(Dhivya et al., 2017)
9	Anti-CD147 Immunoliposomal DOX	Liposomal NP	DOX	Hepatocellular carcinoma	Targeting CD147 overexpressing cells	High production cost, complex synthesis	(Wang et al., 2018)
10	DOPE/CHEMS-based DTX Immunoliposomes	Liposomal NP	Docetaxel	Prostate cancer	Targeted delivery of DTX	Limited cytotoxicity	(Wang et al., 2018)
11	YIGSR-CMChT/PAMAM Dendrimer NP	Dendrimer NP	-	Colorectal cancer	Targeted therapy	Limited validation of affinity	(Carvalho et al., 2019)
12	ICG-Loaded PEGylated BSA-Ag NP	Silver NP	ICG	General photothermal therapy	Photothermal cancer treatment	Ineffective at low concentrations	(Park et al., 2020)
13	TT3-oCB NP@EXOs Exosomal NP	Exosomal NP	-	General tumor treatment	Image-guided photothermal therapy	Toxic degradation products	(Li et al., 2021)
14	Aspergillus Austroafricanus CGJ-B3 AgNP	Silver NP	-	Breast (MCF-7), skin (A431), liver (HepG2)	Antioxidant and cytotoxic against ROS and RNS	Limited toxicity studies in vivo/in vitro	(Danagoudar et al., 2021)
15	Amygdalin Loaded AgNP Chitosan Microcapsules	Silver NP in Chitosan	Amygdalin	Breast cancer	Targeted amygdalin delivery	Lower cytotoxicity vs. free AgNP	(Pandey et al., 2021)
16	Doxil	Liposomal NP	Doxorubicin	Ovarian, sarcoma, myeloma	Kaposi's Cancer treatment Multiple	Costly and complex formulation	(Shafei et al., 2017)
17	Myocet	Liposomal NP	Doxorubicin	Metastatic breast cancer	Anti-tumor therapy	Limited release control	(Batist et al., 2002)
18	Onivyde	Liposomal NP	Irinotecan	Metastatic pancreatic cancer	Tumor-targeted chemotherapy	High production costs	(Ko, 2016)

19	Daunoxome	Liposomal NP	Daunorubicin	HIV-associated sarcoma	Kaposi's AIDS-related Kaposi's sarcoma treatment	Limited tissue penetration	(van Hoogevest et al., 2021)
20	Vyxeos	Liposomal NP	Daunorubicin, Cytarabine	Acute myeloid leukemia	Leukemia treatment	High cost, limited specificity	(Hristova-Panusheva et al., 2024)
21	Ameluz	Liposomal NP	5-Aminolevulinic acid	Actinic keratosis	Targeted skin cancer therapy	Photosensitivity post-treatment	(Hristova-Panusheva et al., 2024)
22	Abraxane	Polymeric NP	Paclitaxel	Breast, non-small lung, pancreatic cancers	Chemotherapy with reduced toxicity	Expensive manufacturing	(Master & Sen Gupta, 2012)
23	Genexol-PM	Polymeric NP	Paclitaxel	Breast, non-small lung, ovarian cancers	Targeted anti-tumor therapy	High cost, lack of long-term studies	(Pillai, 2014)
24	NKTR-102	Polymeric NP	Irinotecan	Breast, ovarian, colorectal cancers	Tumor-targeted chemotherapy	Tumor-targeted chemotherapy	(Tripathy et al., 2019)
25	Opaxio	Polymeric NP	Paclitaxel	Lung, ovarian, cervical cancers	Targeted chemotherapy	Potential toxic side effects	(Cryer & Thorley, 2019)

Cancer has been connected to the downregulation of microRNAs (miRNAs) that maintain gene expression and cellular functions. Oncogenic viruses can accelerate the formation of growth of cancer by altering the regulation of miRNA (Kandeel, 2023). AuNPs@NIPAm-co-AAc microgel composites and SERS (Nanotechnology platforms) enable the accurate detection of miRNA biomarkers, such as miR-21 and miR-29a (Kamali et al., 2024). Circulating miRNAs present the possibility of correct early treatment and diagnostic monitoring (Treerattrakoon et al., 2022). Circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) enter the blood circulation as cancer cells expand, helping in successful diagnosis. One important target for liquid biopsy is the surface protein EpCAM on CTCs. For example, the nanotechnologies NG-PEI-COFTAPB-TFPB and Fe-MOF enhance the immunoassay's sensitivity and ctDNA identification (Guo et al., 2022). Microfluidic chips, 30 times quicker than ELISA, giving effective, cost-effective, and low-energy detection (Wang et al., 2021). CoZnFeONPs and other nanotechnology-based immunoarray devices aid in detecting biomarkers. By putting together enzyme-mediated nanoparticles, they are also utilized to find cancer biomarkers and CEA antigens (Yin et al., 2021). Multiplexed imaging is made feasible by semiconductor quantum dots (QDs), which also enable enhanced tissue penetration, photostability, and brightness, primarily for cancer detection (Mousavi et al., 2022). While PEGylated QDs linked with monoclonal antibodies specifically target tumor tissue, surface-modified CdTe QDs increase anti-tumor therapeutic action (Liang et al., 2021).

Nanomaterial-based Formulations for Reversing Multidrug Resistance

Drug resistance, driven by factors like ABC transporter overexpression and tumor microenvironment conditions, limits chemotherapy effectiveness (Sajid et al., 2023). Nanotechnology, including P-GP inhibitors and mesoporous silica NPs, enhances drug delivery and overcomes resistance, even crossing the blood-brain barrier. Selenium- and tellurium-based NPs also show promise in reversing multidrug resistance, improving treatment outcomes (Domínguez-Álvarez et al., 2022). Cancer drug resistance often results from defective apoptosis and dysregulated Bcl-2 and NF- κ B pathways. Targeting Bcl-2 with chemotherapeutic drugs and siRNA delivery via NPs, along with pro-apoptotic agents like rubusoside and C6-ceramide, enhances therapy (Sankar et al., 2025). Restoring p53 function using NP-based delivery methods also shows promise in overcoming resistance, especially in lung and breast cancers (Jafari-Gharabaghloou et al., 2023). Gene delivery via viral vectors faces challenges in efficiency and targeting, while nanovehicles offer a safer alternative for cancer gene editing. CRISPR/Cas9, delivered through engineered nanosystems, outperforms Bcl-2 inhibitors and RNAi in targeting oxidative stress and triggering apoptosis. Combining CRISPR/Cas9 with immunotherapy, such as CD47 blockage and IL-12 generation, enhances cancer treatment efficacy (Coelho et al., 2022).

AI's Broad Application in Nanomedicine

AI encompasses machine learning, deep learning, computer vision, and NLP, enabling human-like intelligence in complex tasks. In biomedical research, AI accelerates drug discovery and pharmaceutical operations, aiding in compound identification and compliance. In nanotechnology, AI supports scanning microscopy and simulations, with ANN enhancing spectroscopic analysis and material behavior identification (Zohuri, 2020).

Use of AI techniques has been increasingly used to resolve nanotechnology issues, with a focus on creating nanocomputing, useful nanoscale stimulation to decrease processing time, nanosystems, and improve parameter accuracy and estimation (Elemento et al., 2021). AI increases the medical efficacy of drug delivery, facilitating processes such as preparation, customized transport, and stability of bioactive components (Liao et al., 2023). Modern developments in AI assist in the development, characterization, and formation of drug delivery nanosystems through the analysis of biological and genetic data to accelerate drug development and estimate drug behaviors (Sherani et al., 2024). By evaluating immense databases, especially patient DNA and molecular profiles, AI creates customized treatments for cancer. In addition, artificial intelligence accelerates pharmacokinetic modeling and offers more customized dispersion across complicated biological barriers by incorporating various kinds of inputs, like drug and molecule interactions (Cheng & Zhao, 2014).

Cancer biomarkers are important for prognosis, surveillance, risk assessment, diagnosis, and therapeutic response in oncology (Das et al., 2023). Genetic and protein examinations aid in discovering the best medicines, and diverse biomarker profiles permit customized care. To accurately treat cancers without harming healthy tissues, nanomaterials that boost drug delivery the selectivity, and biomarker detection, such

as gold nanoparticles and quantum dots, are crucial (Sajid et al., 2023). Real-time studying of the distribution of drugs and efficiency becomes possible by outstanding imaging, which is crucial for treatment planning. AI-enhanced NP tracking devices, like Malvern's NTA, facilitate imaging and evaluation, providing individualized care and boosting the impact of nanomedicine (Zdobnova et al., 2011).

Advances in nanorobotics now allow microrobots to perform tasks like targeted drug delivery, cellular targeting, and microsurgeries, though challenges in design and biocompatibility remain (Taha et al., 2024). A recent study showcased mesoporous silica NPs with urease and gold NPs functioning as radiolabeled nanomotors, enabling PET imaging for real-time tracking and new therapeutic possibilities (Neague et al., 2024). Nanorobots' integration of AI, sensors, and power sources has improved molecular production even further. AI simulations enhance the design of nanorobots for regulated medication delivery; DNA-based nanorobots exhibit potential for accurate drug delivery and biosensing (Kong et al., 2023). Artificial neural networks enhance tumor detection, while fuzzy logic optimizes intracellular dosing for greater precision (Hassanzadeh et al., 2019).

Nanomedicine has both benefits and drawbacks, even while technological developments, particularly artificial intelligence, have accelerated drug development and optimization (Tiwari et al., 2023b). The consequences of increased permeability and retention (EPR), toxicity, dose accuracy, drug system design, and biocompatibility are all significant factors to take into account. Precise drug administration in nanorobotics is difficult due to issues including noise interference and the ability to distinguish between healthy and malignant cells (Giri et al., 2021). However, by evaluating complex data, improving drug development, and guaranteeing precise dose delivery, AI can assist in resolving these problems (Hassanzadeh et al., 2019). Artificial intelligence (AI) is especially important for genetic programming and cancer genomics, where techniques like fuzzy logic, decision trees, and artificial neural networks (ANNs) aid in the identification of new drugs (Quazi, 2022). Artificial neural networks (ANNs) are excellent at classification and prediction, fuzzy logic improves automated medication scheduling, and supervised associating networks enable response surface techniques. In silico medicine, reinforcement learning is beneficial and might adapt (Mak & Pichika, 2019).

Conclusion

AI-powered strategies enhance medication targeting and biomarker identification, resulting in a more customized treatment regimen. The study highlights the expanding use of cutting-edge nanoparticles that improve therapeutic efficacy and clinical imaging capabilities, such as dendrimers and quantum dots. The concept of nanotheranostics, which combines therapeutic and diagnostic qualities in nanoparticles, enables real-time treatment progress monitoring. Additionally, it has been shown that the production of nanoparticles functionalized with ligands improves the precision of targeting for specific cancer receptors. Despite these advancements, problems with multidrug resistance and ensuring effective tumor accumulation still exist, necessitating additional development of therapies based on nanoparticles.

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Nanotechnology and Rhizobacteria: A Novel Strategy for Enhanced Plant Growth

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Abstract

The continuous use of chemical pesticides and fertilizers in agriculture has raised serious threats and concerns about environmental sustainability and food security. Scientists and researchers are looking into different approaches, like using beneficial microorganisms in biofertilizers. By facilitating better nutrient uptake and functioning as biological regulators, these microbial inoculants promote plant growth while lowering the demand for chemical inputs. Living microorganisms that colonize plant roots or soil to help transform nutrients into forms that plants can use make up biofertilizers. Through processes like the synthesis of phytohormones and nitrogen fixation, they can stimulate growth. Furthermore, applying nanotechnology to agriculture presents promising improvements for biofertilizers, which could increase their efficacy in a range of environmental circumstances. This review highlights the potential of nanoparticles (NPs) to support sustainable agricultural practices by improving the effectiveness of beneficial plant bacteria. These cutting-edge methods seek to establish a more sustainable and profitable agricultural system by lowering reliance on chemical pesticides and fertilizers.

Keywords: Plants, Plant growth-promoting bacteria (PGPB), Nanoparticles (NP), Biofertilizers

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Introduction

The need for food has grown due to population growth and economic development, which has resulted in an overuse of chemical pesticides and fertilizers to raise crop yields (Prasad, 2013; Sharma & Singhvi, 2017). Such approaches have led to ecosystem imbalance, biodiversity loss, water and soil contamination, and soil microbial depletion. Sustainable soil and water management techniques, biopesticides, and biofertilizers can all produce high agricultural yields with little harm to the environment (Kour et al., 2020). Rhizosphere and endophytic plant growth-promoting bacteria (PGPB) are useful biofertilizer ingredients that improve nutrient uptake, boost plant tolerance to stress, and provide phytopathogen protection (Singh et al., 2019). This potential is reflected in the global plant bio-stimulant market, which is expected to reach USD 3.0 million by 2022 at a growth rate of 12% per year (Peter et al., 2020).

Despite their promise, microbial biofertilizers face challenges such as instability and inconsistency under field conditions (Fadiji et al., 2024). Nanotechnology offers solutions through precision agriculture, leveraging NPs to address biofertilizer limitations like reproducibility, storage stability, and sensitivity to environmental factors (Duhan et al., 2017). Nanotechnology utilizes materials with unique properties arising from quantum confinement effects and highly reactive surfaces at the nanoscale. Compared to their macroscopic counterparts, nanomaterials exhibit novel characteristics due to their reduced size, higher surface area-to-weight ratio, and distinct shapes (Rastogi et al., 2019). By integrating nanomaterials with PGPBs, this technology promises to optimize crop systems while providing economic and environmental benefits, paving the way for sustainable agricultural development (de Moraes et al., 2021; Verma et al., 2024).

1. Application of Nanotechnology in Modern Agriculture

The concept of using agriculture techniques along with nanotechnology started in the late 20th century. In the starting era the nanotechnology was only considered for the application in material science and medicinal domains. As the population of the world is increasing day by day at a rapid speed, the importance and need of food security become and significant concern as a global problem (Kumar et al., 2020). Researchers are exploring environmentally friendly nanomaterials to enhance crop production. In agriculture, nanotechnology is applied in areas such as seed science, nano fertilizers, nonherbicides, water management, nanoscale carriers, biosensors, agricultural engineering, and animal science (Ditta & Ullah, 2022; Ghouri et al., 2020).

In smart agricultural systems use of nanomaterials improves nutrient absorption and allow for the regulated release and targeted distribution of molecules, which aid in early disease detection and safeguard the environment (Asrar et al., 2023). A traditional method that uses another synthetic form of NPs, nanoencapsulation, minimizes environmental effects while optimizing efficacy by enabling controlled release of agrochemicals (Chugh et al., 2021). In addition to improving plant uptake of nutrients, this method lowers the total amount of

pesticides required, which supports a sustainable agricultural output (Mondéjar-López et al., 2024).

2. Development of Nanotechnology-Based Biofertilizers

Bacterias such as *Pseudomonas*, *Bacillus*, *Rhizobium*, *Azospirillum*, *Arthrobacter*, *Burkholderia*, *Serratia*, *Flavobacterium*, *Enterobacter*, *Erwinia*, *Acinetobacter*, *Alcaligenes*, etc. support plant health through direct mechanisms such as nutrient uptake (nitrogen, phosphorus, iron) and hormone regulation (auxins, cytokinins, gibberellins) and indirect mechanisms like biotic stress resistance (antibiotics, antioxidants, volatile compounds) (Chandra et al., 2015). However, crops only use 30–50% of chemical fertilizers, which as a result, cause soil saturation and groundwater contamination (Khan et al., 2018). Biofertilizers containing live microorganisms such as phosphorus solubilizers and nitrogen fixers offer an environmentally benign substitute for chemical fertilizers and improve soil fertility, sustainability, and accessibility for small farmers.

Despite its advantages, PGPB application has drawbacks, such as the necessity for physical protection or a suitable microenvironment and the fall in the bacterial population following inoculation as a result of unpredictable soil conditions (Hossain et al., 2023). In order to get around this, PGPB needs carriers for transportation and storage, such as liquid media or peat. New materials, including nanostructures, are being explored to improve inoculum stability, reduce production costs, and enhance effectiveness in field applications. Nanomaterials, whenever applied at the scale of nanometers, have the potential to be the most effective carrier, improving the delivery and bioavailability of nutrients in different aspects (Saritha et al., 2022).

Nanoscale encapsulation and coating technologies are especially important in Nanomaterial-Based Biofertilizer formulations. Microbial cells and culture are protected against different stress environments by encapsulation of PGPB, a process of entrapment or enclosure of microorganisms by a nanomaterial (Vejan et al., 2019). These methods not only provide stability (ability to resist heat, UV light, and desiccation) and more shelf life to biofertilizer but also ensure the release of nutrients in a controlled and manageable way for plant (Jafari, 2017). Another very beneficial feature of enclosing PGPB with inorganic or organic NPs is that it allows very accurate timing of bacterial distribution to target organs (Khalid et al., 2020). For instance, research has shown that nano-urea may be successfully applied to pearl millet cultivation, resulting in notable improvements in nutritional content and dry matter buildup (Sharma et al., 2022).

3. Integrating Nanomaterial with Plant Growth-Promoting Bacteria for Enhanced Plant Productivity

Nanomaterials facilitate biofilm formation abilities to bacteria as well as support in the enhancement of biofilm formation and the enhancement of metabolite secretions (Mohanta et al., 2023). Small-scale NPs also help a bacterium to adhere properly to different surfaces. Carbon nanotubes have been tested and proven to provide antibacterial properties and trigger defense mechanisms in pathogen-infested tomatoes (Ning et al., 2024). Alpha amylases is essential for the breakdown of starch during the seed germination process. Zinc oxide NPs have been reported to increase its production during wheat and maize production (Srivastav et al., 2021). Researchers have studied two functional properties of two bacterial strains, *Pseudomonas* and *Azotobacter*, with NPs in a detailed manner (Yousaf et al., 2024). They have found that this formulation can influence the development of roots by colonization and plant growth by increasing phosphorus availability in soils (Ahmed et al., 2021; Patel et al., 2023). PGPBs (*Agrobacterium*, *Alcaligenes*, *Arthrobacter*, *Azospirillum*, *Azotobacter*, *Bacillus*, *Burkholderia*, *Caulobacter*, *Chromobacterium*, *Enterobacter*, *Erwinia*, *Flavobacterium*, *Klebsiella*, *Micrococcus* *Pseudomonas* and *Serratia*) microbial activity help the soil to solubilize and release plant growth promoting phytohormones (auxins, gibberellins, cytokinin, ethylene and abscisic acid) which help the plant in nutria uptake (Amara et al., 2015).

4. Innovative Ways to Increase Plant Productivity

4.1. Preserving the Rhizosphere Microbiome

Reducing rhizosphere microbiome disruption is essential for improving plant health and agricultural productivity. Bacterial colonies present in the rhizosphere are crucial to the cycling of nutrients, the prevention of disease, and the general growth of plants (Ayangbenro et al., 2022). The stability is maintained by frequently used methods like traditional farming, tillage, pesticide application, and monoculture. Unfortunately, the traditional method can eventually lower crop yields and make crops more susceptible to pests and diseases. Nowadays, several techniques are used to reduce rhizosphere microbiome disruptions. These include organic farming methods that support microbial diversity and soil health, conservation tillage, and cover crops. However, organic methods are resource-intensive and might not necessarily produce results right away (Crystal-Ornelas et al., 2021). With nanotechnology, researchers can create customized fertilizer and biopesticide delivery systems that limit chemical runoff and eliminate the need for broad-spectrum treatments by employing NPs (Ullah et al., 2024).

Nanomaterials have a strong potential to significantly impact the strength of the rhizosphere microbiome and make plants more resilient. Nanomaterials' unique properties have also been linked to improved soil physicochemical properties, which support microbial communities in soil. Studies have reported that NPs can improve water holding capacity, soil pH and nutrient availability, microbial biomass and diversity (de Oca-Vásquez et al., 2020). A study done in the past has demonstrated that the combination of nanogypsum and *Pseudomonas taiwanensis* not only improves soil structure but also enhances plant overall health by promoting beneficial microbial interactions without causing toxicity (Chaudhary et al., 2021).

4.2. Mitigating Effects of Heat and Drought Stress

Extreme temperatures and drought conditions are very crucial in the context of climate change because they present serious obstacles to plant growth and agricultural productivity (Raza et al., 2019). These conditions can make a crop suffer, make it vulnerable to pests, and affect the overall food security by lowering crop yields. However, the scalability and efficacy of these drought-resistant plant varieties, better irrigation techniques, and soil management strategies that improve moisture retention in harsh environments are frequently constrained (Shiferaw et al., 2013).

Nanomaterials (NMs), along with PGPB, have emerged as a promising strategy to enhance plant resilience under extreme weather

conditions (Savanur et al., 2021). Nanomaterials can help a plant to withstand different stress environments through multiple mechanisms. One of the mechanisms is to facilitate the controlled release of nutrients by PGBGs (Thabet & Alqudah, 2024). Secondly, it can minimise nutrient fixation in the soil and make essential elements more accessible to plants (Khalid et al., 2022). Third, it creates a more favorable environment for root development and microbial activity (Zhang et al., 2020). For example, NPs have been reported to increase phosphate-solubilizing bacterial abundance and play a critical role in making phosphorus available to plants (Cheng et al., 2023). This enhances nutrient uptake and improves overall soil health and plant growth under adverse conditions.

4.3. Reduction of Soil Contamination

Researchers are finding new ways to reduce contamination from the environment by using nanomaterial. They have discovered their significant potential in enhancing soil health and mitigating heavy metal toxicity. NPs made up of zinc oxide and silver have been found to improve heavy metal contaminations present in soil, such as iron (Rizwan et al., 2019). *Staphylococcus aureus* is resistant to chromium, and it can transform toxic chromium (Cr VI) into Cr III in soil, which is a less harmful state (Ahmad et al., 2022). The iron NPs act in a way that they can upregulate chlorophyll content and mitigate oxidative stress caused by chromium toxicity (Ulhasan et al., 2022). These capabilities of bioremediation capabilities of heavy metals in soil are crucial for restoring contaminated land and supporting plant growth.

4.4. Soil Remediation

Soil remediation involves improving the nutrient value in soil for plant growth and good water retention. This can be done commonly using three different methods, which are chemical, phytoremediation, and bioremediation. All these traditional methods have some limitations associated with them. For example chemical methods can result in secondary pollution when improperly managed, and bioremediation can be slow and ineffective in removing heavy metals (Rajendran et al., 2022). Studies done in the past for exploring some alternatives have resulted in the introduction of NPs in bioremediation efforts by promoting plant growth and facilitating the breakdown of contaminants. Silver NPs applied with *Bacillus cereus* and *Pseudomonas fluorescens* in a contaminated environment have successfully remediated soil for plant growth. Silver NPs boost enzyme activities linked to stress responses, including catalase and peroxidase, and improve root morphology (Danish et al., 2022). The enhanced enzymatic activities due to microbial interactions and nanomaterial applications contribute to improving soil fertility.

5. Impact of Nanomaterial and Plant Growth-Promoting Bacteria on Global Plant Production

5.1. Nutrient Efficiency

A stable amount of nutrients in the soil and their uptake by plants is necessary for proper development. Nanomaterials paired with PGPB are reported to increase plant nutrient uptake to a very stable amount. They help in various ways to fulfill this requirement, for example, by maintaining physicochemical characteristics, Ph, substrate availability, or water holding capacity of soil (Elsakhawy et al., 2022). It can also help in increasing microbial diversity and better aeration for nutrient transportation in rhizosphere (Agarwal et al., 2024). *Pseudomonas* specie is associated with phosphate solubilization when combined with NPs and make phosphorous readily available for the plant to absorb (Safari et al., 2020). In addition to increasing phosphorus availability, this synergistic relationship promotes beneficial microbial colonization of roots, which improves wheat growth in infected *Fusarium culmorum* soil (Kashisaz et al., 2024).

Applications of nanoparticles can further show a positive effect on the availability of nitrogen in soil. Zinc oxide NPs and PGPB stimulate siderophores and make plants able to perform iron chelation and nutrient uptake (Khan et al., 2024). A study showed that titanium dioxide NPs facilitate PGPBs to adhere to plant roots and create persistent biofilms to support nutrient uptake (Vidya et al., 2024). Stable biofilm formation and bacterial colonization reduce the effect of stress on plants in unfavorable environmental conditions. Silica NPs improve mechanical resistance in plant cell wall which provides extra protection against biotic stress and also stimulates phosphorous uptake for plant (Wang et al., 2022). Copper oxide NPs have been found to stimulate indole acetic acid (IAA) synthesis in certain PGPB strains (Karunakaran et al., 2024). IAA promotes root elongation and branching in plants and provides support for nitrogen absorption from the soil. The role of nanomaterials extends to nitrogen fixation as well. With enhanced microbial activity due to nanomaterial application there is a notable increase in nitrogen-fixing bacteria populations in the rhizosphere.

5.2. Pest and Disease Resistance

Pest and disease management is very critical for a plant to survive in its natural environment as it can possess various threats to plant development. For agriculture sustainability this concern is very problematic because of its compromises the crop yield and quality. World population is expected to become 8.5 billion people by the year 2030 therefore in order to fulfil food requirement it is very necessary to find a solution to this global issue (Oluwole et al., 2023). No doubt there are traditional methods available for pest and disease control such as using chemical pesticides but they have serious disadvantages as well. Chemicals used in pesticides are very harmful for untargeted biotic life like birds, cattle and insects (Naz et al., 2023). They also give rise to generation of super bugs in pest making them resistant to these chemical pesticides (Venkatesan et al., 2022). Microbial biofertilizers face several limitations, including slow action, host specificity and reduced efficacy under extreme environmental conditions (O'Callaghan et al., 2022). Additionally, they often have a short shelf life and require proper storage.

Nanotechnology-based approaches offer effective solutions to challenges in agriculture and the food industry, including increasing food demand, ensuring food safety, managing plant diseases, and addressing climate change. A number of studies have reported the significant potential of nanoparticles to be used as an effective antimicrobial agent. Nano chitosan is highly renowned for its unique potential to microbial colonies, specifically *Meloidogyne incognita* and the associated root galls, achieving reductions between 45.89% to 66.61% in nematode densities and 10.63% to 67.8% in gall density, respectively (Upadhayay et al., 2023). The combination of nanogypsum and *Pseudomonas taiwanensis* has been reported to work to improve soil structure and health and ultimately, it supports plants with more robust defense mechanisms against pests and diseases (T. Ahmed et al., 2023). Strong antibacterial qualities are exhibited by certain nanomaterials, such as carbon nanotubes, which can also trigger plant defense systems against diseases like *Alternaria solani* in tomato crops (González-García et al.,

2021). These results highlight the dual function of NPs as agents that protect against microbial diseases and stimulate growth.

5.3. Enhancing Soil Health

Use of nanomaterial in agriculture leads to improvements in soil health and microbial diversity. The efficiency of PGPB enhanced with nanomaterials in advancing sustainable farming methods is demonstrated by a number of scientific studies. For example, combined effects of PGPB strains (*Azospirillum lipoferum* and *Pseudomonas fluorescens*) and the cyanobacterium *Nostoc piscinale* on maize growth were examined and results over two years indicated that the addition of *N. piscinale* (0.3 g/L) and *A. lipoferum* enhanced grain yield by 31.53% in the second year and 33.20% in the first (Solomon et al., 2023). Furthermore, compared to untreated controls, treated plots showed improved microbial biomass and nutrient availability, as evidenced by increases in soil pH, humus content, and nitrogen levels. In a study *Curtobacterium oceanosedimentum* strain caused a significant increase in root and shoot length of chili plants by 58% and 60% even under the cadmium stress applied in a pot experiment (Patel et al., 2022). Chromium-resistant bacteria alongside NPs can also improve in rice quality by upregulating chlorophyll content and mitigating oxidative stress damage (Basit et al., 2023). These studies provide solid evidence regarding different ways of improving soil and crops health by using NPs.

6. Limitations for Use of Nanomaterial-based Biofertilizers in Agriculture

Nanomaterial combined with PGPBs no doubt provides a significant opportunity for modern agriculture and enhancing crop output, but unfortunately, some limitations hinder the widespread application of this technology. One of the main challenges is the production and adoption cost of nano-based PGPBs industry due to the requirement of advanced architecture at a large scale. The production comprises advanced techniques that require expertise and infrastructure investment, making it impossible for small-scale farmers to obtain (A. Ahmed et al., 2023). A study highlighted that the cost of producing certain nano formulations can reach up to \$1,000 per kilogram, which may deter farmers from transitioning to these innovative practices, especially in regions where traditional farming methods are deeply entrenched (Kesisoglou et al., 2007). Another factor is the toxicity associated with NPs, as it could raise serious environmental concerns. Nanomaterials when left for a long period in soil can cause bioaccumulation in plants and microorganisms present in soil. Studies have found that certain types of NPs, such as silver NPs, can act as a toxic agent for the bacterial population in soil, even if it is present a very small quantity (Kafeel et al., 2022). Titanium dioxide NPs can also adversely affects the Earthworm population that acts as a natural cultivator in soil (Makarenko & Makarenko, 2019). Insects like earthworms are crucial for the maintenance of the health and structure of soil. Additionally, the stability of NPs in various environmental conditions must be ensured to maximize their benefits when applied to crops. Stability is a major hurdle in this regard as storage and transportation logistics can complicate the development of nanoparticles at a large scale. Stability and viability of bacterial colonies during storage and transportation is crucial for their effectiveness to be used as a biofertilizer as the effectiveness can be compromised after a few weeks if not stored in proper environment (Ahmad et al., 2008).

Nanotechnology use in agriculture is a modern techniques and yet the standardization of regulatory frameworks for this is very limited at this stage (Soltani & Pouypouy, 2019). This makes it more complicated for a farmer to implement it as a normal practice. Regulatory uncertainty is a main reason for hesitation among industrials and stakeholders to invest and adopt this modern technology. A report from the European Commission noted that a fewer number of European Union member states have established specific regulations for nanomaterials in agriculture (Amenta et al., 2015).

These challenges must be addressed through research and policy development so that the potential benefits associated with the integration of nanotechnology with PGPBs can be obtained efficiently for sustainable agriculture.

Conclusion

PGPBs provide an effective solution to counter the limitations of chemical fertilizers. However, this requires first obtaining accurate knowledge and understanding of specific plant-microbe interactions. Since different nanomaterials have shown beneficial effects on both PGPB and plant growth, nanotechnology becomes an important tool to improve the effectiveness of microbial biofertilizers. Integration of specific nanomaterials with beneficial bacteria, the viability and environmental resistance of these microbes can be improved which ultimately enhance plant growth. Despite these advantages, concerns regarding the impact of NPs on bacterial metabolism and potential risks to the environment, food safety, and human health necessitate thorough investigation. Factors such as the type of bacteria, characteristics of nanomaterials (including size and concentration), plant species, and environmental conditions play crucial roles in these interactions. Despite these advantages, challenges such as potential ecological risks, cost-effectiveness, and large-scale applicability must be addressed to ensure the safe and effective use of these technologies. Most current research has been conducted under controlled conditions, highlighting the need for field experiments to validate findings. More research and field trials are still needed to implement this technology on a large scale. With continued research and technological advancements, the integration of nanomaterials and PGPB has the potential to revolutionize global agricultural practices, driving sustainable development and food security

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Biomass Conversion through Nanotechnology and Circular Economy

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Abstract

We have seen a huge utilization of fossil fuels due to the rise of energy requirements in the last decade. Biomass fuel production is the best alternative to meet this requirement and to protect the environment from hazards created by conventional energy resources like fossil fuels. Biomass can be converted into biofuel through different methods like gasification, direct liquefaction, and biological processes. Nowadays the commonly used method for biofuel production is a catalytic process. In this regard, nanocatalysts are significant due to their high-quality fuel production and optimal working conditions. Nanocatalysts are more advanced than heterogenous catalysts as the present solution to common issues like limited outcomes, time-consuming processes, etc. As a result, there has been an increasing trend in the development of novel nanocatalysts. This study centers on biofuels and addresses several areas including categorization, manufacturing techniques, and approaches to enhance productivity using nanocatalysts. Ultimately, the study analyzed the prospective prospects and obstacles associated with utilizing nanocatalysts in the conversion of biomass into biofuels

Keywords: Sustainable biofuel production, Green nanocatalyst, Catalytic nanotechnology Circular Economy

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Introduction

Fossil fuels, such as coal, oil, and gas, have emerged as the predominant options for meeting the growing energy needs. Conventional fossil fuels currently meet almost 80% of the total energy demand. However, they also have several disadvantages (Hou et al., 2017). Due to their non-renewable nature, fossil fuels will eventually be depleted, resulting in a significant energy crisis. The growing predominance of energy sources results in a corresponding rise in costs, posing a considerable economic challenge, especially in developing nations. The primary issue at hand is the irreversible ecological harm resulting from using these traditional fuels. Fossil fuel combustion leads to environmental problems that's why there is a need for alternatives that have a positive effect on the environment (Yao et al., 2011; Chen et al., 2018; Yang and Wang 2018). Biofuels are best in this regard as they are environment friendly and broad range of raw materials (Adegboye et al., 2021).

The Biofuel sector has been revolutionized with the application of nanotechnology. The ability of microorganisms to produce biofuel has been enhanced by assisting with nanomaterials like nano-sheets, nanotubes, etc. (Bhardwaj et al., 2021). There are different nanoparticles (NPs) are used in this process, each has its advantages like thermal stability. Catalysts can prevent or minimize the formation of detrimental byproducts during chemical reactions. NPs possess a significant surface area and exhibit strong reactivity, rendering them appropriate for utilization as catalysts or as supports for catalytic processes. The utilization of NPs in catalysts increases their durability, hence reducing the frequency of expensive and resource-intensive replacements or regeneration (Li et al., 2014; Morsi et al., 2018; Ndolomingo et al., 2020; Mishra et al., 2021).

The primary objective of using nanobiotechnology is to decrease the expenses associated with transporting feedstock and enhance the breakdown of feedstock, hence increasing the efficiency of bioenergy production (Abusweireh et al., 2022). Nanobiotechnology holds the capacity to enhance energy efficiency, mitigate environmental impacts, and establish economic viability for bioenergy in comparison to conventional fossil fuels. It can be incorporated into bioenergy research and production operations. Many biorefineries use coated NPs on their equipment to provide corrosion protection and thermal insulation (Thomas et al., 2022), resulting in a more environmentally friendly process. The utilization of nano-metals for energy generation can enhance the commercial feasibility of microorganisms. Nanoscale studies are conducted to investigate enzymatic activity, where the enzymes themselves function as nano-objects. The utilization of nanoscale technologies

has also expanded into research and development (R&D) in other domains.

The objectives of the chapter are given below.

1. Present an outline of modern biofuel production techniques, highlighting the importance of nanotechnology in expanding the effectiveness and sustainability of these methods.
2. Investigate different nanomaterials and their applications in biomass conversion, highlighting their catalytic attributes and potential to increase productivity.
3. Review the challenges and opportunities of integrating nanocatalysts into biofuel production, focusing on the circular economy and environmental sustainability.
4. Assess the potential of agricultural biomass and microalgal biomass as feedstocks for biofuels, as the role of nanotechnology in improving bioenergy production.

What does BIOMASS mean?

Biomass is an organic material obtained from organisms and used for the production of renewable energy. There is a need to produce energy sources with minimal negative effects on the environment. Biomass energy is the only one that does not have any limitations in terms of supply and accessibility. Biomass pertains to the organic matter obtained from living organisms or those that have just ended life, encompassing both plant and animal sources (Asadi, 2020; Jareteg, 2020). Organic materials possess the potential to serve as an energy source through their combustion or conversion into biofuels. Typical instances of biomass encompass wood, remnants of crops, agricultural waste, and specifically cultivated energy crops such as switchgrass and willow. Biomass emerges as a noteworthy renewable energy source that offers potential as an alternative to enhance energy self-sufficiency instead of fossil fuels and mitigate environmental degradation. Biomass exhibits potential as an alternative fuel source that can be utilized as a backup to meet the power grid demands during instances of production losses resulting from the intermittent nature of other renewable sources, which are reliant on weather conditions. Thermochemical conversion methods, including torrefaction, pyrolysis, hydrothermal liquefaction, gasification, and combustion, can be employed to utilize biomass for the generation of energy, biofuels, or chemical compounds. All of these methods are promoted as solutions that have worked very well in changing different types of biomasses into solid, liquid, and gaseous forms that can then be used to make energy, biofuels, and chemicals (Klaas, 2020; Torres, 2020; Zalazar-Garcia, 2022).

Role of Nanotechnology in Biomass Conversion

The latest advancements in nanomaterials technology have attracted significant attention due to their ability to convert various forms of biomass into useful products. The term 'Nano' has its origins in the Greek prefix that is commonly connected with the notion of 'dwarf,' denoting a factor of one billionth (Hulla et al., 2015; Nasrollahzadeh et al., 2019). Nanomaterials are widely employed in several industries such as medical, cosmetics, packaging, nanofiber manufacturing, biosensors, and electronics. The amazing magnetic, catalytic, mechanical, optical, and electrical properties of these entities have generated great interest, making them a prominent area of focus in ongoing research efforts (Thanh et al., 2014; Titus et al., 2019).

Types of Nanomaterials

Nanomaterials can be categorized according to several parameters. One distinguishing factor is the composition of the materials they are made of. Depending on the diversity of the materials, they can be broadly grouped into the following categories as shown in figure 1

Trends in Agricultural Biomass and Current Conversion

Agriculture biomass has been used as a source of energy since 1830 when it was first used to produce ethanol in Ethiopia utilizing the *Euphorbia abyssinica* plant (Smil, 1999). Globally, massive amounts of biomass are produced, with straw of wheat, rice, corn, and bagasse of sugarcane (Sarkar et al., 2012). Sarkar et al. (2012) gathered data on the worldwide disposal of various agricultural wastes and discovered the topmost waste to be straw of wheat. Asia produces the most wheat and rice straw. Throughout the last 3 decades, research in the United States has revealed the highest average potential of 3203 PJ per annum (Aleman-Nava, 2014).

Lignocellulose molecules, which are plentiful in agricultural biomass, are a critical component in biofuel generation. Table 2 shows the configuration of the main agricultural biomass in weight % of dry matter (Ali et al., 2019). According to reports, around 950 million tonnes of biomass are formed yearly in Europe and can be secondhand to make 0.3 billion tonnes of oil equivalent fuel (Stout, 2012).

Conversion of Agricultural Biomass into Various Energy Products

1. Production of Ethanol from Agricultural Biomass

Agricultural biomass contains hemicellulose and cellulose, which can be renewed into bioethanol (Patzek, 2005). Poland is a forerunner in terms of utilizing agricultural-based ethanol additives in petroleum. Approximately 2.5 million tonnes of biomass will be cast off to make bioethanol in Poland (Champagne, 2007; Acharya, 2019). Canada is a world leader in bio-ethanol production with the capacity to produce 5336 million liters of bio-ethanol from agricultural biomass each year (Kim, 2004). The increased use of agricultural biomass to make biofuel reflects a substantial shift in policy and environmental goals, which will result in a big revolution in the fuel market. Global ethanol output was predicted to be more than 30GL (Giga Liters) in 2001, but it climbed to more than 94GL in 2015. The biggest contributors to ethanol production are the United States and Brazil, which account for around 85% of global ethanol output (WFEP, 2017).

2. Fuel Pellets of Agricultural Biomass

Dry leaves, tree bark, and tree pruning from agricultural land are sometimes used to make fuel pellets. The usage of fuel pellets in industrial boilers has increased by 13% (Lehtikangas, 2017). According to studies, logging residue pellets have higher thermal power and can be applied

in ordinary boilers to create power (Swanston, 2005). Pradhan et al. (2018) manufactured comparable quality pellets from orchard biomass exclusive of the use of any binder. The combustion test confirmed the suitability of pellets for domestic cooking. A palletization prototype research was also carried out, which confirmed the feasibility of fuel pellets (Pradhan et al., 2018).

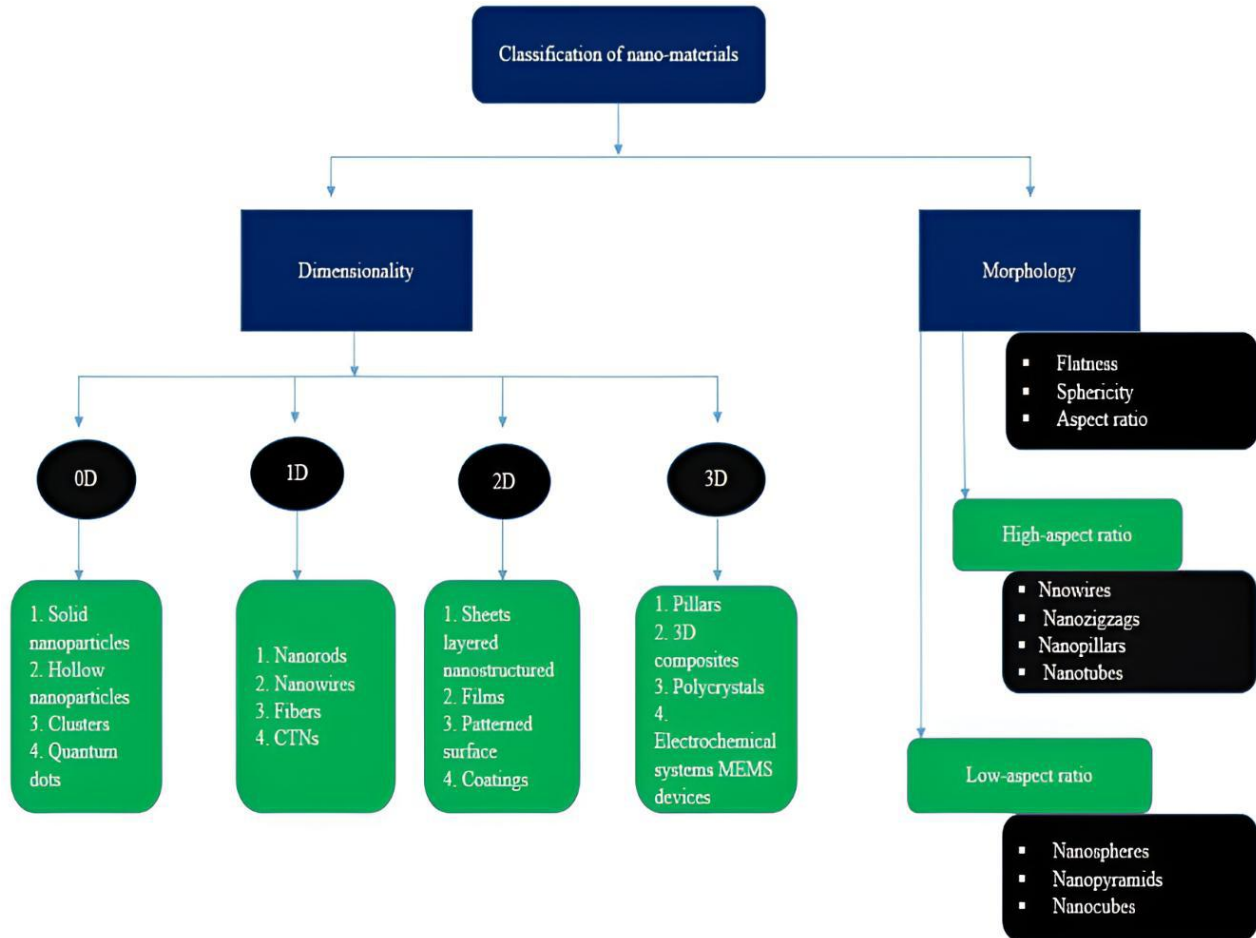


Fig. 1: Demonstrate the schematic classification of nano-materials

Table 1: Key agricultural wastes available globally (Sarkar et al., 2012)

Agricultural wastes	Quantity (million tons)
Rice's straw	731.3
Corn's stover	128.02
Sugarcane' sbagasse	180.73
Wheat straw	354.34

Table 2: Composition of major agriculture biomass

Crop waste types	Cellulose (%)	Hemicellulose (%)	(Lignin %)	Reference
Rice's straw	39.05	20.92	5.72	(Huang, 2010)
Rice's hull	33.48	21.04	18.81	(Mansaray, 1999)
Wheat's straw	43.3	34.2	22.01	(Alemdar, 2008)
Soya's hull	56.5	12.6	18.01	(Alemdar, 2008)
Corn's straw	42.7	21.4	8.3	(Sarkar et al., 2012).
Sugarcane's Bagasse	65.01	33.5	18.5	(Sarkar et al., 2012)
Sorghum's straw	32	24	13	(Saini, 2015)
Barley's straw	40	30	15	(Saini, 2015)
Coconut's husk	24.8	12.27	40.12	(Cabral, 2016)
Rapeseed's straw	32	16	18	(Thygesen, 2012)
Soybean's straw	35	17	21	(Martelli-Tosi, 2016)
Sunflower's straw	32	18	22	(Antonopoulou, 2015)
Peanut's shell	40.6	14.9	26.5	(Bharthare, 2014)

3. Biogas Production from Agricultural Biomass

Biogas is produced from agricultural biomass to meet the energy requirements for heating, cooking, and lighting, and thereafter, stored and transferred for residential utilization. An annual estimate indicates that gasoline consumption in Asia exceeds 3 Tg of methane (CH₄) (Einarsson, 2017). Approximately fifty percent of bio-methane facilities utilizing agricultural biomass are situated in Germany (Reijnders, 2008; McCormick, 2013). A potential application of straw is as a feedstock for biogas production, perhaps resulting in energy generation. Streets (2003) asserts that gasification methods might transform biomass in Poland into 1.5 billion m³ of biogas.

Agricultural Biomass Conversion through Nano-Materials

Animal fats and a variety of other raw materials, including soybean, mustard, and sunflower, have been utilized to make biodiesel, which is currently a more environment-friendly and energy-efficient alternative. Nevertheless, their high cost and low yield have rendered them unsuitable for commercial use. Better substitutes are sustainable resources, such as microalgae with the highest lipid content and rate of growth. Oil is transformed into fatty acid methyl esters (FAME) or biodiesel via the trans-esterification process in the presence of alcohol. This reaction is catalyzed by acid/base/heterogeneous substances or enzymes; the employment of enzymes makes the process more economical. By using NPs, this obstacle can be removed (Gebremariam and Marchetti, 2018; Khanna & Goyal, 2019; Verma and Rani, 2021). The cost of the raw materials plays the most influence in determining the cost of producing biodiesel, together with the facility's size and the value of the byproduct, glycerine. Depending on its source and what is easily accessible, waste, non-edible, and edible oil can all be categorized as feedstock. Producing biodiesel feedstocks from edible vegetable oils, such as soybean and palm oil, is dependable and financially advantageous. Lipases are produced by bacteria, fungi, plants, and animals. The primary issue with producing biodiesel by lipase catalysis is the high expense of the enzyme. Furthermore, there have been instances where immobilized lipases exhibit higher enzyme activity than free lipases. It is feasible to reduce the cost of enzyme use while increasing enzyme activity, stability, and reusability by employing nano-immobilized enzyme systems. During the biodiesel synthesis process, the immobilized lipases were disrupted by shear strain from the batch reaction stirring approach (Zhong et al., 2020).

With its β -1, 4 glycosidic links, cellulose is one of the most prevalent natural polymers in the world. Lignocellulose biomass is made up of 40–60% cellulose, 20–40% hemicellulose, and 10–25% lignin. Out of 181.5 billion tons, only 8.2 billion tons are used, and the remaining is lost as waste. The cellulosic content of lignocellulose can be used to produce bioenergy and it leads to waste degradation without harming the environment (Ashokkumar et al., 2022; Dahmen et al., 2019). Since biomass is a cheap substrate, cellulase, the biocatalytic enzyme, pays the greatest expense in this bioconversion process. The enzyme group known as cellulase is responsible for the production of oligosaccharide from random regions of cellulose by endoglucanase, cellobiose from the oligosaccharide by exoglucanase, and cellobiohydrolase, which converts cellobiose into glucose main products that serve as a precursor for biofuel (Rajnish et al., 2021).

A lignocellulosic biomass (LCB) biorefinery is a facility that uses dry, woody biomass or energy crops to produce bio-based fuels and biochemical products through biological or thermochemical processes (Singh et al., 2022). By enhancing efficiency, the use of nanotechnology in the biofuels production process can facilitate the process. Bioproduct production can be enhanced by using NPs as they improve biomass pretreatment and hydrolysis by chemical catalysts (Chandel et al., 2022). The name of this approach is the Nano Shear Hybrid Alkaline approach. Furthermore, NPs can be very important in the fermentation and enzymatic hydrolysis phases of the biofuel production process (Wang et al., 2013; Koo et al., 2017; Antunes et al., 2019).

Importance of Agricultural Biomass

1) Biofuels from Microalgal Biomass

Algal fuels are ecologically friendly since they help to reduce global carbon dioxide emissions. Plant-based biodiesel production involves the cultivation of oil-producing crops on cultivable land, and most governments limit biofuel feedstock supplies to avoid rivalry with food production on these lands. When compared to plants, algal biomass has a low percentage of lignin, which is one of the benefits that makes them good substrates for biofuels (Kavitha, 2023). Breaking down the tough cell wall that holds the soluble organics in place is the main problem with using algal biomass to make gasoline. Because different types of algae have different cell wall components, it is not possible to get a single pretreatment method that works for all of them. It is accurate to say that the production of biofuel from algal biomass has garnered considerable attention in recent years, the production process is complicated and challenging due to the unyielding and complex cell walls of algae. Algae biofuel production is still in its infancy despite advancements; this is primarily due to the energy and financial investment required for pretreatment (Kavitha, 2023). Further research should be devoted to the development of innovative, cost-effective biomass disintegration techniques.

2) Algal Biomass Conversion Through Nano-Materials

First, second, third, and fourth generations of biofuels are distinguished by their principal raw material sources. FAME is utilized in first-generation biofuels to transform vegetable oil, lipids, carbohydrates, and sugars into bio-alcohol (Vasanthan et al., 2021). A wide range of feedstocks, including cereals, vegetable oils, sugar cane, and animal fats, can be used to create first-generation biofuels. Concerns have been voiced regarding these feedstocks' feasibility, nevertheless. Second-generation biofuels, on the other hand, seek to address the problem of carbon concentration by making use of nonfood feedstocks, particularly lignocellulosic biomass. In the worldwide biofuel development, this idea is gaining popularity (Boscaro et al., 2022).

Second-generation biofuels offer advantages, including the repurposing of waste resources; nevertheless, they also present disadvantages, such as high production costs and technological obstacles. Due to their elevated lipid content, algae are integral to the third and fourth phases of biofuel synthesis. Unlike third-generation biofuels that concentrate on algal production, fourth-generation biofuels utilize metabolic algae to generate carbon reservoirs (Khemthong et al., 2021).

The Department of Energy states that if algae were to entirely supplant petroleum as the fuel source for the United States, an area marginally larger than Maryland—approximately 17,000 square miles—would be necessary (Kushkevych et al., 2019). Zaidi et al. (2018), study on the use of metals (Ni and Co) and metal oxide (Fe_3O_4 and MgO) NPs with green microalgae *Enteromorpha* to increase biogas generation. Geng et al. (2020) performed the BMP Test (biochemical methane potential test) and studied the incorporation of zerovalent iron (ZVI) in the anaerobic digestion of *Microcystis* sp. Sludge can boost methane production.

3) Trends in Forest Biomass Conversion

Current literature features continuous discussions over the significance of forest biomass in biomass utilization for energy generation (Plank et al., 2023; Raihan, 2023d). Raihan (2023e) and Siarudin et al. (2023) delineate two principal classifications of forest biomass: firewood and commercial roundwood. Direct combustion and conversion into bioenergy and biofuels are feasible methods for utilizing fuelwood obtained from forested regions (Manikandan et al., 2023; Raihan, 2023f). Thermochemical transformation, biological conversion, liquefaction, and gasification are conversion processes that can substantially benefit from utilizing fuelwood as a feedstock. According to Manikandan et al. (2023) and Raihan (2023g), this potential is derived from the increased concentrations of macromolecular carbohydrates, specifically cellulose and organic matter. Kalak (2023) suggests two possible approaches for investigating the utilization of forest biomass: first, as a co-combustion agent with fossil fuels; and second, as a standalone fuel source for power production devices, including boilers.

Limitations and Future Trends

Limitations and Challenges in Biofuel Cell Advancements

Despite the significant advancements made by several categories of nano-materials in the field of Biofuel Cells (BFCs), there remain numerous unresolved matters that need to be addressed to attain optimal performance in biochemical conversions. The current era is characterized by several significant problems, which include the attainment of optimal efficiency, effective cost management, the establishment of perfect operational circumstances, and the assurance of long-term technological durability. Presently focuses on the advancement of graphene-based bioanodes and biocathodes as alternative, highly efficient options for many applications. The formation of naturally existing macromolecular materials with porous characteristics. The successful incorporation of Carbon Nanotubes (CNTs) within the metallic structure. The investigation of inorganic biomass fuels. The bioelectrodes that have been recently developed, possess the capability to transform these possibilities into actuality in the coming times (Tawalbeh et al., 2022).

I. Economic Constraints in Biomass Conversion and Algal Biodiesel Production

The financial costs associated with pre-treatment methods of lingo-cellulosic biomass are substantial. It is believed that there exists an alternate method for converting fossil fuels into biodiesel throughout the production process. However, it should be noted that the cultivation of algal biomass for agricultural purposes experiences significant costs, while the extraction of lipids from these algae requires substantial allocation of resources (Assad et al., 2022).

II. The Role of Genetically Modified Microalgae and NPs in Future Bioeconomy

In future studies, it may be beneficial to explore the potential of utilizing genetically modified microalgae strains in conjunction with designed NPs in order to get enhanced and noteworthy outcomes. Therefore, NPs and microalgae possess the ability to serve as elementary components in the development of the bioeconomy characterized by renewable and sustainable opportunities (Dey et al., 2023).

III. Unexplored Avenues in Hydrogen Production Using Nano-Materials

The investigation of an integrated approach for biological hydrogen production with nano-materials remains an unexplored field of study. Regarding the creation of H_2 using nano electrocatalytic and nano photocatalytic processes, the advancement of two-dimensional nano-materials that possess hybrid structures and multifunctional capabilities presents a promising avenue for augmenting their potential in H_2 production by water splitting. The investigation of their production on a wide scale under controlled circumstances is also worthy of examination. There is a need to conduct a computational study on H_2 storage that takes into consideration practical and rigorous situations, as well as handles practical uncertainties. Moreover, there is a notable absence of comprehensive economic analysis on the various methods of H_2 storage in existing scholarly literature (Epelle et al., 2022).

IV. Advancing Biomass-Derived Carbon Electrochemical Sensors

There is a strong recommendation for more studies to look at the ability of biomass-derived nano-materials, particularly in terms of enhancing their inherent properties, hence leading to improved electrochemical performance. Consequently, it is conceivable that the advancement of research in this particular field could facilitate the development of portable electrochemical sensors capable of detecting harmful contaminants. Carbon-based electrochemical sensors made from biomass have gained significant popularity in recent years. However, they have not yet achieved the level of flexibility and portability required for use as detectors. The utilization of advanced technology such as 3D printing has the potential to facilitate the creation of rapid, cost-effective, and highly responsive sensing devices. Furthermore, there is potential for further development of this technology to produce intelligent functionalized devices that will establish the standard. The prevailing standard within this particular industry (Malode et al., 2023).

Conclusion

The transition to sustainable energy alternatives is crucial for addressing the environmental and economic challenges linked to fossil fuels. The conversion of biomass, improved through advancements in nanotechnology, offers a promising pathway to energy sustainability.

Nanocatalysts have transformed the biofuel industry through their remarkable efficiency and eco-friendly properties, enabling enhanced conversion rates, reduced energy consumption, and minimal environmental impact. This article highlights the potential of agricultural, algal, and forest biomass as abundant renewable resources for biofuel production and underscores the importance of nanotechnology in improving their utilization.

Despite significant advancements, challenges such as the high costs associated with nanocatalyst production and issues related to scalability continue to exist. Addressing these challenges requires continuous interdisciplinary research and innovation, as well as policies that support the circular economy. Facilitating collaborations among academia, industry, and government can transform biomass conversion through nanotechnology into a core element of sustainable energy systems

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Nanotechnology in Tissue Engineering and Regenerative Medicine

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Abstract

Nanotechnology has shown incomparable advancements in case of tissue engineering and regenerative medicine and are now considered as advanced techniques instead of other conventional techniques which are used to treat diseases related to human health. With the prominent advantages of utilizing nanotechnology-based techniques such as nanocarriers, gene therapy and stem cell therapy, scientists have utilized these techniques noticeably. With the advancements in the production of nanoscale, scientists and researchers are now being able to use these in the existing and new innovative techniques. However, this chapter briefly reviews a basic overview related to the various nanotechnological techniques which are being analyzed and utilized in the tissue engineering and regenerative medicines, along with some of the challenges and future aspects associated with these strategies which further confirms that tissue engineering and regenerative medicine would be accepted by the patients to a great extent in near future in the place of other conventional approaches available.

Keywords: Nanotechnology, Nanoparticles, Tissue engineering, Regenerative medicine, Stem cell therapy

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Introduction

Nanotechnology is a discipline of science and engineering which further combines chemistry, physics, colloidal science, biology, and other scientific fields and used to manipulates atoms and molecules at the nanoscale, these can be nanomaterials, nanoparticles and others. According to the facts, the simplest terminology used for nanotechnology is “Technology on the nanoscale”. The term nanoscale is used to focus on the objects with the dimensions on the order of 1-100 nanometers (Satyannarayana, 2022). There are various areas where this nanotechnology is applicable. Some of the major areas of applications are shown in Figure 1.

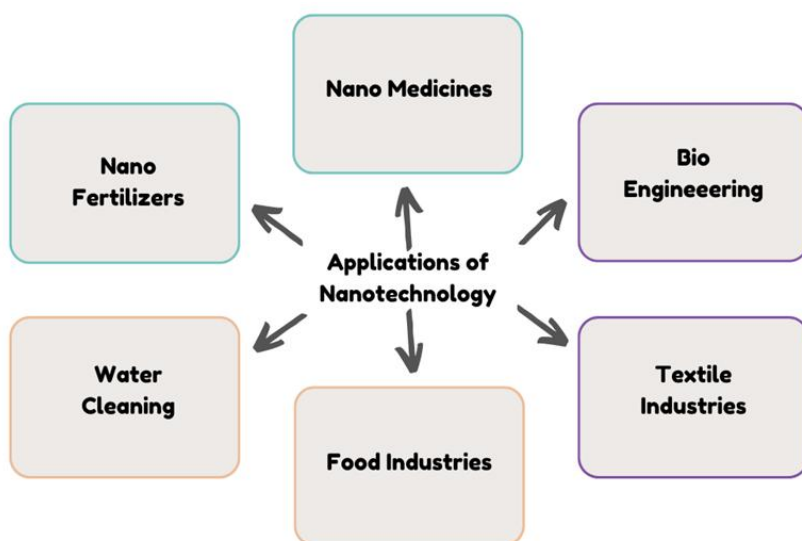


Fig. 1: Utilization of nanotechnology in various fields (Designed by Word)

There are different classifications of nanoparticles (NPs) depending on their size, morphology and chemical properties i.e. carbon based, metal based, ceramics based, polymeric based and lipid based and all these have many applications. There are mainly two methods which are used to prepare nanoparticles i.e. bottom up approach and top down approach (Khan et al., 2019). However, the recent advancements in the

field of nanotechnology have extended many possibilities related to its applications in medicine which includes the enhancement of early diagnosis and its therapy (Malik et al., 2023).

Furthermore, the most recent advances in the field of nanotechnology related to bioengineering are to initiate nano-antimicrobials for the reduction or the prevention of infections along with new nanostructured drug delivery systems and their interaction with cells, tissues, and living systems (Zong et al., 2022).

Nanotechnology in Regenerative Medicine and Tissue Engineering

Nanotechnology has provided a new opportunity for the development of medicines and its constant development has made possible early diagnosis and the precise treatment. However, due to these properties, nanomaterials have been extensively examined and utilized in the medical field. Thus, nanotechnology has now become a powerful tool in regenerative medicine and tissue engineering (Guo et al., 2018).

Regenerative medicine may be defined as a field that aims to develop methods to regenerate or replace injured cells, tissues, or organs to restore their normal functions. It a powerful approach in tissue regeneration which creates nanoscale quality of tissues for cellular adhesion, migration and differentiation. The nanomaterials used in nanotechnology have their unique physical, and chemical properties including optical, magnetic and electrical properties and on the basis of their size and functions, nanomaterials can be used for various techniques such as biomolecule delivery, tissue engineering, in vivo cell tracking and stem cell therapy (Yang et al., 2019).

On the other hand, tissue engineering includes combining of cells, scaffolds, and other growth factors to make functional tissues outside the body. Tissue engineering research is a necessary first step in regenerative medicine therapies (Sharma et al., 2019). However, tissue engineering regenerative medicine (TERM) is a multidisciplinary field that combines bioengineering and medicine to develop alternative therapies to repair tissues and organs as shown in the table 1 (Saini et al., 2021).

Table 1: Characteristics of tissue engineering and regenerative medicine

Characteristics	References
Goals	To create new functional organs by creating new cells or tissues to restore body functions. (Saini et al., 2021)
Techniques	Tissue engineering, gene therapy, cell base transplantation, 3D bioprinting and much more. (Xie et al., 2020)
Materials	Cells, biomaterials, scaffolds. (Babbar et al., 2020)
Benefits	Solves the issue of organ shortage and also provides efficient therapies for many clinical disorders. (Parihar et al., 2022)

Nanomaterials for Regenerative Medicines

Nanodevices

Nanodevices are nanotechnological elements and is a powerful strategy for regenerative medicine which allows the recreation of nanoscale tissue features that can be used for many cellular processes. Some of the examples of nanodevices which are used in regenerative medicines are nanoparticles, biosensors, nanofibers, biodegradable nanocarriers (Yang et al., 2019). Advancements in the technology of microfabrication also creates invention in nanodevices. Some of the nanodevices used in regenerative medicines are biocapsules, biosensors, laboratory on a chip and others.

Biocapsules are the form of nanodevices which can be used for the storage and transportation of molecules which are collected in a controlled way. Bioencapsulation is a process which involves the enclosing of tissues or other biological active substances in semi-permeable membranes. This process has been shown to be effective in copying the natural environment of the cell which further improves the efficiency of many metabolites and different therapeutic agents (Aylanc et al., 2023).

Bioreactors can be used to create a suitable environment such as temperature, pH, pressure for cells and tissues to grow fast in vitro methods. Thus different bioreactors which plays important role in regenerative medicine are cell culture, *in-vitro* organ modeling, stem cell therapy and tissue engineering (Ko et al., 2018).

Biosensors are devices which combine biological and electrical components to detect and measure different abnormalities, toxins, to diagnose or predict diseases related to immune system, to monitor the status of tissue culture, to check protein interactions and to evaluate the effects of drug concentration and can even measure harmful chemicals and pH values. They actually change the biological responses into the electrical signals which may be further measured to check abnormalities and interactions. The biological elements, such as enzymes, antibodies or nucleic acids, interact with the samples or specimens which are being tested. They have high specificity and sensitivity thus can analyze samples rapidly (Alma et al., 2022). On the other hand, nanosensors are the sensor which are able to detect different reactions including biological, chemical or electrical reactions in various local environments. Some of the examples of nanosensors used are quantum dots, fluorescent nanoparticles, metallic nanoparticles and molecule release sensor (Solaimuthu et al., 2020; Rong et al., 2019).

However, there is an industrial technique, known as biomanufacturing which can be used to produce biological materials including human tissues by manipulating different biological techniques. One of the examples is DNA biosensing. The figure 2 elaborates DNA biosensing with the application of 3D printing technology on it. The different type of facilities related to biomanufacturing can also be used to modify cells to manufacture different chemical or molecular products. Biomanufacturing can also be used in different types of industries, including healthcare, food production, and agriculture. However, it is important to control the quality and conditions of the biological structures to produce good quality products, and biosensing technologies can help to control these (Alma et al., 2022).

Nanoparticles (NPs)

The nanoparticles which are used for regenerative medicines mainly focus on delivery systems for genetic material, biomolecules and for reinforcing the bioactivity of three dimensional (3D) scaffolds in tissue engineering. The NPs used in delivery systems includes microspheres, microcapsules, liposomes, micelles and dendrimers as shown in table 2. There are different types of magnetic nanomaterials such as iron oxide

NPs which are considered as the most important for the research of stem cell. Iron oxide NPs are emerging tools for Magnetic Resonance Imaging abbreviated as MRI (Dadfar et al., 2019).

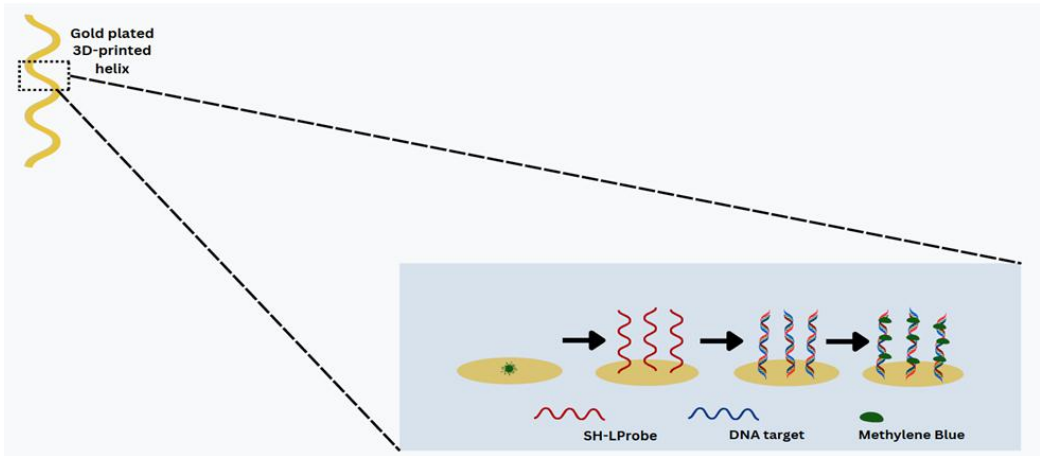


Fig. 2: DNA biosensing by the application of 3D printing technology (Designed by Adobe Photoshop)

Table 2: Types of nanoparticles used in delivery system

Types	Description	References
Microspheres	These are spherical particles made up of biodegradable polymers or proteins which can encapsulate the drugs and release them in a measured way.	(Yusuf et al., 2023)
Microcapsules	These are the carrier systems for pharmaceuticals which can be customized to adhere to the targeted tissue.	(Ladeira et al., 2022)
Liposomes	These are the compact lipid nanostructures which can entrap both hydrophobic and hydrophilic drugs and used to treat diseases like ovarian cancer etc.	(Cheng et al., 2020)
Micelles	These are type of nanocarriers which are formed by the spontaneous arrangement of amphiphilic di-block co-polymers in aqueous solutions.	(Bhardwaj & Jangde, 2023)
Dendrimers	These are the organic nanocarriers which are mostly considered in designing target specific drug delivery systems.	(Ajith et al., 2023)

Nanocarriers

Nanocarriers are used in regenerative medicine to deliver drugs, genetic material, and growth factors, and to monitor cells. They can be used for many purposes in regenerative medicine, for example as drug delivery, cell monitoring, mechanical stimulation, imaging and to overcome multi-drug resistance. They can be generated from a variety of materials, such as ceramics, metals, and polymers, hydrogels, dendrimers, liposomes (Su & P, 2020).

The delivery of biomolecules in a controlled manner is the main thing to consider in the support and enhancement of tissue growths during regeneration processes. Bone regeneration and osteoblast adhesion are found to be enhanced with hydroxyapatite nanoparticles. The multi-functional property of nanocarriers make them ideal for treating MDR cancer. The nanocarriers basically reduces the effects of ABC transporter mediated drug efflux, which is the main mechanism of MDR and further they overcomes the drug resistance as a conclusion (Gao et al., 2024).

Nanotechnology Based Stem Cell Therapy

Nanotechnology and stem cell therapy are two disciplines which show prominent areas of research during the treatment and contributes towards the improvement in human health. The stem cell therapy is also known as regenerative medicine and is a treatment which is done with stem cells. This therapy as shown promising results while treating number of diseases such as cancer, cardiac disorders, diabetes and neurodegenerative diseases. Although, it is very interesting and useful as it integrates two disciplines i.e. nanotechnology and stem cell which further contributes towards human health. The nanotechnology based strategies in the research related to stem cell have now been established by using various techniques and different mechanisms (Ponpandian et al., 2023). This figure 3 shows the process of stem cell briefly as stem cell is isolated from donor (human), then the propagation of stem cells are done by culture methods in laboratories and then nanoparticles associated stem cells are prepared by the combination of nanoparticles with stem cells and then these new stem cells are applied to treat various diseases including cardiac, neurodegenerative diseases, cancer and others. Additionally, there are different factors which involves during the production of nanomaterials based stem cells (Dong et al., 2021).

However, when the conventional therapy does not work then cell based therapies can be an excellent alternative to treat a number of diseases and different types of infections in humans. For this purpose, it is important to understand different processes such as cell cycle and cell differentiation, which will further help to design cell-based therapies in proper way and imaging techniques to check cell imaging. Some of the imaging methods which are used for cell imaging involves MRI, fluorescent imaging, and radioactive cell imaging (Dong et al., 2021).

According to the recent studies, the utilization of nanotechnology in stem cell research has showed better advancements, which are important for this interdisciplinary field. Some of the applications of stem cell nanotechnology includes isolation and identification of stem

cells, lineage and differentiation of stem cell, imaging and tracking of stem cells, gene and macromolecule delivery system of stem cells which further involves the stem cell based therapies for neurodegenerative diseases, cardiac diseases and cancer (Ponpandian et al., 2023). This figure 4 shows the important applications of nanotechnology in stem cell therapy.

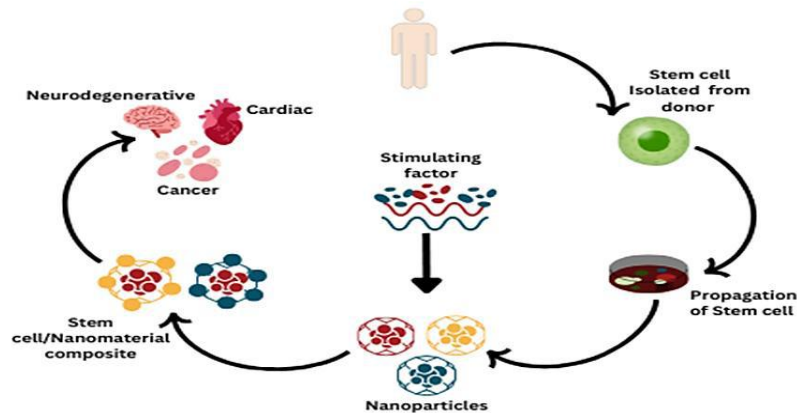


Fig. 3: The process of stem cell therapy (Designed by Adobe Photoshop)

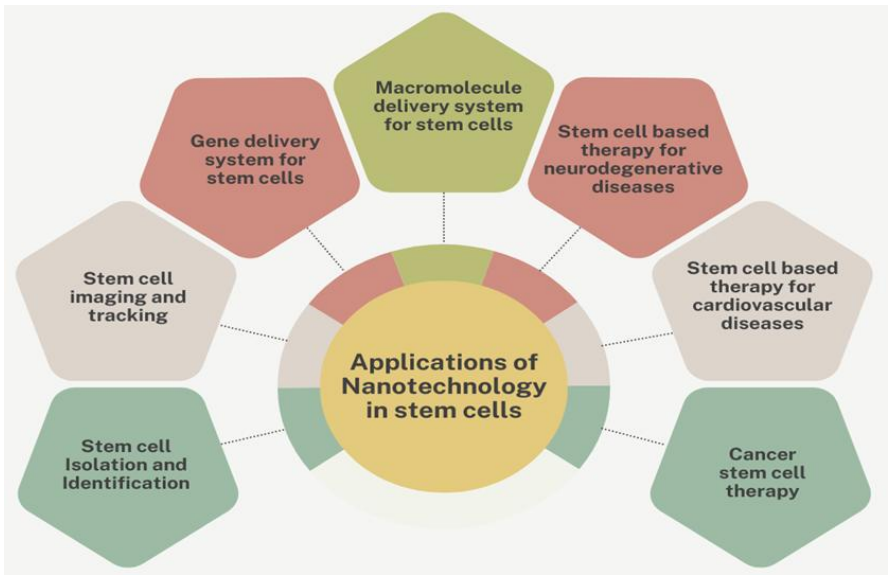


Fig. 4: Utilization of nanotechnology in stem cell therapy (Designed By Word)

Why Carbon Nanoparticles are Suitable for Tissue Engineering

The properties of nanostructures depend on the nanomaterials used. Carbon nanomaterials are mostly used in tissue engineering research along with drug delivery process because as compared to some traditional strategies because the carbon nanomaterials have the capability of large surface areas, have excellent mechanical, electrical and thermal features, strong enough and are suitable to use in drug delivery and tissue engineering after modifications. Additionally, some of the properties of carbon nanoparticles such as their high drug and tissue loading property, their good biocompatibility and long duration of action, make them good and suitable to use in tissue engineering. However, cells which attach directly onto carbon nanotube containing structures which further produces good cell growth (Zheng et al., 2022).

Types of Carbon Nanotubes used in Tissue Engineering

Some of the types and properties of carbon nanotubes are shown in table 3, as they as suitable and considered best for tissue engineering.

Table 3: Types of carbon nanotubes used in tissue engineering

	Single-walled carbon nanotubes	Multi-walled carbon nanotubes	References
Diameter	Their diameter is between 0.5 to 2.5 nm	Their diameter is between 7 and 100 nm	(Omrani et al., 2019)
Aspect ratio	Their aspect ratio is typically greater and goes up to 10,000.	Their aspect ratio is between 50 and 4,000	(Aminul Islam et al., 2024)
Description	These types of nanotubes consist of a single layer of graphene rolled into a hollow cylinder	These types of nanotubes consist of multiple layers of graphene sheets rolled up into a tube shape	(Anzar et al., 2020)
Applications	- Cancer treatment - Bio-imaging - Drug delivery	- Bone regeneration - Drug delivery - Drug delivery	(Krishnaveni et al., 2022)

Carbon Nanotubes in Bone Tissue Engineering

Carbon nanotubes are considered more suitable biomaterial for bone tissue engineering because of some unique features such as mechanical strength, electrical conductivity, and chemical stability. Their electrical conductivity can be controlled by changing their length or diameter accordingly, which can make them as electron cell biosensor. According to their characteristics, they support bone tissue regeneration in many ways and can be used to deliver drugs and biomolecules and can also be used to bind with other molecules including antibodies and radioisotopes. They can also be used to regulate the morphology of the cell (Chen & Li, 2022).

Carbon Nanotubes for Neural Tissue Engineering

As previously discussed, that carbon nanotubes are considered suitable bone tissue engineering, they are also suitable for neural tissue engineering as they have some unique properties and has potential to promote neural development. As they have excellent electrical conductivity, good strength, which makes them good for neural development, as they interact with neurons and thus promotes neural development which is important in the engineering of neural tissues. However, the aim of this technique is to develop future strategies to repair tissues which further promotes the functional recovery after any kind of damage related to the brain (Redondo-Gómez et al., 2020).

Carbon Nanotubes in Cardiac Tissue Engineering

The unique electrical conducting feature of carbon nanotubes makes them suitable choice to use in cardiac tissue engineering. Their integration along with polymeric scaffold is an ideal approach in cardiac regeneration as their conductivity has an improving effect on cardiac tissues. The research has made success with the production of scaffolds with nanoscale features which aims to regenerate the cardiac tissues to restore cardiac functions. Additionally, regenerating cardiac tissues would be able to improve the chances of recovery of cardiac disorders such as heart failure and other cardiovascular diseases. Overall, they have shown their great prospects to develop new platforms for the repairing of cardiac tissues which further enhanced the function of cardiac tissues (Barrejón et al., 2021).

Current Challenges Associated with Regenerative Medicine

The most challenging aspects of regenerative medicine when they are used to treat diseases are their efficiency and safety issues. For example, during the stem cell therapy, there are many challenges which are faced such as which cell type would be the best choice and which approach would be the suitable one. Additionally, the major challenge in the therapeutic applications of stem cell therapy is the production of a fast, easily operated and low cost techniques to purify the expected cells from the available cell mixture and also to reduce the cell variability in the culture. However, there are also many technical issues which slow down the applications even there are many recent advancements done in this field (Altyar et al., 2023).

Moreover, the use of nanoparticles in diagnostic and therapeutic procedures are somehow restricted due to their safety concerns. On the other hand, the continuous development of gene delivery systems also represents an emerging challenge for regenerative medicine. However, the complications in the wide range of applications are due to lack of knowledge to understand the mechanism of actions between the nanoparticles and the stem cells (Xuan et al., 2023).

Challenges Associated with Tissue Engineering

The major problem of tissue engineering is the neovascularization which is necessary to supply oxygen and nutrients to a cell. It is not possible to expect the neovascularization for a cell scaffold construct in case of *in-vitro* tissue engineering (Brady et al., 2023). Additionally, the four primary issues in tissue engineering involves biomaterials, cell sources, vascularization, and design of drug delivery systems as biomaterials and cell sources should be specific for the engineering of every tissue (Chandra et al., 2020).

Future of Regenerative Medicine and Tissue Engineering

Several research teams have started working to create new treatments techniques to overcome the current strategies due to the limitations of methods currently available for regenerating many vital organs. Consequently, this will allow for significant advancements in regenerative medicines in the near future. Many of the novel regenerative medicine concepts have begun to provide encouraging benefits and outcomes (Altyar et al., 2023). The coming decade is expected to see more advancements which would be considered successful. It is expected that tissue engineering would become recognized medical specialty along with more acceptance of this technique for various treatments among patients instead of other conventional therapy in future (Chandra et al., 2020).

Conclusion

Nanotechnology plays an important role in regenerative medicine as well as in tissue engineering as it creates new functional organs to restore the normal functions of the body. Stem cell therapy is the prominent therapy which is used to treat various diseases including cardiac, neurodegenerative disease and even cancer. Additionally, carbon nanoparticles including single-walled and multi-walled carbon nanotubes are considered good for tissue engineering because of some of the properties of carbon nanoparticles which make them suitable to use in various strategies including bone, cardiac, and neural tissue engineering. Moreover, there are also many challenges associated with tissue engineering and regenerative medicine that's why the use of nanoparticles in diagnostics and therapeutics are somehow restricted in many cases due to their safety issues and due to the lack of knowledge related to the mechanism of actions, creating many complications but many researchers have started working to overcome the current challenges which are associated with the limitations of methods currently available for regenerating many vital organs for significant advancements in regenerative medicines in the near future. Overall, it is expected that tissue engineering regenerative medicine would be accepted more among patients for various treatments in future instead of other conventional therapies.

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Innovative Approaches: Nanotechnology and Nanomedicine in the Fight against Hydatid Disease

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Abstract

Hydatidiosis is a zoonotic helminthic parasitic disease that is caused by *Echinococcus granulosus* that affects different hosts, and it is life-threatening. It is disturbed throughout the world, mainly in rural regions. For decades, millions of individuals have been aware that hydatid cysts are a prevalent medical condition. Individuals who have this illness may not exhibit any symptoms for years and only show up when their hydatid cysts, which are liver cysts, burst. The potential for nanotechnology to improve chemotherapy against hydatid cysts could pave the way for a revolution in medical care. This book chapter outlines how nanotechnology affects chemotherapeutics against hydatid disease. Delivering therapeutic drugs more precisely and effectively, targeting hydatid cysts more effectively, and reducing interaction with surrounding tissue are all made possible by nanotechnology. Nanotherapeutics do, however, present issues with resistance, toxicity, and biodistribution. In conclusion, there are a lot of challenges associated with using nanotechnology for treating hydatid cysts, despite the possibility of success. Additionally, nanobiosensors are used in diagnostic methods to aid in earlier and more precise patient diagnosis.

Keywords: Hydatidiosis, Echinococcosis, Nanotechnology, Nanomedicine, Treatment

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Introduction

Hydatid disease, or unilocular cystic echinococcosis disease, is a zoonotic helminthic disease caused by the metacestod stage (hydatid cyst) of *Echinococcus granulosus*, presents significant health challenges globally, particularly in endemic regions (Moro & Schantz, 2009), and is mostly responsible for the increasing prevalence of echinococcosis worldwide (Budke *et al.*, 2006). The classical treatment of hydatid cysts till now depends on the surgical removal of the cyst and the use of drugs such as albendazole, but the use of drugs has side effects and drug resistance (Lupia *et al.*, 2021, Karshima *et al.*, 2022). *Echinococcus granulosus* forms cysts with a vibrable size, ranging from a pinhead to football size, and depressing the body organs and tissues (Alvi & Alsayeqh, 2022). If left without treatment, it will lead to fatal problems in humans and animals (Casulli *et al.*, 2022). This parasite has a complex indirect life cycle and includes the carnivores as the final host and the herbivores, including humans, as the intermediate host. The intermediate hosts are infected by the ingestion of eggs of this parasite that pass with feces of the carnivores such as dogs and foxes (Zhang *et al.*, 2003; Zhang *et al.*, 2012). Several broad-spectrum antibacterial activities have been used for the treatment of this parasite as an antiparasitic agent, including azithromycin, azithromycin with paromomycin, rifaximin, nitazoxanide, and albendazole (Rossignol *et al.*, 2006, Checkley *et al.*, 2015). It works well for minor infections but is ineffective against moderate and severe illnesses (Diptyanusa & Sari, 2021).

The classical anthelmintic treatment of echinococcosis is albendazole and mebendazole, which inhibit the growth and proliferation of hydatid cysts (Adetunji *et al.*, 2021, Chai *et al.*, 2021). The using of these two anthelmintics has several side effects such as gastritis, and enteritis (Wang *et al.*, 2020, Erfani *et al.*, 2023). The treatment of echinococcosis is extended for months and up to years, therefore the prolonged using of these anthelmintics, resulted in the emergence of resistance (Taghipour *et al.*, 2021, Alvi *et al.*, 2023). Many problems still exist even if conventional chemotherapy is an effective treatment for hydatidosis (Wen *et al.*, 2019). Working with large cysts or those located in complex anatomical areas may require altering the procedure (Kern *et al.*, 2017). Many medications struggle to reach the parasite cores because of the challenges of breaking through cyst walls. Taking the patients' existing medical problems into account as well as any factors that might.

Early detection of hydatid cysts is essential for efficient treatment (Habibi *et al.*, 2023). Unfortunately, because of its deceptive character and current diagnostic limitations, it is still challenging to detect this illness swiftly and reliably. However, because hydatid cysts can frequently be mistaken for other cystic lesions, imaging methods like ultrasound are helpful for offering first insights but are sometimes misconstrued (Dietrich *et al.*, 2020). Magnetic resonance imaging and computerized tomography scans can provide high-resolution imaging, but they are costly and ineffective at differentiating between different types of cysts (Caraiani *et al.*, 2020; Calame *et al.*, 2022).

There are serological methods for screening for particular antibodies against *E. granulosus* antigens, such as Western blotting and ELISA, but these are also limited (Meftahi *et al.*, 2021, Alvi *et al.*, 2023). A Western blot continues to be more accurate than ELISA. Nevertheless, the

probability of a false positive gets higher due to requiring specific resources and experience. It may be more challenging to figure out hydatid cysts because of their similarity to other cystic tumors (Alshoabi et al., 2023). Additionally, the current screening method typically finds cysts after they have significantly expanded, delaying early management that could improve results (Chouhan et al., 2019). In many cases, a definite diagnosis requires aspiration and biopsy (Khalili et al., 2023). However, there are risks associated with these treatments, including the potential for rupture and the development of cysts. When it comes to inert cysts or cysts that have calcified over time, serological testing is frequently ineffective (Paramita & Wibawa, 2023). The absence of advanced imaging and diagnostic technology in low-tech settings makes cancer identification more challenging (Borhani et al., 2021). More studies on hydatid cysts are needed, as are more precise and easily available diagnostic techniques.

Recent decades have seen the fusion of technological advancements and research innovations to give rise to a new field of study called nanotechnology, where system components are measured in billionths of meters and engineered and designed at the nanoscale, requiring extremely precise measurements (Sadr et al., 2023). This field is able to cross traditional boundaries, giving scientists basic control over matter (Sahu et al., 2021). The development of nanotechnology has great promise for the next several decades to transform medicine by providing a plethora of new opportunities that may fundamentally alter therapeutic approaches (Prasad et al., 2021, Sindhvani & Chan, 2021).

1.2. Nanoparticles

Dealing with materials that are nanometers in size (ranged between 1-100 nanometers) (Cho et al., 2013, Hasan, 2015, Mishra, 2016), for medical applications, nanomedicine is regarded as a relatively emerging area of science and technology. Drug delivery, imaging, diagnosis, medical devices, vaccinations, and antimicrobial therapy are only a few of the medicinal and diagnostic uses of nanomedicine that are currently available in contemporary medicine (Machado et al., 2015, Zhu et al., 2014). In light of the use of nanomedicine to treat microbial diseases, numerous studies have documented the antimicrobial properties of both organic and inorganic nanoparticles, including chitosan, synthetic cationic polymers, cationic peptides, and metal and metal oxide (Sengul & Asmatulu, 2020).

Inorganic nanoparticles are metal-based and metal oxide-based nanoparticles are two more subcategories for them. The preparation of metal-based nanoparticles involves either constructive or destructive methods of turning the metals into nanoparticles. It is possible to produce nanoparticles from any kind of metal (Salavati-Niasari et al., 2008). Aluminum, cadmium, cobalt, copper, gold, lead, silver, and zinc are frequently used to create nanoparticles. Surface area-to-volume ratio, pore size, surface charge density, and high surface charge are some of the unique properties of these nanoparticles (Geetha et al., 2016). By altering the matching metal-based nanoparticles, metal oxide nanoparticles are created. Iron (Fe) nanoparticles oxidize to iron oxide at room temperature when oxygen is present. When their efficiency and reactivity rise, metal oxide nanoparticles are created (Tai et al., 2007). Zinc oxide, silicon dioxide, titanium oxide, iron oxide, magnetite, aluminum oxide, and cerium oxide. These tiny particles differ from the equivalent metals in a few special ways (Samy et al., 2022).

Organic nanoparticles are made of polymers such as liposomes, dendrimers, ferritin, and micelles. Drugs can be transported by these specific nanoparticles since they are non-toxic, and stable. Heat, light, and radiation sensitivity are associated with the hollow centers of liposomes and micelles, also known as nano-capsules (Tiwari et al., 2008, Gehrke et al., 2015). They are an effective drug delivery way because of these qualities. Because of their effectiveness, these kinds of nanoparticles are frequently employed in the field of medicine. Targeted drug delivery methods send nanoparticles to particular body parts. The material's composition, shape, size, flexibility, and surface quality all affect the attributes of nanoparticles (Muthu et al., 2009). Lipids and a wide variety of synthetic polymers made up of different substances make up nanoparticle composition. The most synthesized used polymers in the production of nanoparticles are dextran's, a polyanhydrides, and poly lactic-co-glycolic acid, and the nature polymer like elastin-like polypeptides. The production process, toxicity, and compatibility with loaded pharmaceuticals all influence the utilization of these nanoparticles (Macewan & Chilkoti, 2012). Shape and structure have an impact on nanoparticle efficiency as well. Spherical nanoparticles are less effective than rod-shaped nanoparticles at reaching specific tissues (Cao et al., 2019).

1.2.1. Application of Nanoparticles as a Treatment for Hydatid Disease

Much research has investigated the potential role of nanoparticles in treating cystic echinococcosis to inhibit the infective stage of *E. granulosus* (Norouzi et al., 2020). There are several nanoparticles are used as anti-cystic echinococcosis such as zinc oxide, copper, and silver (Shnawa, 2018).

The use of nanoparticles has many potential applications including targeted delivery of therapeutic agents which can improve the effectiveness of therapies against cystic echinococcosis. They are very tiny which helps them cross blood-brain barriers, and carry drugs specifically to infected organs and tissues, minimizing side effects. Such targeted therapy significantly enhances the efficacy of the treatment; it also reinforces the potential of these nanoparticles in the battle against this disease (Arshad et al., 2021, Malik et al., 2023). Research remains focused on innovative designs for nanoparticles aimed at enhancing drug release (Zhou et al., 2023, Wang et al., 2022). However, as this occurs, rules and regulations are evolving to safeguard patients while still permitting new ideas and inventions. These advancements could lead to improved treatment options for cystic echinococcosis and various infectious diseases. Although continued collaboration among researchers, clinicians and regulatory bodies is essential, achieving optimal therapeutic outcomes will require concerted effort (Casulli et al., 2022). It is essential to invest in nanoparticle research to bring out their characteristics. It is proposed that prospective studies must scrutinize both the long-term influences and specific duties in different patient groups in distinct healthcare sections.

Nanomedicine enhances the therapeutic efficacy by reducing side effects. Additionally, modifications can enhance drug delivery and retention within the cysts. Effective targeting is crucial for improving treatment outcomes and reducing the likelihood of drug resistance (Huang et al., 2022). Furthermore, tailored surface properties can facilitate better cellular uptake and release kinetics. These advancements promise to significantly improve the management of hydatid cyst infections and enhance overall patients' safety (Donahue et al., 2019).

To distribute praziquantel through nano-based delivery systems, the medication is encapsulated in a variety of nanomaterials, including

copper, zinc, silver, gold, and zinc oxide, all of which are made of a combination of metals (Król et al., 2023, Boudier & Le Faou, 2023). Nanoparticles act as transporters and have the ability to enhance the outcomes of medication. Napooni et al. (2019) suggested that the Au nanoparticle can inhibit the protoscolices. The using of gold nanoparticles with praziquantel and albendazole for treating hydatid disease reduces the side effects that are produced by the chemical drugs and these two drugs will work better with nanoparticles. Jelowdar et al. (2017) recorded that chemoprophylaxis works better than praziquantel and albendazole in the treatment of cystic echinococcosis.

The silver nanoparticle (Ag) originated from the fungus named *Penicillium aculeatum* and has protoscolicidal properties and is safe and effective in the treating of echinococcosis, because it is nontoxic and has fewer side effects than albendazole (Rahimi et al., 2015, Nassef et al., 2019).

Lashkarizadeh et al. (2015) reported the protoscolicidal properties of Ag nanoparticles, essential oil of *Foeniculum*, amphotericin B, and hypertonic saline.

There are several advantages of using nanoparticles for treating of cystic echinococcosis such as due to their effective solubility, directed drug delivery, and they controlled the drug release (Kesharwani et al., 2014, El-Say & El-Sawy, 2017, Pandian et al., 2021). The use of nanoencapsulated albendazoles and mebendazoles is a potential benzimidazole anthelmintic technique (Shukla et al., 2021). Numerous nanostructured carriers, such as lipid nanoparticles, polymeric nanoparticles, and liposomes, have been used to encapsulate these medications (Shukla et al., 2021).

Nanoparticles have antiparasitic properties, like the triggering of apoptosis (Khashan et al., 2020, Ezzatkhah et al., 2021). Albendazole sulfoxide and albendazole sulfoxide-loaded poly (lactic-co-glycolic acid)-PEG was assessed against protoscolices in an in vitro investigation by Naseri et al. (2016). According to Soltani et al. (2017), Solid lipid nanoparticles loaded with albendazole and albendazole sulfoxide had excellent physicochemical and controlled release characteristics. This suggests that the particles can function as extremely effective drug-delivery vehicles. These results imply that the treatment of cystic echinococcosis may benefit from the use of such materials.

1.2.2. Toxicity of Nanoparticles

Parasites are the most pathogenic microorganisms for humans and animals than other microorganisms because they cause chronic illness (Prajitha et al., 2019, Srivastava et al., 2021). Parasites have a complex life cycle and, therefore have the ability to live within the host and in the environment for many years (Gagne et al., 2022). Different parasite morphological stages result in different sensitivity to the same medication (Gupta & Xie, 2018). The continuous use of antiprotoscolix which leads to resistance, and this issue is resolved by using nanoparticles which enhance the drug delivery (Rehman et al., 2021, Yin et al., 2022). Resistance to nanotherapeutics also occurred as antimicrobial resistance (Prajitha et al., 2019). There is proof that the environment that is produced by interactions between biological systems and nanoparticles aids in the development of resistance mechanisms within these systems (Wang et al., 2017). The nanoparticles can change the sensitivity of medication, which can aid in developing resistance to antibiotics (Chenthamara et al., 2019).

2. Discussion

The treatment of hydatid cysts with classical drugs is difficult and has several side effects (Manterola et al., 2023), first due to the location of cysts and it is difficult for drugs to reach it site or a low concentration of drug can be reached which results into a poor treatment outcome (Aminu et al., 2020), and second due to the cyst surrounded by a protective thick wall (Majumder et al., 2019). Therefore, nanotechnology and nanomedicine have the ability to enhance the delivery of drugs (Geramizadeh, 2017). Nanoparticles can be used with medication and encapsulated then increase their stability, solubility, and bioavailability cysts (Devadasu et al., 2013, Momčilović et al., 2019).

The early diagnosis and identification of cystic echinococcosis play an important role in the treatment of the disease. The most common diagnostic methods used for the diagnosis of hydatid cysts are ultrasound, and computed tomography, with aids of serological testing (AlGabbani, 2023). However, these methods may give a false negative result (Aljanabi et al., 2021). However, there is no sensitivity to using serological tests in the early diagnosis (Deng et al., 2019). Recently, the combination of nanotechnology with chemotherapy in the treatment of hydatid cysts has been successful (Cheraghipour et al., 2023). This is why nanotechnology developed (Ullio Gamboa et al., 2019). Also, resolved the problem of the solubility of the drugs by nanocarriers, and boosted the stability of the drugs (Muraleedharan & Chhabra, 2018). The main idea of the development of nanotechnology was that medication can reach the locations of cysts without any side effects, also, the drugs can be reached within the cysts effectively through nanocarriers by circulatory ways (Xu et al., 2022). This way is safer and more targeted (Nikam et al., 2022). The main problem of the classical treatment of echinococcosis was the development of resistance and is resolved by using nanocarriers (Şenel & Yüksel, 2020). The use of nanocarriers can postpone the process of the emergence of resistance.

Nanotechnology is a good technique for treating hydatid cysts, but still has some side effects such as their hazardous nature (Olawoyin, 2018). Several studies are required to determine the using nanoparticles and their effects on the human's health (Abdussalam-Mohammed, 2019). It is also important to monitor the hydatid cysts and resistance to nanotherapeutics. To avoid these researches are needed to do by using of different drugs from different classes should be combined with nanocarriers.

Conclusion

As known cystic hydatid disease is a zoonotic helminthic disease and it needs an early diagnosis and treatment. Classical medications have been developed drug resistance and this issue was resolved by introducing nanotechnology and nanomedicines. Nanotechnology and nanoparticles are recent developments used in the diagnosis and treatment of parasitic diseases. In the case of hydatid disease, the nanoparticles have efficient protoscolicidal properties and are used as antiprotoscolixes effects. More studies are necessary to comprehend the mechanisms of action of nanoparticles in order to create safe diagnostic and therapeutic alternatives.

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Role of Nanotechnology in Treatment of Bovine Mastitis

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Abstract

Mastitis is an inflammatory transformation of the mammary along with chemical and microbiological changes. Mastitis is a serious problem in dairy animals as it affects both their welfare and productivity and is associated with economic loss and public health concerns. Antibiotics have a key role in mastitis control programs, although there's a continuous search for new effective therapeutic alternatives. Another public health concern about mastitis is the antibiotic residues in milk owing to the improper use of antibiotics in treatment and control and the withdrawal time, which is not considered. These residues may cause a severe allergic reaction and sensitization in normal individuals when present at a low level. Drug delivery depending on nanotechnology allows medications to be deposited, maintained, and released gradually at specific sites, addressing some of the drawbacks of traditional medications, such as antibiotic resistance. To overcome antibiotic resistance Nanoparticles have emerged as new tools against bacterial infections. Metals, including copper, silver, and zinc, have been used due to their antibacterial properties. This chapter presents an overview of alternative solutions that may become popular in mastitis treatment.

Keywords: Nanotechnology, Bovine mastitis, Metal nanoparticles, Drug delivery, Antibiotic resistance

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Introduction

Mastitis, an inflammatory retort of the udder tissue due to mammary gland infection, is an intricate, multifactorial, chronic, and deadly disease in cattle (Argaw 2016; Shoukat, et al. 2018). It was classified as contagious and environmental according to the causative agent. The contagious is classified into clinical, subclinical, and chronic mastitis. Mastitis is a crucial problem that affects dairy animals and influences their milk production, leading to heavy culling (Cobirka et al. 2020). Mastitis is the biggest economic burden of the dairy industry, and its control is a global challenge (Gad et al., 2025). Various conventional and advanced therapeutics and methodologies are used for mastitis control (Cheng and Han 2020). Traditional treatment of subclinical mastitis includes intramammary broad-spectrum drug administration however, the limitations of this therapy are well known (Ruegg 2017; Klaas and Zadoks 2018). Bacteriophages, bacteriocins, probiotics, stem cell therapy, herbal therapy, dry cow therapy, nutritional, genetic selection, vaccination, and nanoparticle-based therapeutics were tested for their effect on mastitis treatment and control (Gomes and Henriques 2016; Sharun et al. 2021). Antibiotics, such as penicillin, are considered the most used strategy for mastitis treatment (Gomes and Henriques 2016). It is believed that 80% of the antibiotics administered in dairy animals are used for the control of mastitis globally (Ganda et al. 2016a) but detection of the pathogens using a drug sensitivity test is important before starting antibiotic treatment (Koskinen et al. 2010). Although misusing and overusing antibiotics, in addition to their cost, in the case of bovine mastitis could introduce a serious problem of resistance and introducing resistant bacteria to the food chain (White and McDermott 2001). Being intracellularly residing, the bacteria within the mammary glands form abscesses and are hard to kill because of the restriction of their contact with antibiotics (Gomes and Henriques 2016). Moreover, another disadvantage of antibiotics is the presence of their residues in bovine milk which could represent a public health concern due to its human consumption (Motaung et al. 2017). Also, biofilm formation could contribute to antibiotic-resistant infections and recurrent mastitis (Babra et al. 2013). As no milk is produced during this period, a dry cow is considered the best period to control mastitis (Biggs 2017). Also, using strict biosecurity protocols and strategic culling could be effective in preventing and controlling the virulent strains of *S. aureus* and *S. agalactiae* (Kefee 2012). An alternative approach, such as using bacteriocins, antimicrobial peptides produced by bacteria, offered many advantages better than the traditional antibiotic choices (Twomey et al. 2000). Additionally, combining antibiotic treatment and culling of unresponsive cows declined the transmission rate of mastitis (Halasa 2012). Another approach involved subcutaneous injections of different concentrations of Selenium, Copper, Zinc, and Manganese (Machado et al. 2013) which reduced

cases of subclinical mastitis and retained udder health without any effect on milk quantity or quality (Ganda et al. 2016b). This chapter concentrated on the application of nanotechnology as an antibiotic substitute in the treatment of mastitis.

Nanotechnology in Mastitis Treatment as Alternatives to Antibiotics

Nanotechnology research has been known since the previous century. Nanotechnology was introduced by Nobel laureate Richard P. Feynman in his celebrated 1959 speech "There's Plenty of Room at the Bottom", this topic has seen several ground-breaking advancements (Feynman, 1960). Different kinds of materials were created at the microscopic level using nanotechnology. Materials that have one dimension smaller at least than 100 nm are referred to as nanoparticles (NPs) (Laurent et al., 2010). 0D, 1D, 2D, or 3D materials can be used, relying on the general form (Tiwari et al., 2012).

NPs could be generically divided into many classes built on their shape, chemical, size, and shape makeup, this classification is according to the chemical and physical properties (Khan et al., 2019). The unique chemical and physical features of inorganic nano-sized particles, whether simple or complex, make them an increasingly significant component in the invention of novel nanodevices with a large range of biological, physical, pharmacological, and biomedical approaches (Loureiro et al., 2016; Khan et al., 2019). For the assembly of NPs, a variety of techniques can be used, two classes are broadly categorized into two classes: (i) top-down approaches and (ii) bottom-up approaches (Wang and Xia, 2004; Iravani, 2011; Bayda et al., 2019) (Fig. 1).

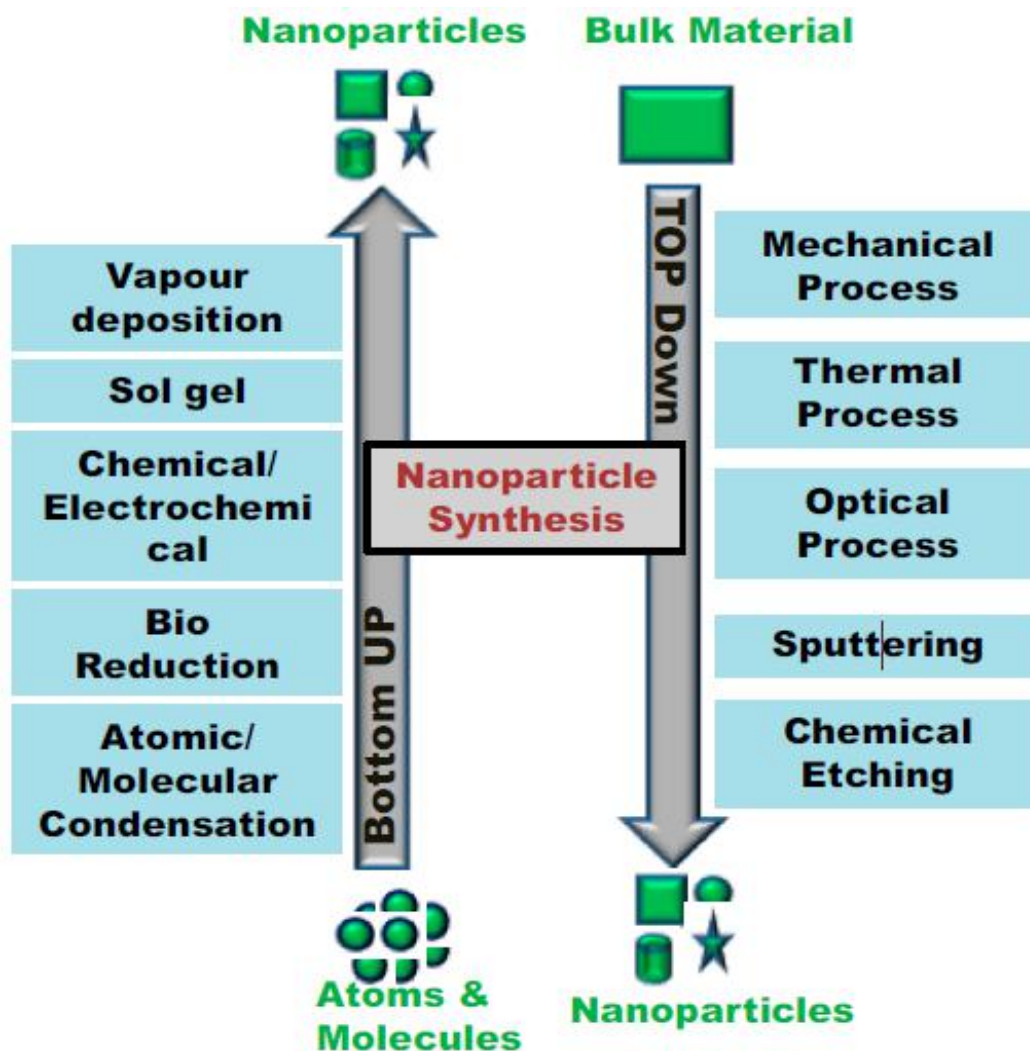


Fig. 1: The concept of top-down and bottom-up technology: different methods for nanoparticle synthesis (Bayda et al., 2019)

Three layers make up NPs (i) a superficial layer that could be functionalized with a range of polymers, tiny molecules, metals, and surfactants; (ii) an outer shell layer; and (iii) a core moiety that is the exact term for the NPs. As nanotechnology develops and new NPs are produced, the famous structure of NPs is changing, especially via bio-NPs as well as co-assembly (Noman et al., 2022; Wang et al., 2022).

Drug delivery depending on nanotechnology allows medications to be deposited, maintained, and released gradually at specific sites, addressing some of the drawbacks of traditional medications, such as antibiotic resistance (Ferreira et al., 2021; Li et al., 2023). Release of adherent drug from the surface of nanoparticles, through the erosion, diffusion, and the diffusion/erosion of the NPs are the main three key factors that affect the release of drug rate from the NPs. Thus, diffusion of drug and polymer biodegradation will control the pace of the released drug from the nanoparticles. In addition to deeper understanding the physiological parameters implicated in this procedure,

the composition of the NPs (e.g., pH-sensitive and thermosensitive substances) and their engineering (e.g., nanoparticles, nanocapsules, monolayer and multilayer) can be used to control the time and location of the released drug (Klymchenko et al., 2020; Tan et al., 2021; Harish et al., 2022) (Fig. 2).

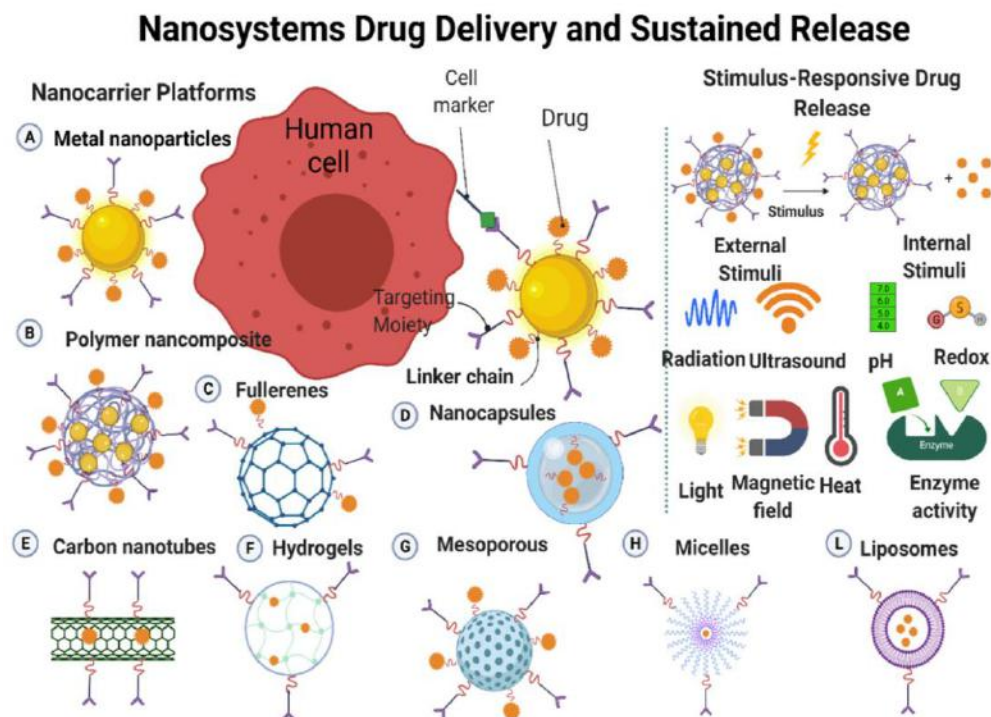


Fig. 2: Characteristics of nanomaterials that can cross the biological membranes to deliver a drug to a specific site and mechanisms influencing controlled drug release (Harish et al., 2022)

Since tiny molecules can alter the biological characteristics of nanomaterials, their use in surface functionalization has opened up new possibilities for biomedical applications. Antimicrobial resistance can be further prevented in this way by mediating the engagement to cell receptors (Masri et al., 2019; Spirescu et al., 2021) (Fig. 3).

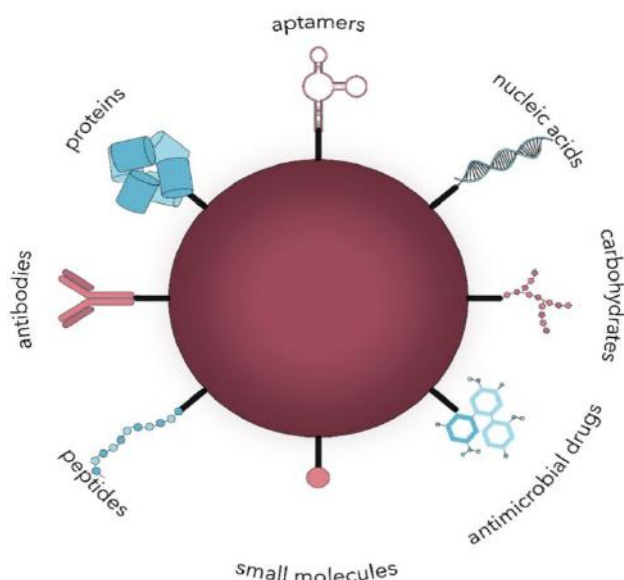


Fig. 3: The main types of biomolecules used for the surface modification of nanoparticles for active microbial targeting (Spirescu et al., 2021)

Nano Particles and Mastitis

To overcome antibiotic resistance Nanoparticles have emerged as new tools against bacterial infections. Metals, including copper, silver, and zinc, have been used due to their antibacterial properties (Haider et al., 2023) (Fig 4). With advances in nanotechnology, functional nanomaterials have been developed and widely used in various fields such as cosmetics, device coatings, and food preservation (Yilmaz et al., 2023). Zhou et al. (2019) recorded that treatment of cows with *S. aureus* mastitis, with tilmicotin nanogel showed a greater rate of recovery than a group receiving traditional treatment. Silver nanoparticles and cinnamon oil both had bactericidal effects on *S. agalactiae*. Phyllanthus emblica, Terminalia, Citronella, Dandelion, and cinnamon were among the polyherbal nanocolloids that demonstrated effective, dose-dependent antibacterial activity against microorganisms obtained from mastitis (Abd El-Aziz et al., 2021; Ranjani et al., 2022).

Nano minerals are reported to produce unexpected biological responses when fed to cows due to their significant physical, chemical, and biological activities. The translocation of 100-nm nanoparticles is 15–250 times more than that of micromolecules. They improve the health and production of bovine at even lower doses. Being nanometer-sized, nano minerals can easily cross the animals' small intestines and spread into blood, brain, lung, heart, kidney, spleen, liver, intestines, and stomach. However, many

factors, like, size, shape, zeta potential, other ligands, surface chemistry, age and species of animal, intestinal health, and dose of use, may affect the absorption and metabolism of these particles (Yilmaz et al., 2023).

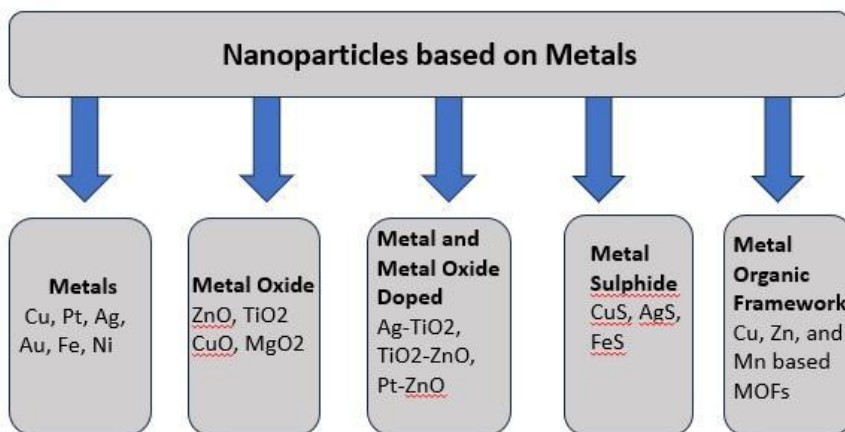


Fig. 4: Various types of metal-based nanomaterials

Metal Nanoparticles

Silver nanoparticles (AgNPs) are medical nanomaterials used commonly between the varied kinds of metal nanoparticles (metallic and metal oxide), they are detected to be most efficient against viruses, bacteria, and many other eukaryotic microbes because of their noticeable antibacterial characteristics and low toxic effect (Franci et al., 2015; Sharma et al., 2009; Chamundeeswari et al., 2010; (Mohamed et al., 2024). It is thought to substitute antibiotics in the future due to its significant effect against many of the resistant pathogens. Silver ions work by allowing exposure of bacteria to harmful external factors as a result of depriving it of its protection when it interacts with its cell wall and cell membrane causing rupture and death of the cell (Siddiqi et al., 2018). They are also found in nucleic acids, disturb ribosomes, and basic functions of the cell (Salas Orozco et al., 2019; Haider et al., 2023) (Fig 5).

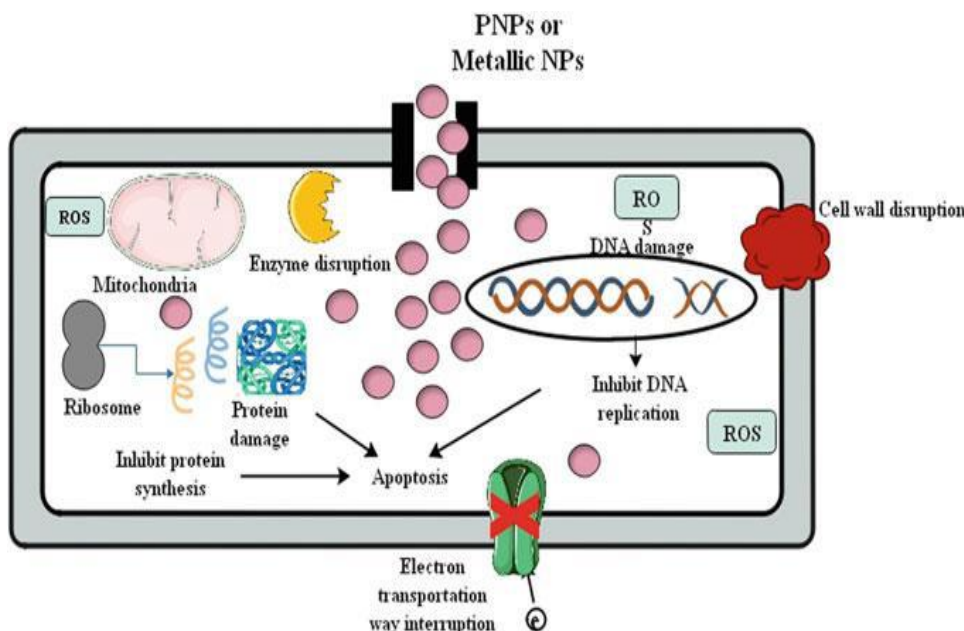


Fig. 5: Metal-based nanoparticle's general mechanism for antimicrobial potential (Haider et al., 2023)

There is an amplified antibacterial effect against both *S. aureus* and *E. coli*, which are common species of Gram-negative and Gram-positive bacteria, such as, when silver (Ag) nanoparticles and antibiotics including amoxicillin, penicillin G, vancomycin, and erythromycin are combined (Shahverdi et al., 2007; Fayaz et al., 2010). Moreover, green synthesized Ag NPs showed significant results against isolates of *Aspergillus species* and *Candida species* isolated from the milk of mastitis cows (Hasanin et al., 2022).

Copper nanoparticles (Cu NPs), have a high surface attention, and easy surface activation with other components so they have great potential as antimicrobials (Ingle et al., 2014). According to Seo et al. (2018), copper nanoparticles act on *Methylobacterium* species through inhibition of the growth of its biofilm, as well as highly resistant *Pseudomonas aeruginosa spp.* (LewisOscar et al., 2015; Mohamed et al., 2024).

Zinc Oxide, (ZnO) NPs can manufactured under harsh conditions and exhibit a specific toxic effects on bacterial cells, Additionally, it's thought that ZnO nanoparticles interfere with the cell membrane of bacteria, leading to the final bacterial death. (Sawai 2003). On the other hand, it has minimal effect on animal and human cells. Zinc oxide nanoparticles are considered as a potential medication carrier due to their antibacterial function against essential food-borne pathogens and because they are biocompatible and relatively harmless to humans (Roselli et al., 2003; Brayner et al., 2006).

Titanium Dioxide, (TiO₂) NPs were found to be the most for photocatalytic antibacterial activity (Gelover et al., 2006). Strong antibacterial action obtained by TiO₂ nanoparticles when exposed to UV beams. The Antimicrobial effect relies on the size, wavelength of the light source of

the TiO₂ and intensity. The effective concentration to kill microbes is between 100 and 1000 parts per million. Furthermore, it was detected that the photocatalytic efficacy of TiO₂ as antimicrobial nanoparticles was reliant mostly on the thickness of the cellular membrane of the microbe (Kühn et al., 2003).

Gold, (Au NPs) have been employed to treat bacterial infection by irradiating with an appropriate wavelength (Sekhon and Kamboj, 2010). The antimicrobial activity of gold nanoparticles (Au NPs) was exhibited through Strong electric attraction to the cell membrane with a negative charge (Johnston et al., 2010). For example, gold nanoparticles (Au NPs) combined with anti-protein A that aim at the bacterial surface, have been found to selectively destroy *S. aureus* (Pissuwan et al., 2010). Bacteria were mostly destructed by the hyperthermic actions that were influenced by clustered gold nanoparticles (Au NPs). Strong antimicrobial effects obtained by gold nanoparticles coated with antibiotics, like streptomycin, neomycin, and gentamicin, have been searched in numerous studies against strains that are highly resistant to antibiotics, as well as both Gram-negative and positive (Grace and Pandian, 2007).

Chitosan is a polymeric nanoparticle and has an antimicrobial effect; the action of chitosan against variant kinds of bacteria, fungi, and yeasts is still not known (Guarnieri et al., 2022; Haider et al., 2023). The interactions between the microbial cell membranes which are negatively charged and the positively charged NH₃⁺ sites of chitosan interfere with microbial cell permeability, which resulted in the release of intracellular material considered the most common mode of action of these particles (Tsai and Su, 1999; (Mohamed *et al.*, 2024); Chung and Chen, 2008) demonstrated that disruptions in the structure of *S. aureus* and *E. coli* spp. Occurred through the binding of chitosan to microbial enzymes and nucleotides. Chitosan exerts antibacterial action against both types of Gram bacteria (positive and negative) bacteria, where the difference in cell membrane structure is the main determinant of how chitosan acts.

Nanoemulsion, surfactant molecules coating a thin oil diffusion in aquatic solution, the mean size of this emulsion (ranged from 0.1 to 600 nm) can be affected by the concentration and mechanical energy of this surfactant. Nanoemulsions save protection and stability to active compounds by encapsulating them (Machado et al., 2020). Several studies were done on the antimicrobial activities of nanoemulsions and showed how they amplify the effect of antimicrobial drugs; this antimicrobial action is controlled by the physicochemical structure of nanoemulsions (Girgin and Nadaroglu, 2024).

Panchal et al. (2024) demonstrated that higher effect of copper-oxide nanoparticles as antimicrobials compared to common antibiotics. Due to the toxic effect of higher concentrations of metal nanoparticles, so they are applied in a limited form. Triphala and Chitosan nanoparticles could be the solution to overcome copper toxicity in cattle.

Conclusion

Bovine mastitis is a significant challenge for veterinarians and academics. Further research is necessary to effectively manage mastitis. Microbial mutations causing antibiotic resistance pose a significant concern in the treatment of infectious diseases like mastitis. Antibiotic resistance is a global topic, addressed by both pharmaceutical businesses and academic researchers. Nanomaterials can improve antimicrobial medicine efficacy and open up new possibilities for antibacterial agent development due to their unique physicochemical properties. Nanoparticles can operate as antibiotic transporters, potentially addressing antimicrobial resistance. Nanoparticles have been studied as effective nano-antibiotics and delivery strategies to prevent antimicrobial resistance, potentially overcoming antibiotic resistance. This chapter discusses the role of nanoparticles in controlling and treating bovine mastitis.

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Nanotechnology and the Future of Medical Imaging: Enhancing Diagnostic Accuracy

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Abstract

Through medical imaging improvements, nanotechnology implementation enhances diagnostic techniques through better resolution power and improves sensitivity and specificity at the same time. Point-based analysis demonstrates how gold nanoparticles and iron oxide nanoparticles, together with quantum dot nanoparticles as well as polymeric nanoparticles, function as imaging agent enhancers for CT scanners and MR scanners as well as PET scanners and ultrasound scanners, and optical image systems. Higher-resolution imaging at both cellular and molecular levels becomes possible through nanoparticles, which enhances disease detection at an early stage and enables precise identification of abnormalities primarily during cancer diagnosis. Nanoparticle inclusion in theranostic imaging techniques makes it possible to perform battery-powered medical procedures that simultaneously detect and treat diseases, for tailoring precise medical care. Real-time imaging implementations enabled by nanotechnology allow doctors to monitor diseases as they evolve alongside therapeutic responses in patients. Complete realization of nanoparticles within medical imaging demands resolution of biocompatibility and safety issues, along with regulatory requirements. Precision medicine receives significant advancement through nanoparticle-based imaging technologies, which this chapter discusses recent developments alongside existing challenges and future possibilities.

Keywords: Nanoparticles, Medical Imaging, Contrast Agents, Theranostics, Precision Medicine.

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Introduction

Medical imaging serves a fundamental role in cancer diagnosis by helping to locate abnormal areas and direct biopsy procedures and determine disease spread for deciding appropriate treatments between surgery and radiation or chemotherapy. Barentsz et al. (2006) noted that tracking therapy response constitutes a common practice which also functions as a substitute endpoint during drug discovery. Each technique has unique advantages, but they have certain limitations like resolution, sensitivity, and specificity (Wang et al., 2022). Images produced by CT scanners are used to support anomaly diagnosis and other therapeutic assessments. X-rays are generated from different angles using this method, and computers analyze them to create tomographic images (Gallamini et al., 2014). Highly innovative re-created photos have been made by this sophisticated computer-based technology. The skeleton, head, neck, kidney, and bladder can all be diagnosed with CT, which is an efficient method for identifying various tumors. Rapid high-resolution images can be generated with CT scanning (Stock, 2012; Sera, 2021).

PET uses small amounts of radioactive material called radiotracers, which are absorbed by the body and generate positrons, which produce gamma rays when combined with the electrons (Crişan, G et al., 2022). The PET scanner detects these gamma rays and generates an image that can be used to identify cancer. Other metabolic disorders, neurological disorders, and heart disease are also diagnosed with PET scans (Gallamini et al., 2014). Strong magnetic fields and radio waves are used in this non-invasive medical imaging method to create incredibly detailed pictures of the body's internal organs, including soft tissues. It can identify abnormalities such as tumors, blood clots, and soft tissue injuries (Kasban et al., 2015).

High-frequency sound waves are used in ultrasound to create a real image of the body's organs and tissues without the use of ionizing radiation. It is frequently linked to prenatal imaging, which enables medical professionals to track a fetus's growth and development. The heart, blood arteries, pelvis, and abdomen can all be examined by ultrasound (Duck et al., 2020). Medical imaging faces some challenges that impact its efficacy and reliability. The primary issues include resolution limitations, sensitivity concerns, and data management complexities (Haleem et al., 2023). Recent advancements in imaging technologies tackle these issues. However, sophisticated algorithms and processing techniques are required to optimize and improve the imaging modalities (Gull & Parah, 2024).

1.1 Introduction to Nanotechnology in Medical Imaging

Nanotechnology is revolutionizing medical imaging by significantly increasing diagnostic precision and imaging quality. By employing

nanoscale materials and technology to improve traditional imaging techniques, this novel approach tackles significant problems in healthcare diagnosis (Han et al., 2019). Gold nanoparticles and quantum dots are examples of nanomaterials made possible by nanotechnology, which has been used to diagnose cancer at the molecular level. Nanomaterials are being utilized in the detection and treatment of cancer (Hanif et al., 2021; Salar et al., 2024). Nanotechnology allows for precise viewing of biological processes and improves imaging quality and diagnostic accuracy through multimodal capabilities, real-time monitoring, and enhanced contrast agents. MRI, CT, PET, and fluorescence imaging are among the techniques whose sensitivity and specificity are improved by improved contrast agents and multimodal imaging (Liu et al., 2023). Early disease detection is facilitated by real-time nanoscale monitoring, which is essential for prompt interventions. Furthermore, nanotechnology facilitates less invasive procedures and tailored medicine, lowering patient risk and improving comfort while enabling accurate, customized diagnosis and treatment planning (Han et al., 2019).

2. Nanotechnology in Medical Imaging

The handling of materials One billion times smaller than a meter at the nanoscale is the focus of nanotechnology, a groundbreaking avenue for scientific advancement. In actuality, nanotechnology refers to any nanoscale technique that has a wide range of practical uses (Hasan et al., 2018). Nanotechnology literally encompasses the development and use of chemical, physical, and biological systems at sizes ranging from single molecules or atoms to submicron dimensions, as well as the integration of the resulting nanomaterials into larger systems. (Nasrollahzadeh et al., 2019). It is well known that nanoparticles are minuscule materials with sizes between 1 and 100nm. To put it more simply, nanoparticles are nano-objects that have three exterior dimensions at the nanoscale. They are frequently divided into many classes according to their characteristics, sizes, or shapes. The different types include metal nanoparticles, ceramic nanoparticles, polymeric nanoparticles, and fullerenes. (Haleem et al., 2023).

2.1 Nanoscale Contrast Agents

Various forms of cancer are detected and diagnosed using medical imaging technologies. Numerous studies have lately focused on the creation of novel nanoparticles as contrast agents for medical imaging that can be used to identify cancer early (Mhlanga et al.,2024). Different types are shown in Figure 1.

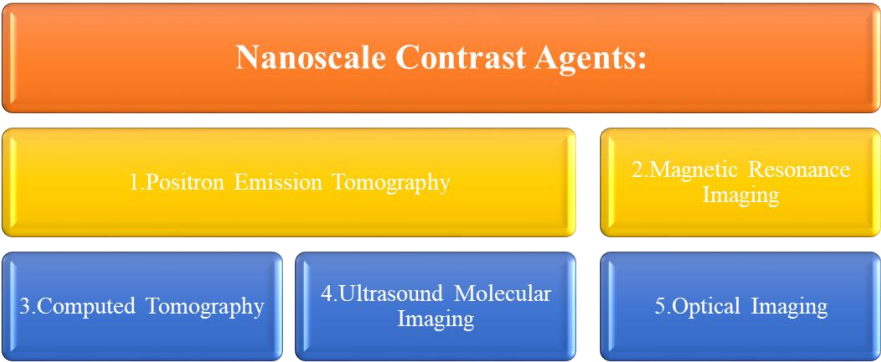


Fig. 1: Nanoscale Contrast Agents: Using Nanoparticles to enhance image contrast and detail.

i. Positron Emission Tomography

The paired 511keV gamma rays produced by the annihilation event of a positron and an electron are intended to be detected by the PET method. Along a line, the annihilation photons go in opposite directions, 180° apart. The target can be surrounded by a PET detector that can prepare signals and transform them into tomographic pictures (Casali et al., 2021).

ii. Magnetic Resonance Imaging

The interaction of nuclei with a nonzero magnetic moment in an external magnetic field is the fundamental basis of magnetic resonance imaging (MRI). Comparably high temporal and spatial resolution, strong tissue contrast, nonionizing radiation, non-invasiveness, and the simultaneous gathering of anatomical and functional data are some of MRI's outstanding qualities (Jiang, M et al., 2021).

iii. Computed Tomography

In medical imaging facilities, CT is a particularly helpful X-ray imaging technique for diagnosing cancer. 2D cross-sectional images of the human body's internal architecture are provided via a CT scan. Consequently, CT can examine translucent tissues, including malignancies. However, CT's capacity to discriminate between adjacent tissues was diminished by a poor signal-to-noise ratio (Mhlanga et al., 2024).

iv. Ultrasound Molecular Imaging

It is a unique modality since it may be used for both therapeutic and imaging applications. Microbubble (MB) is a novel form of contrast agent used in the US modality for diagnostic reasons. MB may improve this modality's sensitivity and specificity for detecting malignancy (Gharat, S. K et al., 2022).

v. Optical Imaging

Through the use of nonionizing radiation, such as visible, ultraviolet, and infrared light, optical imaging noninvasive technique for viewing inside the body, significantly lowers the patient's exposure to dangerous radiation. By stimulating electrons, these kinds of light produce pictures without causing harm that certain other imaging methods that involve ionizing radiation can. (Shahbazi-Gahruei et al., 2019).

2.2 Enhanced Resolution and Targeting

Nuclear medicine focuses on molecular imaging for noninvasive diagnosis and treatment using radioisotopes, both free and molecule-bound (Wozniak et al., 2022). Recent advances integrate isotope-labeled probes with PET and SPECT, expanding beyond radioactive injections. Nanostructures aid personalized therapies, including hyperthermia, which raises tissue temperature (40–45°C) to enhance cancer treatment (Huang et al., 2024). Superparamagnetic iron oxide nanoparticles (SPIONs) exhibit high magnetic sensitivity without coercivity or remanent magnetization, behaving differently from bulk iron oxide in an alternating magnetic field (Pucci et al., 2022). Effective targeting requires biocompatible stabilizers for colloidal stability and functionalization, binding ligands via electrostatic or chemical interactions (Hu et al., 2023).

2.3 Early Disease Detection

It is essential to discover CNS disorders early because this allows for early therapy, which stops the pathology from getting worse. Unfortunately, because the brain is inaccessible, it is particularly difficult to detect brain-related disorders in their early stages. The absence of diagnostic biomarkers and the decreased blood–brain barrier (BBB) penetration of diagnostic probes is only two of the many drawbacks of the current methods. Furthermore, molecular diagnostic methods cannot replicate real brain activity; they can only identify surrogate endpoint indicators. Numerous Nano diagnostic methods, including contrast-enhanced drugs and imaging probes, have been developed thus far. Probes that are very sensitive and selective with excellent temporal characteristics, tissue penetration, and spatial resolution have been used to study CNS illnesses thanks to recent advancements in diagnostic tests (Hanif et al., 2021).

For the clinical diagnosis of malignancies and neurodegenerative illnesses, a number of imaging modalities are essential, including computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), photoacoustic (PA), and fluorescence (FL) imaging. One of the main forms of brain cancer is GBM Extreme heterogeneity and variation in tumor appearance within the white matter are characteristics of GBM. The molecular mechanisms that cause GBM disease to begin can be identified with the use of emerging molecular techniques (Yang, K et al., 2022). AD is a common neurodegenerative illness that affects several cellular processes and proteins. The amyloid cascade theory is a major focus of the development of AD medications. This hypothesis primarily explains how A β monomer self-assembles into insoluble fibrils and soluble oligomers (A β Os), which in turn cause synapse dysfunction and cognitive impairment. Early or progressive loss of neurotraumatic neurons is linked to Parkinson's disease. Currently, imaging and genetic testing are used to diagnose Parkinson's disease (Raj et al., 2021).

3. Types of Nanoparticles and Their Application in Imaging

3.1 There are four different types of nanoparticles as mentioned in Figure 2, and their application is described below.

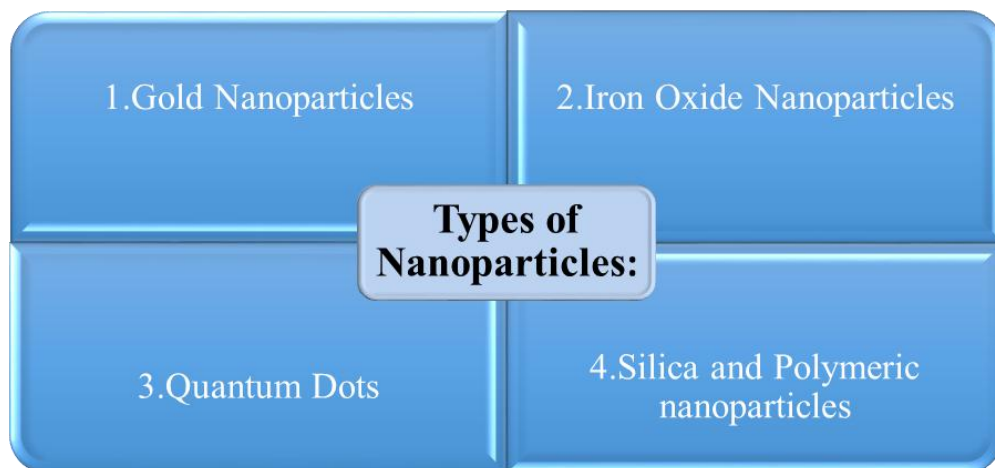


Fig. 2: Types of nanoparticles.

3.2 Gold Nanoparticles (AuNPs)

Much research has been done on gold nanoparticles (AuNPs), which are recognized to have significant medical uses. AuNPs can be created using a variety of techniques, however they can be broadly divided into two categories: chemical and physical synthesis. The half-life of iodinated CT contrast agent in the vasculature is brief. A more robust contrast agent would be very helpful in the domain of intervention techniques grow (Oumano et al., 2021). The feasibility of using gold nanoparticles as a vascular contrast agent for CT that lasts was examined in our study. A modified Turkevich process was employed to create the gold nanoparticles, which were then coated with methoxy-polyethylene glycol-thiol chains and contrasted using a contrast agent based on iodine that was administered to mice. Contrast compounds were examined in vivo by injecting them into the tail vein after being CT-imaged in tubes at 40, 60, and 140kVp (Luo et al., 2021). Two mice were given an iodine-based contrast agent, nine mice were given gold nanoparticles, and one was given saline. Mice were CT-scanned right away at 60kVp, six hours, and twenty-four hours after injection (Jeon et al., 2021). When gold nanoparticles were separated into tubes, their radiographic density was higher than that of an iodine-based contrast agent at 40kVp and was similar in the other CT voltage ranges. Gold nanoparticles in mice produced a strong contrast enhancement that made it possible to see the renal arteries and abdominal aorta clearly, which would not have been possible without a contrast agent (Jiang et al., 2019). This continued until the final time point evaluated, which was 24 hours. Immediately following injection, there was contrast enhancement of the vasculature using a contrast agent based on iodine, but this vanished six hours later (Mahan et al., 2018).

3.3 Iron Oxide Nanoparticles

For a long time, iron oxide nanoparticles (IONP) have been utilized extensively as contrast agents (CA) for magnetic resonance imaging (MRI) because of their exceptional biocompatibility and unique magnetic characteristics (Zhao *et al.*, 2022). One of the most common contrast agents used in magnetic resonance imaging (MRI) in therapeutic settings is based on gadolinium chelates. However, the Food and Drug Administration has repeatedly warned about their possible retention in patients' systems, raising safety concerns, and their toxicity results in serious adverse effects. The benign and biodegradable characteristics of iron oxide nanoparticles (IONPs) makes them a potentially alluring substitute (Jeon *et al.*, 2021).

3.4 Quantum Dots

Over the past twenty years, studies on nanocrystals of fluorescent semiconductor, sometimes referred to as qdots, or quantum dots, has progressed from electrical materials science to medical applications. Vascular endothelial cells will come into direct touch with the quantum dots in the blood when they are utilized as fluorescent probes or drug tracers for in vivo imaging (Xu *et al.*, 2021). Therefore, research into whether quantum dots, when injected into blood arteries as imaging agents, can impact endothelial function is required. Therefore, research into whether quantum dots, when injected into blood arteries as imaging agents, can impact endothelial function is required. We go over the most recent methods for creating, soluble, and functionalizing qdots as well as how they are used in animal and cell biology (Huang *et al.*, 2024). They have recently been used experimentally to use near-infrared emission during surgery to locate lymph nodes in live animals and to track the spread of individual glycine receptors in vivo neurons. Long-term in vivo tracking of cell trafficking, tumor targeting, high-resolution cellular imaging, diagnostics, and the investigation of intracellular functions at the level of individual molecules are all made possible by the new generations of Qdots (Hu *et al.*, 2020).

3.5 Silica and Polymeric nanoparticles

A basic overview of deep learning network architectures is provided for applications involving classification, detection, segmentation, and generation of medical imaging in the most recent deep learning applications to ultrasound imaging (Kasban *et al.*, 2015). After that, A few sample imaging investigations of the unborn head, kidney, liver, thyroid, heart, and breast are examined and summarized, along with ultrasound applications for picture processing and diagnosis. Over time, the use of ultrasound (US) imaging in medicine has grown in acceptance (Avola *et al.*, 2021).

Some important advantages of US technology include its low cost, safety, and ability to give real-time feedback. However, it also has significant disadvantages, like a high degree of noise and poor image quality, which are being addressed by research in this area. Presenting the developments in US medical imaging techniques is the goal of this survey. It tries to arrange the research in this area into three categories: segmentation, classification, and miscellaneous, and describes the studies on the many organs that the US employs the most. This latter category comprises the works that attempt to improve the quality of the obtained US images/volumes or aid during surgical procedures. To the best of our knowledge, this is the first review that examines the many methods used on a wide range of bodily parts (such as the brain, thyroid, heart, breast, fetus, and prostate) in the three subfields of study (Palma-Chavez *et al.*, 2021).

4 Applications of Nanotechnology in Medical Imaging

Figure 3 shows three different applications of nanotechnology in medical imaging.

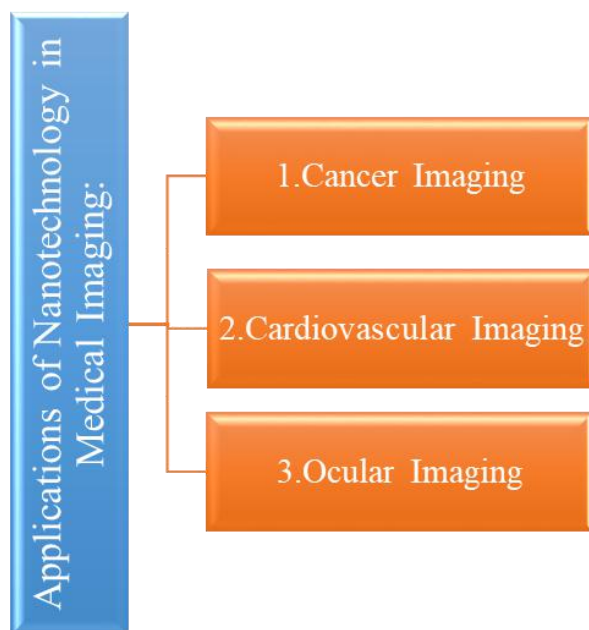


Fig. 3: Application of nanotechnology in medical imaging.

4.1 Cancer imaging

Cancer imaging with nanotechnology focuses on two key areas: (1) nano detection for identifying proteins and cancer cells and (2) nanoparticle-based contrast agents for enhanced imaging. Nanoparticles are being developed for early cancer detection in body fluids, with a focus on capturing circulating tumor cells, though existing methods struggle due to low cell concentrations (Kus-Liśkiewicz *et al.*, 2015). Nanoparticle devices with cancer-specific antibodies or ligands could improve this process. MRI remains a common non-invasive imaging tool, but nanoparticle-based contrast agents offer greater sensitivity and specificity for tumor detection, potentially enabling earlier diagnosis of metastases. However, this approach risks overdiagnosis and overtreatment. For instance, Harsinghani's research showed that nanoparticle-enhanced MRI could upstage cancers by detecting lymph node metastases outside typical resection areas, which, if applied prematurely, could lead to unnecessary tissue removal and increased patient morbidity (Gunasekera *et al.*, 2009).

4.2 Cardiovascular Imaging

Cardiovascular diseases are a leading global cause of death, with myocardial infarction posing challenges for full cardiac regeneration. Stem cell therapy promotes therapeutic angiogenesis, but viral vectors for gene delivery have limitations. Biocompatible nanoparticles (NPs)

offer a promising alternative, with liposomes protecting genes and polymers enhancing target specificity (Wang *et al.*, 2021). Chitosan-alginate NPs delivering growth factors have shown improved cardiac function in studies. Additionally, NPs like SPIONs and quantum dots enable long-term stem cell tracking. For hypertension, nanotechnology-based drug delivery systems such as lipid and polymeric nanoparticles offer improved bioavailability and targeted treatment, addressing limitations of conventional antihypertensive medications (Hu *et al.*, 2022).

4.3 Ocular Imaging

Drug delivery through the eye remains difficult because multiple defensive barriers form an intentional challenge, including the tear film and both the ocular surface epithelium and blood-ocular barriers. The delivery of drugs via NPs becomes possible thanks to their small dimensions and customizable surfaces, which enable safe delivery through barriers. Most NPs have a biodegradable composition, which eliminates the requirement for surgical intervention after their drug release operation (Woźniak *et al.*, 2015). Nanotechnology systems help treat cataracts and keratitis, as well as corneal injuries, by both increasing drug penetration intensity and lengthening drug retention durations. Posterior eye disorders, including glaucoma, macular degeneration, and retinoblastoma, usually need interocular injections that produce known adverse effects. Posterior eye drug delivery has become more efficient through Nano-based solutions that combine nanovesicles, Nano implants, NPs, and hydrogels (Pakzad *et al.*, 2020).

5. Innovative Techniques

Allowed by Nano-knocking Nanotechnology has revolutionized medical imaging by enabling innovative techniques that significantly increase diagnostic accuracy and therapeutic results. The key procedure is molecular and functional imaging, displaying Theranostics and real-time imaging. These Nano approaches allowed the transformation of how the disease is diagnosed and monitored, and offer an unprecedented insight into biological functions (Xu *et al.*, 2015).

5.1 Molecular and Functional Display

The molecular display focuses on the visualization of biological processes at the molecular level. Nanoparticles (NP), such as quantum dots and gold nanoparticles, are designed to target specific biomarkers, allowing highly specific display of cellular activities. For example, fluorescent quantum dots provide detailed visualization of tumor edges that help in accurate cancer diagnostics. Functional imaging enhances this ability to quantify dynamic processes such as blood flow or metabolic activity. Molecular and functional applications of nanomaterials have resulted in increased detection of cancer using link gold nanoparticles (Truong *et al.*, 2024). Monitoring neuronal activity of the brain in real time with magnetic nanoparticles. Cardiovascular imaging of nanoparticles based on lipids improved the detection of atherosclerotic plaques (Thakur & Kumar, 2024). The specificity of the Nano-blind molecular display reduces the likelihood of false positives, which is a critical restriction of conventional imaging modalities. Functional imaging supplemented by nanoparticles also increases our understanding of physiological processes under pathological conditions. (Wehn *et al.*, 2024)

5.2 Theranostic Imaging

Theranostic imaging combines diagnostic and therapeutic abilities into a single nanomaterial that makes personalized medicine easier. For example, iron oxide nanoparticles serve two purposes: it acts as contrasting substances to display magnetic resonance imaging (MRI) and add therapeutic agents directly to the destination. This approach is particularly useful in oncology, where real-time monitoring can lead to treatment (Anani *et al.*, 2021). The benefits of theranostic display. Example of benefits of functions: Combined diagnostics and therapy make the treatment of MRI treatment more efficient. Reduced systemic toxicity. Localized therapy minimizes the side effects of targeted chemotherapeutic nanoparticles. Adaptive processing monitors feedback in real time. Theranostic imaging is preparing a way to more efficient and less invasive treatment. By integrating therapeutic delivery with diagnostic feedback, it also reduces the time and cost of clinical intervention (Parashar *et al.*, 2022). Table 1 shows Innovations in Real-Time Imaging.

5.3 Real-time Imaging

Real-time imaging also facilitates minimally invasive diagnostics, where physicians can monitor the success of procedures such as stent placements or tumor ablations in situ.

Table 1: Innovations in Real-Time Imaging

Innovations	Nanomaterial	Use Case	References
Drug Delivery Monitoring	NIR fluorescent nanoparticles	Visualizing drug distribution dynamics	Lee et al., 2021
Organ Transplant Viability	Gold nanorods	Assessing transplant perfusion in real time	Gupta et al., 2022
Metabolic Monitoring	Zinc oxide nanoparticles	Measuring glucose levels continuously	Ahmed et al., 2023

6. Challenges and Future Direction

6.1 Biocompatibility and Safety

Because of their incredibly high surface-to-volume ratio, materials produced as nanoparticles (NPs) have shown distinct behaviors from their bulk counterparts. In general, the cytotoxic impact of nanoparticles increases with their size (Khan *et al.*, 2022). AuNPs have been synthesized and their cytotoxicity evaluated in a variety of forms, including spherical, rod-shaped, triangle-shaped, star-shaped, octahedron-shaped, plate-shaped, and prismatic. Even though nanoparticles have shown great promise in TE applications like improving biological, mechanical, and electrical qualities, having antimicrobial effects, delivering genes, and creating engineered tissues, there are still a lot of obstacles to overcome before they can be widely used in clinical settings (Xu *et al.*, 2021). For instance, there is a strong need for improved

instruments and techniques for evaluating the toxicity, carcinogenicity, and teratogenicity of nanoparticles. Second, nanoparticles' toxicity, carcinogenicity, and teratogenicity are all strongly influenced by exposure and dosage (Hasan *et al.*, 2018). The regulatory instruments now in use are not nano-specific; for example, the data requirements for chemical notice, classification criteria, and safety data sheet labeling requirements are still not generally accessible. Biocompatibility and biological safety are typical prerequisites for several beneficial uses of AuNPs (Kus-Liśkiewicz *et al.*, 2021).

6.2 Regulatory and Ethical Concerns

To guarantee patient safety and treatment effectiveness, navigating the clinical approval process necessitates adherence to stringent regulatory criteria. Prolonged schedules, strict data requirements, and intricate approval processes are typical obstacles. Researchers must simplify trial designs, guarantee reliable data collection, and communicate with regulatory bodies early in order to overcome these obstacles (Mehta *et al.*, 2024).

Patient welfare, informed consent, and fair access to therapies must be given top priority in clinical research ethics. Resolving issues like trial bias, data openness, and possible hazards is crucial to preserving public confidence. In order to strike a balance between patient rights and innovation, ethical review boards and continuous ethical evaluations are essential. Researchers can promote more seamless approvals while maintaining ethical integrity in clinical developments by combining regulatory compliance with robust ethical frameworks (Grunwald *et al.*, 2020).

The FDA is the main regulatory body in the US tasked with safeguarding the public's health by making sure pharmaceuticals, biological products, and medical devices are safe, effective, and secure. The regulatory supervision provided by the FDA includes all phases of the product lifecycle, including manufacturing, distribution, post-market surveillance, preclinical research, and clinical trials (Teli *et al.*, 2024). The European Medicines Agency (EMA) is a key player in pharmaceutical regulation throughout the European Union (EU), coordinating the assessment and oversight of pharmaceuticals to guarantee uniform effectiveness, safety, and quality requirements. Based on scientific information provided by manufacturers, the agency's Committee for Medicinal Products for Human Use (CHMP) thoroughly evaluates new medications to make sure that only those that satisfy strict regulatory requirements are authorized for sale (Olawale *et al.*, 2024).

6.3 Improving Targeting Precision and Stability

Since targeted treatments seek to selectively disrupt biological pathways or proteins implicated in the development and spread of cancer, they have emerged as a crucial weapon in the battle against the disease. Monoclonal antibodies and small-molecule inhibitors are two of the most vital instruments in the field of targeted treatment, which focuses on two major areas: angiogenesis and apoptosis. Nanoparticles with targeted alterations have demonstrated greater efficacy and reduced toxicity as compared to non-targeted medicines. A key component of the evolving nanocarrier targeting technique is the EPR effect, which enables nanoparticles to passively target tumors by taking advantage of leaky vasculature and inadequate lymphatic drainage (Chehelgerdi *et al.*, 2023). Maintaining vascular homeostasis, controlling vascular tension, promoting SMC proliferation, and preventing inflammation and thrombosis are only a few of the vital functions performed by vascular endothelial cells. A variety of cell surface proteins, such as P-selectin, vascular cell adhesion molecule-1 (VCAM-1), intercellular cell adhesion molecule-1 (ICAM-1), and platelet endothelial cell adhesion molecule-1 (PECAM-1) are also upregulated as a result of the activation. Endothelial cells and their cell adhesion molecules have been thoroughly investigated as essential drug-delivery targets to prevent or reduce the progression of atherosclerosis since endothelial dysfunction is the first stage of the disease (Zhao *et al.*, 2022).

Conclusion

The integration of nanotechnology into medical imaging has significantly advanced diagnostic precision, therapeutic monitoring, and early disease detection. Nanoparticles, including gold, iron oxide, and quantum dots, have improved imaging contrast, resolution, and targeting at cellular and molecular levels. These innovations enhance imaging modalities such as MRI, CT, PET, and ultrasound, enabling real-time visualization and theranostic applications. In cancer, cardiovascular, and ocular imaging, nanotechnology has improved disease detection, targeted drug delivery, and treatment monitoring. However, challenges such as biocompatibility, regulatory hurdles, and ethical concerns must be addressed for widespread clinical adoption. Ensuring nanoparticle stability, optimizing targeting precision, and refining safety assessments are crucial for future advancements. Despite these challenges, nanotechnology continues to revolutionize medical imaging, providing non-invasive, highly sensitive, and patient-specific diagnostic and therapeutic solutions. As research progresses, nanotechnology-driven imaging will play an increasingly vital role in precision medicine, improving healthcare outcomes and advancing early disease intervention strategies.

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Innovations in Nanotechnology and Biotechnology for Combating Cancer, Malaria and Neurodegenerative Diseases

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Abstract

Nanotechnology is shifting the healthcare field through atomically modifying materials, especially in the areas of diagnostics and therapy. Nanoparticles with a size range from 1 to 100 nanometers are at the forefront of these developments and are utilized in targeted therapy, early illness detection, and precise drug administration. Early cancer diagnosis is accelerated by nanotechnology through the use of methods such as NIR quantum dots, gold nanoparticles, and nanoshells. It improves specificity and lessens damage to healthy tissues during medical operations, including radiation, chemotherapy, and X-ray therapy. Nanobiotechnology has increased the effectiveness of therapy for malaria through nanoparticle-based delivery techniques and nano vaccines, and it has improved diagnostic sensitivity using nanoparticle-functionalized biosensors. In treating neurodegenerative diseases such as Alzheimer's and Parkinson's disease, nanostructures like polymeric nanoparticles, nanocapsules, and nanomicelles present promising ways to get around obstacles like targeted drug delivery and the blood-brain barrier. This chapter discusses the latest developments in biotechnology and nanotechnology for the treatment of diseases like neurological disorders, cancer, and malaria.

Keywords: Nano-biotechnology, Cancer, Malaria, Neurodegenerative diseases, Drug delivery

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Introduction

Nanotechnology is the field of applied science and technology that focus on developing materials with novel and advanced properties at the atomic and molecular scale. Nanotechnology is the study and application of structures of different sizes ranging from 1-100nm (1nm= 10⁻⁹m) (Lamberti, 2008). However, nano-biotechnology includes biological screening, chemical engineering, material science, mechanical synergy, electro-spinning, and microelectronics. Nanobiotechnology is the application of nanomaterials or nanodevices to biological processes, such as illness therapy. Nanotechnology helps the medical field grow quickly by combining engineering and medicine (Asadipour et al., 2023).

Nanoparticles are particles smaller than 100nm that possess new size properties in contrast to larger particles. Based on their properties, nanoparticles are categorized into a number of types as shown in Figure 1, including drug-conjugated protein nanoparticles, which are a type of nanomedicine that uses proteins to deliver drugs, liposomal nanoparticles, which are spherical nanocarriers used to deliver drugs and other bioactive materials, polymeric nanoparticles, which are solid particles made of natural or synthetic nanosized polymers (Malam et al., 2009). The other different sorts incorporate dendrimeric nanoparticles, which are circular, nano-sized particles with a clear cut structure and utilized in different applications, like medication conveyance and diagnostics, and hydrogels, which are three-layered networks made of hydrophobic polymers that are made by crosslinking water-solvent polymers (Tiwari & Tiwari, 2013).

The main progression in nanobiotechnology is the creation and utilization of nanoparticles and their uptake by the objective tissue. Nanobiotechnology provides excellent models to improve patient care (Asadipour et al., 2023). Nanotechnology offers different chances to work on the treatment of illnesses. It is recommended that nanobiotechnology convey the right medicine to the objective tissue at the right second with exactness, proficiency, speed, and security (Jain, 2005). Nanomedicine, also known as nano-biotechnology, is a rapidly developing field and the most innovative use of it is in the manufacturing of drug delivery systems at the moment. In the drug delivery system, the particles are designed in such a way that they are attracted toward the cells of the patient and make the environment perfect for the cells to receive the targeted treatment. This makes early diagnosis of disease and less damage to healthy cells (Wilczewska et al., 2012). This chapter explores the innovations in nanotechnology and biotechnology for combating cancer, Malaria, and neurodegenerative diseases.

Nano-biotechnology in Cancer

Cancer is the main cause of death and a significant global health problem. It was estimated that there would be 9.6 million deaths due to cancer and 18.1 million new cases of cancer by 2019 (Dakubo & Dakubo, 2019). Cancer is a disease that occurs when cells proliferate out of control and move to other areas of the body, and cause death. Early identification and therapy of tumors are essential for decreasing sickness spread and mortality. These days, quite possibly the most well-known approach in disease research is nanotechnology (Chaturvedi et al., 2019).

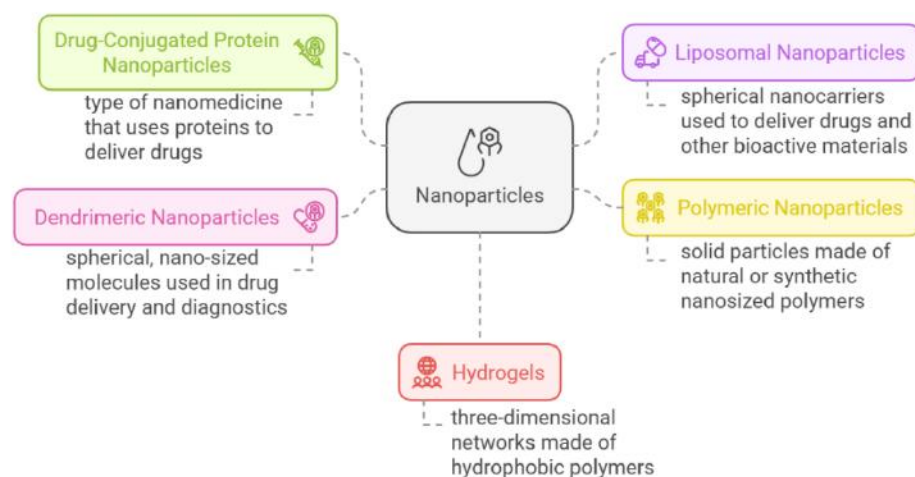


Fig. 1: Types of nanoparticles (Biorender)

Nano-biotechnology in Cancer Diagnosis

Tumors can be classified as malignant and benign. Benign tumors are restricted to the site of disease and don't spread to local tissues while malignant tumors are not restricted and effectively produce cells that spread to local tissues and different organs (Purysko et al., 2014). Early detection and stopping the growth and spread of cancerous cells to neighboring tissues are the goals of cancer diagnostic and therapeutic strategies. Computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and ultrasound are important early cancer diagnosis techniques (Saisho & Yamaguchi, 2004). These imaging techniques are restricted by their failure to give huge clinical information on the stage and different types of cancer. As a result, it can be difficult to get a comprehensive assessment of the disease that permits the administration of the most effective therapy (Bi et al., 2019).

According to studies published in different researches shows that cancer imaging at the tissue, cell, and subatomic level can be examined using nanotechnology (Moiz et al., 2025). For instance, the pH reaction to fluorescent nanoprobe can be utilized to recognize fibroblast-enacted protein-a on the cell film of growth-related fibroblasts (Dutta et al., 2025).

1. Near Infrared (NIR) Quantum Dots

Close to Infrared Quantum Dots are fluorescent gadgets that produce light in the near infrared locale (700-900nm) of the electromagnetic range. They are more reasonable for imaging lymphoma, pancreatic disease, liver malignant growth, and colorectal malignant growth (Cho, 2021). A second close infrared (NIR) window (NIR-ii, 900-1700 nm) has been created to make malignant growth imaging simpler. This wavelength range provides a higher temporal and spatial resolution and can penetrate deeper into tissue (Kenry et al., 2018). The creation of silver-rich Ag₂Te quantum dots (QDs) via a sulfur source has been explained as allowing for the identification of higher spatial goal images across a wide infrared spectrum (Sung et al., 2024).

2. Nanoshells

Dielectric cores with a diameter of 10–300 nanometers are called nanoshells. They typically consist of silicon and have a thin coating of metal, usually gold. These nanoshells can be optically adjusted flexibly using UV-infrared emission/absorption arrays and function by converting electrical energy mediated by plasma into light energy. Nanoshells are desired because their imaging lack of heavy metal toxicity, but the fact that their huge size restricts their application (Malhan et al., 2024).

3. Colloidal Gold Nanoparticles

Gold nanoparticles (AuNPs) can both actively and passively target cells. The permeability tension effect (EPR) in tumor tissues defines the passive targeting concept, which is a collection of gold nanoparticles to upgrade imaging. However, in order to achieve AuNP active targeting of tumor cells, AuNPs are coupled using tumor-specific targeted medications, for example EGFR monoclonal antibodies (Georgeous et al., 2024). Using X-ray imaging, researchers that combination AuNPs with liver cancer cells discovered the collection of the cancer cells in the gold nanocomposite set were noticeably larger and powerful than those in the liver cancer cells alone. These findings significantly affect early detection because the method can identify cancers as tiny as a few in the body millimeters in diameter (Her et al., 2017).

Cancer treatment using Nano-biotechnology

The treatment of cancer is one of the current issues facing medical science. Current therapies may include chemotherapy, radiation, and surgery, however, the results of these techniques may damage not only the tumor but also healthy tissue (Debela et al., 2021).

Nanobiotechnology is capable of revolutionizing the diagnosis and treatment of cancer. Nowadays, there are three ways to cure cancer: chemotherapy, radiation therapy, and surgery (Jin et al., 2020). These therapies also cause concerns for healthy tissues, which further explains each of these approaches and aids in the use of nanoparticles in these treatments (Mosleh-Shirazi et al., 2022).

A) Chemotherapy

Chemotherapy causes malignant tissue to accumulate TNF α , a tumor-killing factor. TNF attaches itself to the polyethylene glycol-coated gold nanoparticle (which is made from THIOL), making it immune system invisible. This will prevent the nanoparticle from being attacked as it moves through the bloodstream (Bhatia & Bhatia, 2016).

B) Radiation Therapy

Auro-Shell™ is a novel radiation therapy technique for eliminating cancerous tumors. Auro-shells are around 20 times smaller than red blood cells and consist of a silica core encased in a thin covering of gold (Sindhu et al., 2021). Auro-Shell™ nanoparticles enter through the bloodstream of the patient to cancer tissue vasculature. When nanoparticles accumulate inside tumor tissue, the tissue is exposed to infrared radiation. This radiation is absorbed by Auro-Shell™ nanoparticles, which then cause the tumor cells to specifically degrade through heat accumulation (Asadipour et al., 2023).

C) X-ray Therapy

Among the nanoparticles that have a strong potential for X-ray therapy-induced tumor tissue destruction is NBTXR3. In this procedure, NBTXR3, also known as PEP503, is directly injected into tumors using a syringe. X-rays stimulate the NBTXR3 nanoparticles, and electrons are released from these nanoparticles that destroy tumor tissue. As such, the tumor cell is broken down. Healthy cells and tissues are least in danger from this sort of radiation. (Asadipour et al., 2023).

Nano-biotechnology in Malaria

Plasmodium parasites spread malaria, an infectious disease that is conveyed by infected Anopheles mosquitoes. Malaria is a serious global health issue, particularly in places with limited access to medical care (Kogan & Kogan, 2020). Malaria is one of the biggest causes of morbidity and mortality worldwide and with estimation, it caused 229 million cases and over 400,000 fatalities in 2019 alone (Patel et al., 2024). Rapid diagnostic tests (RDTs) and microscopy are instances of traditional demonstrative techniques with restricted awareness, particularly for people with low parasitemia. Two significant obstacles for antimalarial drugs are emerging resistance and inadequate absorption (Hanboonkunupakarn & White, 2022). Nanotechnology offers better approaches to take care of these issues with delicate diagnostics, further developed drug conveyance strategies, and precise focusing (Dessale et al., 2022).

Nano-biotechnology in Malaria Diagnosis

For the management and control of malaria, a prompt and precise diagnosis is crucial. Nanotechnology can improve the sensitivity, specificity, and accessibility of conventional malaria diagnostic methods in detecting low parasitemia cases particularly (Guasch-Girbau & Fernàndez-Busquets, 2021).

Rapid diagnostic tests (RDTs) are utilized to analyze malaria in view of their convenience and speedy reaction (Wongsrichanalai et al., 2007). The use of nanoparticles, such as gold nanoparticles (AuNPs) and magnetic nanoparticles (MNPs), has improved performance on RDT platforms. When contrasting AuNPs functionalized with antibodies or aptamers to standard RDTs, the first may detect malaria-specific biomarkers at lower parasite levels due to their higher sensitivity (Ha et al., 2018).

Nanostructured biosensors have a high sensitivity and specificity for detecting malaria biomarkers (Krampa et al., 2020). These biosensors record and transform molecular interactions into measurable signals and offer immediate identification. Nanomaterials' affinity for malaria antigens is enhanced when functionalized with specific receptors or aptamers, allowing immediate diagnosis with minimal sample preparation (Ragavan et al., 2018).

Nano-biotechnology in the Treatment of Malaria

Nanobiotechnology targets the parasite directly and offers effective treatment options for the eradication of malaria. The following are a couple nano-biotechnological drives that make treating malaria simple and secure.

a) **Nanoparticle-based Drug Delivery Systems:** Nanoformulations increase the effectiveness of currently available antimalarial medications by improving absorption, extending their half-lives, and targeting parasites within host cells (Keleş et al., 2024). To enhance absorption by infected cells and prevent degradation, hydrophobic antimalarial medications like chloroquine or artemisinin derivatives can be encapsulated in lipid-based nanoparticles, polymeric nanoparticles, or nanocrystals (Alven & Aderibigbe, 2020). Antimalarial drugs can be precisely delivered to erythrocytes or hepatocytes infected with *Plasmodium* using functionalized nanoparticles. Modifying the surface with ligands specific to parasite receptors encourages selective absorption, lowering side effects and the amount of medication needed (Kunjiappan et al., 2021). This method improves medication effectiveness and delays the emergence of drug resistance.

b) **Nanovaccines and Immunotherapeutics:** Nanotechnology gives novel platforms for the development of malaria vaccines by facilitating controlled release kinetics, boosting immunogenicity, and improving antigen storage (Borgheti-Cardoso et al., 2020). Adjuvants with a nanostructure, including lipid-based nanoparticles or virus-like particles (VLPs), encourage strong immune responses and provide persistent protection against Plasmodium species. It is possible to create nanoparticles to alter immunological responses, strengthening the host's defenses against malaria parasites. When paired with antimalarial medications or vaccines, immunomodulatory nanoparticles loaded with cytokines, immunostimulatory molecules, or RNA-based therapies enhance both innate and adaptive immune responses and provide synergistic effects (Lima et al., 2023).

Nano-biotechnology in Neurodegenerative Disease

The term "neurodegeneration" describes the state in which neurons in the central and peripheral nervous systems deteriorate. When it affects the central nervous system, it results in symptoms such as amyotrophic lateral sclerosis, Parkinson's disease, Huntington's disorders, Alzheimer's disease, and other less frequent illnesses (Jellinger, 2010). Alzheimer's disease (AD) causes approximately 60% of dementia, which affects over 24 million people globally. Alzheimer's disease affects 1% of people between the ages of 50 and 70, and its prevalence rapidly rises to 50% of people over 70 (Association, 2019). Alzheimer's disease is a biological process that starts when amyloid plaques and neurofibrillary tangles, which are protein accumulations, accumulate in the brain. As a result, the brain gradually shrinks and its cells die (Ahmed et al., 2018).

The most common symptoms of Parkinson's disease (PD) include bradykinesia, rigidity, and resting tremor, which are caused by the irregular deterioration of nigrostriatal dopaminergic neurons in the midbrain and a subsequent decrease in brain dopamine (DA) levels. One percent of those over 65 have Parkinson's disease (PD). At most 5% of cases are familial or hereditary, indicating that genetic aspects are distinctly rare (Radhakrishnan & Goyal, 2018).

The biggest challenge to treating all NDs remains the delivery of drugs to the due to the numerous protective barriers that envelop the central nervous system. The development of nanotechnology may provide a way to overcome these challenges with Alzheimer's disease and Parkinson's diagnosis and neurotherapy (Ning et al., 2022). Therefore, nanotechnology can be used to create tools for diagnosis and delivery systems that can bypass the blood-brain barrier to enable both traditional and innovative neurotherapeutic approaches.

Nanostructures used in Neurodegenerative Disease Treatment

Most drug delivery technologies used in nanotechnology to treat NDs are polymeric nanoparticles. The ability of polymeric nanoparticles to penetrate tight cell junctions, travel the blood-brain barrier, attain target the mutagenic proteins and possess a high drug-loading capacity in Alzheimer's disease and Parkinson's disease makes them suitable for treatment (Kumar et al., 2022).

Polymeric Nanoparticles, Nanocapsules, and Nanospheres

Nanocapsules and polymeric nanoparticles have a size range of 10–1000nm. Their strong drug-loading capabilities and ability to prevent degradation of the incorporated drug load increase the probability that the drug will reach the brain (Zorkina et al., 2020). Their capacity to change their surface properties to stay away from reticuloendothelial framework macrophage discovery makes them dependable and equipped for conveying medications to the focal sensory system (Wu et al., 2023). Drugs are dispersed all through thick polymeric lattices called nanospheres, which are made by miniature emulsion polymerization. Though the flimsy polymeric envelope of a nanocapsule encases an oil-filled empty, the strong center of a nanosphere is encircled by a thick polymeric grid.(Khalid & El-Sawy, 2017).

Polymeric Nanogels and Nanosuspensions

Networks of cross-connected polymers, known as nanogels, are made by the emulsification dissolvable dissipation strategy and commonly involve ionic and nonionic polymeric chains. (Mauri et al., 2021). Particles like oligonucleotides, siRNA, DNA, proteins, and low-sub-atomic mass prescriptions can be remembered for nanogels on the grounds that they enlarge in water. Drug-stacked nanosuspensions comprise of glass like drug particles balanced out by lipid blends or nonionic surfactants. The straightforwardness, high medication stacking limit, and reasonableness for a large number of prescriptions for CNS conveyance are a portion of the primary advantages of nanosuspensions (Zingale et al., 2022).

Polymeric Nanomicelles

Polymeric nanomicelles have a center shell structure, with a hydrophilic polymer block shell encompassing a hydrophobic center. The center can forestall early medication debasement and delivery by amounting to 20-30% w/w of hydrophobic drugs. (Movassaghian et al., 2015). While keeping the nanomicelles steady, the shell prevents the medication from communicating with serum proteins and bothersome cells. After arriving at the objective cells, the medicine is delivered through dispersion. (Tewabe et al., 2021).

Polymeric Nanoliposomes

The vesicular designs known as nanoliposomes are made out of uni-or multilamellar lipid bilayers encasing inward water compartments. Presenting similarly a lot of medications to the lipid bilayers or the fluid compartments of liposomes is conceivable. (Bozzuto & Molinari, 2015). Longer fundamental dissemination times can be accomplished by nanoliposomes with changed surfaces that lessen opsonization in plasma and the liver and spleen's capacity to perceive and eliminate them. To assess nanoliposomes for designated CNS drug conveyance, various applications have been examined.(Terstappen et al., 2021).

Conclusion

Biotechnology and nanotechnology have made it possible to identify, cure, and prevent neurological disorders, malaria, and malignant development. Nanotechnology has significantly enhanced cancer imaging through NIR, quantum dots, nanoshells, and gold nanoparticles while also improving treatment outcomes and reducing damage to healthy cells. For malaria, nanotechnology has improved rapid diagnostics by using nanostructured biosensors and treatment efficacy by developing novel nanoparticle-based drug delivery systems and nanovaccines. Nanostructures have shown extraordinary potential in the treatment of neurodegenerative diseases by precisely focusing on the harmed brain regions and crossing the blood-brain barrier (BBB). Even though nanobiotechnology is still in its beginning stages of research, it can profoundly change medical care all around the world. These technologies have the potential to greatly improve patient outcomes, treat illnesses more effectively, and help create a future where complex diseases are treated more precisely and with fewer side effects if they can overcome their current limitations.

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Integrating Nanotechnology and Biotechnology in Holistic Health: New Frontiers in Therapeutics

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Abstract

Nanotechnology and biotechnology are transformative fields that offers a prime potential for providing advancement in health and therapeutics. Nanotechnology involves application of tools that allow for direct control of materials at the atomic or molecular level by modifying such substances that can be used to create drug delivery systems at the nanoscale, nanoscale diagnostic or therapeutic agents. On the other hand, biotechnology utilizes the biological components of living organisms to provide treatments as gene therapies, recombinant proteins and vaccines. Integration of nanotechnology with biotechnology marks the key trend of the today's medical world that led to the age of precision medicine where the concept of targeted drug delivery system to improve the effectiveness of the treatment while minimizing side effects. Nanobiotechnology has applications of curing ailments as cancer, neurodegenerative disorders as well as some infectious diseases. Nanobiotechnology, this cross-disciplinary approach presents the possibility of introducing a new therapeutic method that could revolutionize total health care and result in better care of patients all over the world. This chapter will analyze the close connection between these two crucial fields and will focus on innovative strategies that address critical challenges in medical science.

Keywords: Nanotechnology, Biotechnology, Nanobiotechnology, Therapeutics, Holistic health, Gene therapy

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Introduction

Holistic health appears frequently in the literature that has a wide range of implications. A person is considered healthy if he is free from mental as well as physical disorders (Akyildiz et al., 2015). In order to improve health and reduce illness, it aims to maintain a balance of the entire living organism (Levine et al., 2022). Holistic health is frequently considered as a substitute to traditional drugs and occasionally coupled with complementary therapies, that's why it is termed as integrated medicine (Song et al., 2022). To create the most effective medical care around worldwide, the modern, updated system of healthcare should aim to integrate the best aspects of whole-person health and traditional care (Levine et al., 2022).

Humans have been studying "nano"-sized existence for a long time and Richard Feynman's 1959 speech at the American Physical Society dinner, "There's plenty of room at the bottom," contained the first scientific report on nanotechnology (Jain & Jain, 2008). Nanoscale research and nanotechnology are predicted to make significant progress in the fields of the agricultural sector, electronics, healthcare, and energy (Ghorbanpour and Hatami, 2015). In addition to detecting a wide range of physical ailments (Akyildiz et al., 2015), it is anticipated that Internet of Bio-Nano Things (IoBNT)-based health care will be used extensively to treat psychological issues as well (Bonoiu et al., 2009). The focus of modern biotechnology on human healthcare extends across decades through research in drugs and diagnoses as well as treatments of different diseases and genetically modified food production alongside genetic therapies. Additionally, the human genome project operates as part of biotechnology to both interpret human genetic code and substitute defective genes. All methods and techniques associated with biotechnology have demonstrated exceptional growth during the recent years. Scientists must continue their major efforts to develop new vaccines and drugs and genetically modified crops as well as resistance against multiple pests through multiple biotechnological approaches (Gupta and Chaphalkar, 2016).

Nanobiotechnology has developed a wide range of fields including drug delivery, diagnostics, therapeutics, regenerative medicine and point-of-care diagnostics (Haleem et al., 2023). It can enable the formulation of innovative nanomedicines with minimum side effects. Furthermore, this innovation has made it practical to use molecular self-assembly to study the overall structure of matter in materials science (Xue and Mansoori, 2010). Lithography, ion exchange, adsorption, drug design, catalysis, composites, and plastics are a few examples of these advanced techniques. The intersection of biotechnology and nanotechnology is a revolutionary area of scientific research, especially in the study of human health. Nanobiotechnology uses the special qualities of nanoparticles to solve problematic issues in the medical field (Malik et al., 2023). Nanobiotechnology provides a better future and has the ability to considerably deal with a number of global concerns, featuring avoidance of illnesses, food availability, and sustainability of the environment (Iqbal et al., 2024). In this chapter, we will discuss the integrative role of nanotechnology and biotechnology to improve the approaches to treatment, diagnostics and healthcare.

Biotechnology in Holistic Health

The concept of biotechnology was first brought into use by Karl Ereky in 1919 (Gupta et al., 2017) and the term refers as the use of biology or molecular engineering to manufacture and deliver biologic products for the treatment of ailments (Evens and Kaitin, 2015). It incorporates virtually all branch of scientific use in different fields as health and food production. It applies the chemical processes occurring in living organisms, molecular biology and the use of cells to provide new methods of production and product development approaches i.e. production of vaccines against diseases, bacteria that are useful in oil spillage cleaning or genetically modified plants (Gupta and Chaphalkar, 2016). Biotechnology today is an essential tool in the gene therapy diagnostics, fabrics and clothing, development of drugs, fish farming, chemical manufacturing, crime scene investigation and much more (Ghaffar et al., 2024). They help in the reduction of food toxins, availability of health related products through disease resistance crops, cloning organs transplantation, high quality food production, transgenic animals, that play useful roles in the survival of humans and ensuring food security for the world population (Awais et al., 2010).

Biotechnology allows industries to create completely revolutionary products at a faster pace, and with lesser time and money (Gupta et al., 2017). Biotechnology is integrated in the healthcare industry through diagnostics test kits as well as biological therapeutics labeled with radioactivity for imaging (Afzal et al., 2016). Immunological assays and DNA based methods, Polymerase chain reaction (PCR) and NAAT along with microarray technology is used in diagnosing different diseases and in identifying gene mutation. Furthermore, the application of biotechnology is useful in the preparation of single cell protein, spirulina, enzymes and solid state fermentation in food processing sector (Gupta et al., 2017).

Genetic Engineering and Gene Therapy

Gene therapy can be defined as a process of genetic enhancement of cells by direct modification of its mutated genes or through site specific planned intervention for therapeutic purposes. This therapy has potential due to the development of vectors to deliver extrachromosomal material to targets cells as facilitated by genetics and bioengineering. One of the important criteria of this technique is the choice of the delivery vehicles usually it includes: plasmids, nanostructures or viruses (Goncalves and Paiva, 2017). Classification of gene therapy depends on the type of disease being treated: genetic or complex acquired conditions, gene delivery system: integrating vs non-integrating and on vector administration: *in-vivo* and *ex-vivo* (Anguela and High, 2019). Gene therapy is mainly practiced in research laboratories all over the world and its use is not limited, it has the potential for the treatment of recessive gene deficiency diseases including hemophilia, muscular dystrophy, cystic fibrosis, sickle cell anemia and other acquired inherited diseases as certain virus infections, as AIDS (Misra, 2013).

Biotechnology in Medicine and Nutrition

Progress in today's biotechnology has reached a level that creates the enabling technologies needed to treat these rare and devastating diseases. Major specific objectives of medical biotechnology are biopharmaceuticals, recombinant vaccines, DNA vaccines, bioinformatics, gene therapy, genomics, proteomics and biomedicines. Ever since the humans' genome was sequenced in 2001 biotechnologists have made tremendous effort in pinpointing specific genes that correspond to certain disorders. Many genes associated with diseases including cardiovascular diseases, cancer, respiratory diseases, mental disorders have been identified. Duchenne muscular dystrophy, Huntington's disease, thalassemia, phenylketonuria, hemophilia, Lesch-Nyhan syndrome and sickle cell anemia are some of the promising candidates for gene therapy (Zand and Narasu, 2013).

Vaccination is one of the most important product of biotechnology and has brought tremendous values to human beings. Vaccines are biological agents formulated to induce immunity so as to make body recognize and destroy the pathogen against which an individual has been vaccinated (Bobbala and Hook, 2016). One of most important weapons at the global level for controlling the spread of communicable illnesses are vaccines. They have been of immense usefulness with the excision of smallpox in 1979, the cattle virus Rinderpest in the year 2011 (Greenwood, 2014). Biotechnology is being utilized in two key ways to enhance human nutrition: through raising crop availability particularly home-grown preferred staple crops in the developing world and through improving the quality of those foods in order to benefit populations in both the developed and the developing world. Crops which have been genetically altered to be immune to local pests are expected to enable even the small holder farmer to increase yields for the same investment in an eco-friendly manner. Furthermore, the existing genetic engineering technologies are being used to introduce vaccines into the foods we eat (Mackey, 2002).

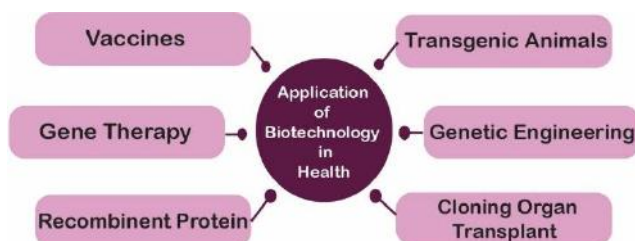


Fig. 1: Applications of Biotechnology in Holistic Health: Vaccines, gene therapy, transgenic animals, recombinant protein, gene engineering and cloning organ transplant.

Nanotechnology in Holistic Health

The science of nanomaterials and nanotechnology offer promise for material engineering and they are now the fastest-growing and most advanced scientific fields. It is the study of managing, constructing, and regulating systems according to their atomic or molecular requirements. Different nanoparticle formulations for medicinal and diagnostic uses have been developed as a result of recent developments in nanotechnology. The purpose of diagnostic nanoparticles is to show diseases and enhance comprehension of significant (pathos-) physiological fundamentals of different illnesses. Many therapeutic nanoparticles are currently used in clinical settings. Some well-known examples of clinically approved therapeutic nanoparticles are Doxil (PEGylated, doxorubicin-loaded liposomes, Janssen, Horsham, PA), Abraxane (paclitaxel-containing albumin nanoparticles, Celgene, Summit, NJ) and AmBisome (liposomal amphotericin B, Gilead, Foster City, CA); numerous other nanomedicine formulations are presently undergoing preclinical and clinical trials (Phillips et al., 2014).

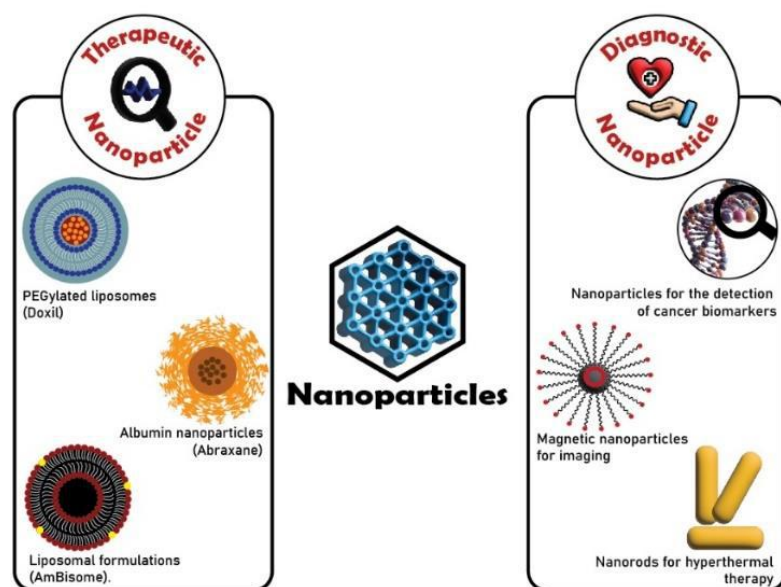


Fig. 2: Therapeutic properties of Nanoparticles: PEGylated liposomes Doxil), Nanoparticles for the detection of cancer biomarkers, albumin nanoparticles (Abraxane), liposomal formulations (AmBisome), magnetic nanoparticles for imaging and nanorods for hyperthermal therapy.

Diagnostic applications of nanoparticles are still trailing behind therapeutic ones. It is an easy way to manipulate the size, shape, and surface functionality of nanoparticles at the nanoscale through recent developments in nanomaterial technology. There are numerous opportunities to use nanomaterials for early cancer diagnosis and treatment because the majority of biological activities, including those linked to cancer, take place at the nanoscale (Lee, 2007). For instance, a variety of hollow nanoparticles particularly liposomes, porous silica nanoparticles, gold nanoparticles, carbon nanotubes and silicon nanowires for the detection of cancer biomarkers, quantum dots and magnetic nanoparticles for in vivo imaging of early-stage tumors and gold nano-shells and nanorods for hyperthermal therapy are among the many engineered inorganic and organic nanomaterials being used in preclinical medicine (Gobin et al., 2007).

Drug delivery nanoparticles are typically less than 100 nm in at least one dimension and are made of many disintegrating substances, including metals, lipids, and natural or manmade polymers. Since nanoparticles are more readily absorbed by cells than bigger micromolecules, they may be employed as efficient delivery and transportation vehicles (Stylios et al., 2005). Drug bioavailability, pharmaceutical targeting, and the absorption of less soluble medications can all be enhanced by the use of nanoparticles in precise drug delivery at the site where disease occurs. Nanomaterials have been successfully used in the preparation of anti-cancer drugs such as doxorubicin, dexamethasone, 5-fluorouracil and paclitaxel (Suri et al., 2007; Salar et al., 2024).

Different nanotechnological approaches including liposomes, liquid crystal (LC) systems, microemulsions, polymeric nanoparticles, solid lipid nano-particles (SLNs) and precursors systems for liquid crystals (PSLCs) have been developed to overcome this interfacial barrier. This multidisciplinary approach to drug formulation is capable of modifying the structural and functional attributes of the drug as well as altering its performance in vivo and these innovations have revolutionized the field of targeted drug delivery. In addition to enhancing the use of active ingredients, the new drug delivery systems can reintroduce other ingredients that were previously removed from the formulation because they were not useful (Mara Mainardes et al., 2006). Moreover, the method is equally more appealing with the possibility of enhancing new compounds before commercialization or therapeutic application, including enhancing selectivity and usage, avoiding thermal or photo degradation, reducing side effects, and controlling the release of active constituents (Bonifacio et al., 2018).

There is an increased demand for tissue engineering and regenerative medicine (TERM) due to the various disadvantages of tissue and organ transplantation, such as the lack of donors, the need for immunosuppression and the low success rate (rejection of the transplant) (Fathi-Achachelouei et al., 2019). The objective of the new broad field of regenerative medicine is to maintain, enhance or restore tissues and consequently the functions of organs. Living cells, which will give biological functioning and materials, which serve as scaffolds to enable cell growth, can work together to regenerate tissues (Engel et al., 2008).

Drug delivery, heart muscle and vascular grafts are a few of the cardiovascular tissue engineering fields for which nanomaterials and nanotechnologies have been extensively examined so far. There are several phases of nanotechnologies of cardiovascular regenerative therapy in this special issue (Omidian et al., 2023). The cardioprotective effect of drugs in patients with cardiovascular disease can be enhanced by nanomaterials that deliver such drugs. There are several applications of nanomaterial-drug delivery systems in cardiovascular imaging and treatment of various cardiovascular diseases (Deng et al., 2020). Cardiovascular diseases are usually diagnosed by biomarkers or molecular imaging (MOI). The sensitivity, specificity and accuracy of the assay in the early stages of cardiovascular diseases remain challenging to attain. Cardiovascular disease (CVD) is presently diagnosed with cardiac biomarkers and imaging methods. The application of various nanotechnologies to improve the efficiency of cardiac immunoassays and molecular imaging to diagnose cardiovascular diseases in their initial stages was also in consideration (Shi et al., 2020).

Overview of Intersection of Nanotechnology and Biotechnology

Biotechnology and nanotechnology are the most remarkable new fields of research in the current century. Nanobiotechnology is the intersection of these two fields of research, which uses both nanotechnology and biotechnology to construct a broad range of applications as

well as examine and construct nanobiosystems to address a range of challenges (Amin et al., 2011). The intersection of nanotechnology and biotechnology has revolutionized the scientific research, particularly, in the domain of human health. Materials exhibit specific features at the nanoscale to allow an accurate manipulation and interaction with the biological system, thus creating a variety of possibilities that would assist in dealing with major problems globally (Hassan and Fathi, 2024). Subsequently, nanotechnology and biotechnology work together to transform diagnosis, treatment, and medicine (Podutwar et al., 2024).

Table 1: Applications of Nanobiotechnologies

Nanobiotechnologies	Applications	References
Electrochemical biosensors	Detection of cancer cells	(Karnwal et al., 2024)
Nanosphere's Clear Read	Detection of SNP	(Alharbi and Al-Sheikh, 2014)
Nanoparticles-based liquid biopsy	Detection of ctDNA, circulating tumor cells, protein, peptide, miRNA and exosomes	(Kim et al., 2024).
Nanofluidic Chip	Dignosis of eurological disorders, infectious diseases, cardiovascular diseases (CVDs), and autoimmune diseases	(Kim et al., 2024).
Lab-on-a-chip (LoC) technology	Analyse bacterial,viral, and parasitic diseases	(Rosenberg and Restifo, 2015)
(CRISPR)/Cas9 system	Gene therapy	(Kim et al., 2024).
Nanoparticle-based drug delivery systems	Cancer treatment and transportation of anticancer agents,	(Elumalai et al., 2024).
Nano-stent	Regeneration of islet β cells, retinal tissue, wound tissue and nerve tissue cells	(Li et al., 2022).

Applications of Nanobiotechnology

Recently, nanobiotechnology has been revolutionizing important areas of molecular biology, including cellular and molecular diagnosis and therapy (Mohanty et al., 2009). In comparison to traditional methods, cancer cells can be diagnosed and treated using nanobiotechnologies including biosensors, nano-probes, and contrast enhancers (Sun et al., 2024). In electrochemical biosensors, gold nanoparticles (AuNPs) can be functionalized by binding specific biomolecules, including antibodies, DNA probes, or aptamers, enabling the extremely sensitive and selective detection of target analytes (Karnwal et al., 2024). A microarray-based technique for the detection of numerous single nucleotide polymorphisms (SNP) in complete human genomic DNA is made possible by Nanosphere's Clear Read nanoparticle technology, despite the requirement for target amplification by PCR (Alharbi and Al-Sheikh, 2014). One of the newly emerged techniques, nanomaterial-based liquid biopsy, utilizes optical nanomaterials for the detection of circulating tumor DNA (ctDNA), protein, peptide, miRNA, exosomes, and circulating tumor cells (CTCs) in biofluids, making it possible to detect a wide range of diseases, including cancer. Similarly, nano/microfluidic chip technology is utilized to diagnose neurological diseases, infectious diseases, cardiovascular diseases (CVDs), and autoimmune diseases (Kim et al., 2024). Moreover, most of the bacterial, viral, and parasitic infections such as HIV/AIDS, malaria, and chronic respiratory infections are diagnosed and treated using Lab-on-a-chip (LoC) technology. Furthermore, cancer detection and targeting is achieved by imaging with quantum dots (Chakraborty et al., 2011).

Additionally, in nanobiotechnology nanomaterials can be utilized in particular therapeutic interventions such as photothermal therapy (PTT) and sonodynamic therapy (SDT) that can be applied together with other therapies in order to enhance the efficiency of treatment (Ji et al., 2023). One of the most important part of gene therapy, the gene-editing tool known as the clustered regularly interspaced short palindromic repeat (CRISPR)/Cas9 system utilizes nanomaterials as non-viral vectors for the recognition and cleavage of particular sites of DNA (Kim et al., 2024). Nanoparticle-based drug delivery systems (liposome- or dendrimer-based systems) are utilized in cancer therapy to enhance the delivery of anticancer drugs, minimize widespread toxicity, and enhance the efficiency of treatments (Elumalai et al., 2024). Nanomaterial-based technologies are commonly used to regenerate bones, cartilages, muscle, skin, and teeth. Nanomaterials play a central role in the advancement of regenerative medicine because nanomaterials improve cell adhesion, tissue regeneration, and cell proliferation scaffolds (Fathi-Achachelouei et al., 2019). Besides this, nano-stent is also a potential method for regenerating islet β cells, retinal tissues, wound tissue and nerve tissue cells. Most nanoparticles also accelerate the process of wound healing and provide other benefits that have overcome many issues in the clinical use of regenerative medicine (Li et al., 2022).

Nanobiotechnology is a rapidly growing field that produces new products for a variety of industries by merging the concepts of biology with nanotechnology. Nanobiotechnology has gained considerable interest in the recent times owing to its potential to completely transform the food, pharmaceutical, packaging, nutrition, and agriculture sectors. Promising results in various medical fields including, tissue engineering, and drug delivery medical imaging have been shown by nanobiotechnology. Nanobiotechnology-based antimicrobials have also been developed to combat the increasing problem of antibiotic-resistant bacteria. In short, nanobiotechnology is paving the road for a better future and has the potential to significantly solve numerous global concerns, particularly preventing diseases, food security, and a sustainable environment (Iqbal et al., 2024). On the other side, nanobiotechnology has several constraints including nanoparticles toxicity, potential environmental concerns, relatively inexpensive, and minimal input of energy, that have to be managed (Tripathi and Prakash, 2022).

Challenges and Future Directions

Nanobiotechnology is encountering numerous obstacles that must be overwhelmed. Developing effective tools to measure nanomaterial contact with air and water is one of the main obstacles. To avoid negative effects, human intake of air and water contaminated with nanomaterials must be regulated. This issue becomes more detrimental while discussing the contamination of consumables, such as food items, by nanomaterials. However, it would be unavoidable to do in vivo research using animal models to comprehend how these nanomaterials affect the environment and human health (Qamar et al., 2019). Since nanomaterials are so small (less than 100 nm), they can interact with biological

structures such as cell walls, organelles and nucleic acids to influence internal biochemical reactions. This is one of the key issues that can damage healthy and normal cells (Dutt et al., 2022).

Being able to find unique treatment plans for patients with serious medical conditions as cancer, heart disease and neurological disorders will be further improved in the future by the combination of nanobiotechnology with high-throughput genomic sequencing, transcriptomics and proteomics innovations. Specific medical advancements will be triggered by nanotechnology, which will make it possible to create distinct treatment strategies that are specific to each patient's needs and illness. By combining nanotechnology with modern imaging methods and techniques for machine learning, it will be possible to observe the progression of diseases in real time, reveal structural changes and provide personal therapy suggestions, all of which will enhance patient clinical results and standard of life (Qamar et al., 2019).

Studies must also concentrate on raising attention about the development of nanobased diagnostic tools. Nanotechnology related studies in medicine also need to speed up with FDA approval in order for physicians to effectively use in vivo trials as a preventive tool in hospitals. The concept of using herbal nanoparticles to transport chemotherapy medication into a selected tissue may also attract certain possible research teams and have noticeable effects. Thus, the use of "herbal remedies" within Nan-companies will increase their ability to treat a variety of chronic illnesses along with medical treatments (Arulanandraj et al., 2018). Nanobiotechnology has the potential to lead to significant advancements in personal health care in the near future. The accuracy and precision of the examinations could be further improved by employing nanodiagnostics. Accurate illness detection and therapeutic interventions may result from the discovery of novel and more distinctive nanoparticles (Qamar et al., 2019).

Conclusion

In conclusion, the integration of nanotechnology and biotechnology has played a significant role in holistic health and therapeutics. The coordination of these two fields has created opportunities for development of solutions to many health issues. The progressive developments in targeted drug delivery, individualized treatment, and regenerative medicine represent are the most promising ones. Moreover, the ability to manipulate biological systems at the molecular level offers the promise of safer, more sustainable therapies. These innovations could lead to breakthroughs in drug delivery systems, gene therapies, and diagnostic tools as PCR, addressing complex health challenges more effectively than ever before. As research progresses, the synergy between these fields will likely open new frontiers in medicine, leading to transformative approaches for treating a wide range of diseases and promoting overall well-being. This chapter highlights the new frontiers of nanotechnology and biotechnology, the potentials shall be realized as the risks are tempered. The future of holistic health can be without a doubt characterized as rather promising, as these new therapeutic approaches will shape the world's healthier and wealthier future.

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Role of CRISPR Technology in Prostate Cancer

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Abstract

Prostate cancer ranks at the top of the maximum communal forms of cancer in males. Prostate tumors develop gradually in the prostate gland and may not affect the prostate gland much, but are localized. Basic and applied research on beneficial gene modification has been at the lead of public scientific discourse for decades. Genome editing using applications like Cas9-based technology can be used to treat human diseases according along with ongoing clinical trials. Gene Therapy research and clinical trials emphasize prostate cancer research and treatment. Gene therapy is a propitious treatment possibility for prostate cancer due to some factors, involving anatomical considerations that allow direct tumor sampling and injections, provide preclinical immune-competent models, and recognize tumor-related antigens that may serve as targets for an induced immune system. “Chimeric Antigen Receptor” (CAR) T cell therapies and novel technologies utilizing CRISPR-Cas9-assisted technologies, such as vaccine-based immune stimulating treatments, are very promising and are now being researched in both the lab and the clinic. Future research holds enormous potential for the establishment of gene therapy in prostate cancer treatment, even though laboratory and preclinical advancements have not yet produced oncologically relevant outcomes in the clinic

Keywords: Oncology Research, CRISPR Technology, Global Health Challenge, CRISPR-Cas9, Gene therapy.

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Introduction

Every year, there are 1.6 million cases of prostate cancer (PCa) and 367,000 deaths due to the disease. PCa may be a frequent kind of cancer in the U.S.A and the 2nd worst killer of men from cancer (Mabjeesh et al., 2002). PCA in men can be treated majorly by androgen deprivation therapy (ADT) because androgens are important elements that encourage the growth of PCa cells (Mucci, 2018). The first line of treatment for this disorder is “Androgen Deprivation Therapy” (ADT), even though the condition typically advances to a more destructive form of the disease called “Castrate Resistant Prostatic Adenocarcinoma” (CRPC). To develop new prostate cancer treatments, there is an vital requirement to comprehend the molecular pathophysiology of CRPC and find fresh pharmacological targets (Huang et al., 2005).

2. Characteristics Associated with Prostate Cancer

Adenocarcinomas, which make up the majority of prostate tumors, have a lot in common with other common epithelial malignancies, including breast and colon cancer. The following are some crucial elements of prostate cancer that are important for examining the disease mechanisms.

2.1. Aging

Prostate cancer is closely linked to the aging process, with advanced age being the most critical risk factor for its development. While earlystage lesions, such as “Prostatic Intraepithelial Neoplasia” (PIN), can appear in men as young as their twenties and become increasingly common by their fifties, invasive prostate cancer typically becomes clinically detectable between the ages of 60 and 70. Notably, precursor lesions are far more prevalent, affecting approximately one in three men, compared to invasive carcinoma, which develops in only one in nine men (Bechis et al., 2011). This disparity highlights the distinction between the early initiation of cellular changes and the less frequent progression to invasive disease, which is heavily influenced by aging.

2.2. Environmental and Nutritional Factors

Epidemiologically, prostate cancer is a global problem but it is more prevalent in western countries as compared to Asia. Dietary habits,

environmental and personal patterns may be a major reason of this disparity as (Oczkowski et al., 2021; Yahya et al., 2021). Different investigations revealed that processed food like meat, milk and other items can also have impact on microbiota which ultimately imposed strong effects on prostate gland leading to cancer so pattern and choice food consumption is a highlighting concern (Matsushita et al., 2020).

2.3. Genomic Factor

Genetic affects are responsible for prostate cancer upto 10-20%. The early development of disease is mostly linked to genetic aspects. Various genetic aspects like BRCA1, BRCA2, HEK2 and PALB2 are recognized as causing agents of prostate cancer. Ovarian cancer and Breast cancer is also linked with these genetic aspects. Furthermore, mutations in genes like “PMS2, MLH1, MSH2, and MSH6”, linked to Lynch syndrome have been concerned in prostate cancer risk. While rare, germline alterations in high-risk genes can significantly influence treatment decisions and screening strategies in affected individuals (Abate-Shen et al., 2000; American Cancer Society, 2023; MedlinePlus Genetics, 2025).

Additionally, alterations in the “HOXB13” gene have been associated with early-onset prostate cancer, highlighting its role in familial cases. Despite advancements in identifying genetic risk factors, the molecular basis for the link between hereditary P.Ca and other cancers, such as breast cancer, remains unclear. Current research aims to uncover additional genetic variations that may contribute to prostate cancer susceptibility and improve clinical management

2.4. Effect of Steroids

Signaling of Steroid receptors is critical in all phases of prostate cancer development. In particular, there is a typical age-related decline in the proportion of androgens versus estrogens in men, which may be a contributive aspect in the instigation of prostate cancer (Bosland, 2000). Recent studies throw light on a major symptom of PCa that is alterations in androgen independency (Soronen et al., 2004).

3. Molecular Mechanisms of Prostate Cancer

Various variations in molecular mechanisms like genetic, signalling pathways and epigenetic variations lead to PCa. Alterations in TP53 gene and PTEN gene along with changes in oncogens i.e. ERG also leads to PCa. More oftenly observed alterations include combination of TMPRSS2 and ERG which causes aberrant transcriptional activity leading to PCa (Abate-Shen & Shen, 2010; Testa et al., 2019). Castration therapy is distributed by reduction of PTEN that promote cell multiplication and division by P13K/mTOR pathway (Taylor et al., 2010). Androgen receptor is crucial for development of PCa. Structural changes are observed in AR, when androgen such as testosterone and dihydrotestosterone bind to AR, like protein movement into nucleus from cytoplasm and also initiates transcription that control cell growth and reproduction (Ho & Dehm, 2017).

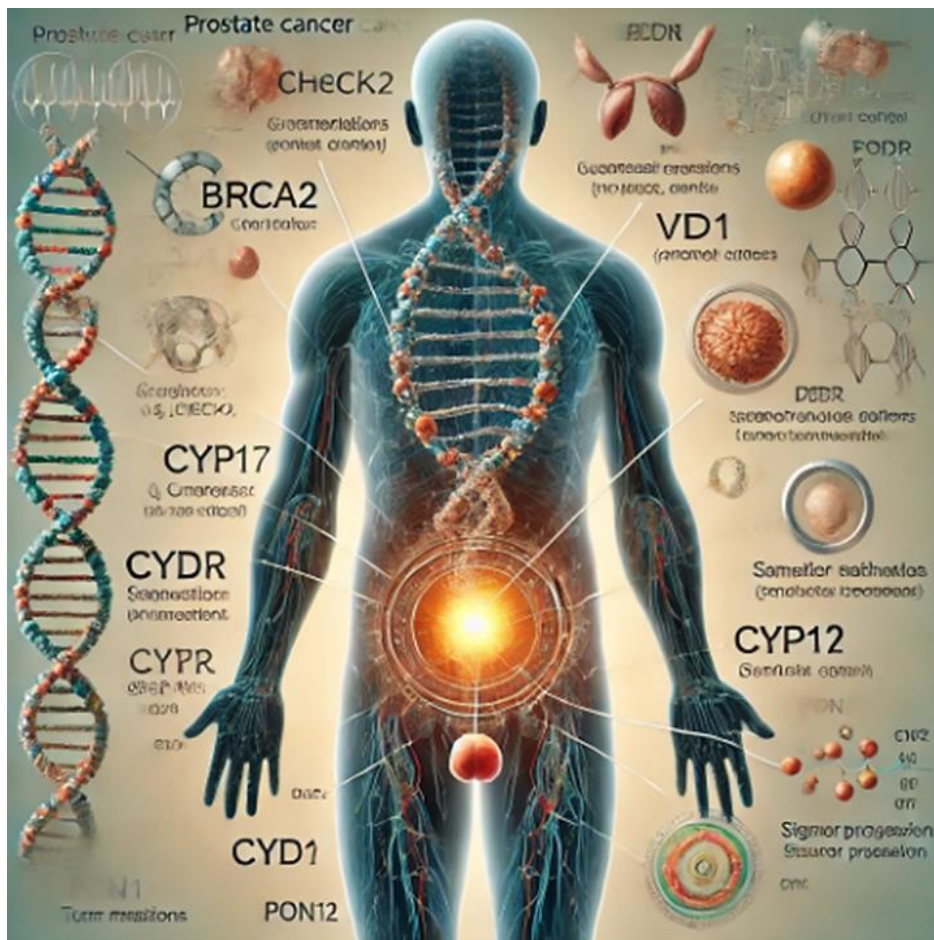


Fig. 1: Molecular Mechanism of Prostate Cancer

In PCa, gene methylation and histone alteration are essential genetic changes. These changes lead to oncogen ignition and may inhibit tumor suppressor genes (Figure 1). For instance, hypermethylation of PTEN is associated with malignant disease profile. Micro RNAs, including miR-379, has been found to play a crucial role in regulating metastasis in PCa. During metastasis, PCa cells often undergo epithelial cell into the mesenchymal transition, a process characterized by loss of cell polarity and adhesion properties. This process is frequently associated with down regulation of E-cadherin, a key molecule involved in cell adhesion. Due to this cancer cells penetrate extracellular matrices and also travel to bone marrow stroma. Matrix metalloproteinases (MMPs) are proteolytic enzymes which promote the metastatic dissemination. These studies about molecular mechanisms gives knowledge related to onset of disease, advancement of disease and resistant property of disease. Developing research including epigenetics, microRNA and immune checkpoint inhibitors offers advanced precision therapies of targeted disease (Ho & Dehm, 2017).

Histone modification and methylation of genes are critical epigenetic changes observed in PCa. These alterations can silence tumor suppressor genes or activate oncogenes. For example, hypermethylation of PTEN has been linked to aggressive disease phenotypes. Additionally, microRNAs such as miR-379 have been shown to regulate metastasis by modulating cell adhesion properties, providing potential therapeutic targets. PCa metastasis often involves E.M.T where cells lose polarity and adhesion properties mediated by E-cadherin downregulation. This enables cancer cells to invade extracellular matrices and migrate to distant sites like bone marrow stroma. Proteolytic enzymes such as matrix metalloproteinases (MMPs) also play a role by degrading barriers for metastatic spread. Understanding these molecular mechanisms provides insights into prostate cancer initiation, progression, and resistance to treatment. Emerging research on epigenetics, microRNAs, and immune checkpoint inhibitors offers promising avenues for developing targeted therapies.

4. Genes Related to Prostate Cancer

4.1. GSTP1

Prostate cancer frequently involves alterations to the glutathione S-transferase pi gene (GSTP1), and one typical mechanism that inhibits its interpretation is excessive methylation of its promoter region. An early event in prostate carcinogenesis, this epigenetic alteration is seen in approximately 6% of proliferative inflammatory atrophy (PIA) samples, 70-75% of prostatic intraepithelial neoplasia (PIN) cases, and 92.95% of prostate cancer cases (Nakayama et al., 2004). The detoxifying enzymes encoded by GSTP1 catalyze the conjugation of glutathione with toxic electrophilic chemicals, which can be generated internally or come from outside the body (Hayes & Pulford, 1995).

For cells to be protected from carcinogenic substances, this protective function is essential. Hypermethylation-induced decrease of GSTP1 expression highlights its tumor suppressive role by increasing oxidative DNA damage and promoting cancer cell survival under extended oxidative stress (Lin et al., 2009). Hypermethylated GSTP1 has been identified as a potentially useful prostate cancer diagnostic sign. The possibility for non-invasive diagnosis was demonstrated by the effective detection of GSTP1 hypermethylation in bodily fluids using techniques such as methylation-specific PCR (Jerónimo et al., 2002). Additionally, studies show that GSTP1 silencing is associated with the evolution of the disease from healthy tissue to malignant prostate cancer morphologies and preneoplastic lesions (PIN) (Yegnasubramanian et al., 2008).

Apart from methylation-induced silence, GSTP1 polymorphisms also affect the risk of prostate cancer. Variants such as Ala 114 Val and Ile 105 Val have been linked to changes in enzyme activity and regulatory effects on pathways including MAP K-JNK signaling, which affects the mechanisms of DNA repair, apoptosis, and proliferation in prostate cancer cells (Wang et al., 2012). But by totally suppressing GSTP1 expression in the later phases of the illness, promoter hypermethylation negates these polymorphic effects (Nakayama et al., 2004). All things considered, GSTP1 contributes significantly to prostate carcinogenesis through both genetic and epigenetic modifications. In addition to aiding in the growth of tumors, its early silencing through hypermethylation is a useful biomarker for prostate cancer risk assessment and early detection. (Yegnasubramanian et al, 2008; Lin et al., 2009)

4.2 NKX 3.1

The most likely factor for the frequently reported 8p deletion in prostate cancer is the “Human homeobox gene NKX3.1”, which is located at 8p21. Although, the deletion of the gene is probed in prostate cancer, the residual allele has not yet been found to have any mutations. However, it has been demonstrated that advanced tumour stage and hormone-refractory illness are related to the decrease of NKX3.1 expression. The likelihood of haploinsufficiency as a method to remove the tumour suppressive effect of NKX3.1 has been raised due to the nonexistence of alterations in the remaining allele of NKX3.1. Moreover, “NKX3.1p” (heterozygous) / and “PTENp/” compound mutant mice develop prostate cancer (Abate-Shen & Shen, 2010).

4.3 PTEN

The PTEN tumour suppressor gene is situated at 10q23, a location where cytogenetics, LOH, and CGH have frequently detected deletions in prostate cancer. Dual specificity phosphatase, which is encoded by the EN gene, controls important signal transduction pathways.

Phosphatidylinositol 3,4,5-trisphosphate is the primary target of its primary lipid phosphatase activity (PIP-3). PTEN downregulates the Akt/PKB signaling pathway, which encourages cell survival and opposes apoptosis, by dephosphorylating PIP-3. Molecular mechanisms of prostate cancer (Abate-Shen & Shen, 2010).

4.4. TP53

A crucial cycle regulator i.e. Tumor Protein TP53 gene which shifts G1 To S phase in cell cycle when mutated ultimately leads to malignancies. When DNA damage is present, TP53 can either cause apoptosis or stop the cell cycle to allow for DNA repair (Wyman & Kanaar, 2006).

4.5. AR

The relationship between androgens and prostate cancer development has been understood for more than 50 years. The androgen signaling pathways are reactivated throughout the advancement of hormone-refractory prostate cancer, according to more recent cDNA

microarray studies. A particular receptor mediates the action of androgen i.e the androgen receptor (AR), triggers in the target cells (AR). Analysis of genetic AR changes in prostate cancer is thus natural (Abate-Shen & Shen, 2010).

5. Pros of CRISPR/Cas9 Technology

In molecular biology, genome editing accurate and effective change is attained by causing breakage of double-stranded DNA, which often involves the attachment of a specific DNA-binding domain sequence to a non-specific binding domain, thus activating the DNA repair mechanism (Wyman & Kanaar, 2006). Recent research have highlighted the importance of nucleases enzymes as they are not only effective for diseases like sickle cell anaemia but also for cancer. Traditionally, two discrete genome editing methods, i.e., “Transcription activator-like effector nucleases (TALENs)” and “zinc-finger nucleases (ZFNs)” have been used for DNA repair by targeting the desired gene. The specificity and affinity of the nucleases are the only factors that affect these procedures. (Qu et al., 2013; Hazafa et al., 2020)

Inactivated Cas-9 (d-Cas9) can be used to act on the epigenome by repressing the enzymatic action of HNH domains without disturbing the sequence. “CRISPR/Cas9” has various other varieties which can be implemented in other cases. Similar to this, another study found that HeLa cells; endogenous genes, such as CXCR-4 and CD-71, were strongly suppressed by CRISPR-I. (Gilbert et al., 2013). As per literature survey, it is confirmed that advance technology i.e CRISPR/Cas9 is more 80% more effective as compared to other methods for editing human pluripotent stem cells.

6. Methodology of CRISPR Screen

6.1. Library

You can browse the pooled libraries for KO screens on Add gene, including the Ge CKO, H1/H2, Brunello, and TKO-CRISPR-KO libraries. These libraries contain almost 4 to 10 sgRNAs and almost 17,000 genes. The activation screen libraries for CRISPRa and SAM and the repression screen libraries for CRISPRi are also shared. Particularly interesting investigations can benefit from custom libraries (Tsujino et al., 2021)

6.2. Packaging

In a pooled screen using the CRISPR/Cas9 technology, the first step is to make a library of damaged cells by using lentiviral infection of an sgRNA library. Transfecting a sgRNA library into the proper host cells, such as the highly capable HEK 293FT cells, results in the creation of viruses. By estimating virus titer, a low (0.3) multiplicity of infection (MOI) can be ensured, which prevents uncertainty in the event that the host cells absorb multiple sgRNAs, targeting various genes within each cell / his stage has a drawback that should be noted: some PCa models, such as NCI-H660 and VCAP cells, make it difficult to apply tools using lentiviral methods (Tsujino et al., 2021).

6.3. Viability-Based Screens

Finding genes that affect cellular fitness is the basic strategy used by researchers. The idea behind negative selection screening is that as the screening process goes on, gene disruptions that lower fitness will become less common or disappear completely. Negative selection screens are widely used in cancer biology to identify tumor cell dependencies linked to certain mutations, copy number variations, and expression patterns, among other things. The simplest negative selection screening technique for determining critical growth genes entails long-term, continuous cell culture. Through the use of these screening methods, researchers have been able to identify the precise genes required for the growth and survival of specific cancer cell lines (Smith et al., 2021). A different negative selection screening method in specific genetic background cell lines identifies synthetic lethal interactions through the dual suppression of genes that leads to decreased cell viability. Researchers found synthetic interactions which will allow targeted therapy against cancer cells because drugs will function solely on cells with particular alterations and provide a fresh method for cancer treatment. The positive selection screen operates by identifying enriched cells over time instead of eliminating unwanted cells like the negative selection screen does. These screens have helped to find perturbations that provide resistance against small molecules and different conditions, including pathogen infections. During positive selection screening, the majority of the population is eliminated while the surviving perturbations become enriched by more than 100-fold. Through one screening process, researchers can obtain both positively selected and negatively selected phenotypic results. A viability-based knockout screen in cancer cells helps identify which oncogenes become depleted and which tumor suppressors become enriched. Intermediate dosages of small molecules often result in the identification of both sensitization genes and resistance genes (Tsujino et al., 2021)

6.4. Marker Selection Screen

Expression of molecule is directly related with genetic factors so selection screen is used to identify those markers & mutation is used for determining the phenotype that affect the marker protein rather than cell survival. In this type of screening, the correspondent can be genetically altered by replacing the fluorescent marker with a gene coding sequence. Finally, fluorescence-activated cell sorting permits the identification of upstream expression regulators by isolating cells with sgRNAs that target genes affecting marker expression (Bock et al., 2022).

6.5. Analysis (Algorithms)

Polymerase Chain Reaction is used for the extraction of DNA and to analyze the gene causing the defect. Next-generation sequencing technology is used to evaluate the areas encoding sgRNAs using large-scale parallel sequencing. Several algorithms, such as Model-based Analysis of Genome-wide CRISPR/Cas9, CRISPR Analyzer, Bayesian Analysis of Gene Essentiality (BAGEL), and Platform-independent Analysis of Pooled Screens using Python (PinAPL-P), can be used to analyze the variations in sgRNA abundance between control and phenotypic samples (Butz & Patócs, 2019).

6.6. Authentication

Through screen analysis, a prioritized list of putative genes associated with the trait is found. To find out which genes affect the phenotype and how much, validation is necessary. Introducing single guide RNAs (sgRNAs) that target the gene of interest and determining if the predicted phenotype is consistently replicated is one of the most dependable validation techniques. As long as many sgRNAs targeting the same genomic region provide the same phenotypic results, recent improvements in sgRNA specificity eliminate the need to validate target binding (Smith et al., 2021).

However, when required, methods like Western blotting, RT-qPCR, and genomic PCR can be used to evaluate functional alterations in the targeted gene. It is important to recognize that off-target effects can still occur even after on-target activity has been confirmed. For ongoing phenotypic validation, it is therefore advised to use numerous sgRNAs per gene, particularly those with the highest on-target activity. Rescue experiments can also be used to ascertain whether a characteristic is due to a genetic component. These research seek to determine if CRISPR/Cas9-edited cells return to their wild-type condition when candidate gene expression is restored to normal levels (Johnson & Lee, 2022).

7. CRISPR Screens in Prostate Cancer

There are many types of screen. Below mentioned are some noticeable screening strategies till date

7.1. Detection of Potential Target

In the beginning of 2014, genome editing technology got significant revolution and 1st screen for “CRISPR” Knockout was published. The 1st genome-wide CRISPR-KO screen in prostate cancer (PCa) cells was later reported by Fei et al. (2017). This study utilized the GeCKO v2 library for a viability-based screen in LNCaP cells and employed custom-designed MAGeCK and MAGeCK-VISPR algorithms to identify heterogeneous nuclear ribonucleoprotein L (HNRNPL) as a critical gene essential for PCa growth. The study revealed that HNRNPL directly regulates its RNA targets, including those encoding androgen receptor (AR), either through back-spliced circular RNA formation or linear alternative splicing. Notably, PCa exhibits abnormal expression of both HNRNPL and its RNA targets, emphasizing their potential therapeutic significance. The authors suggested that HNRNPL could serve as a viable therapeutic target in PCa treatment (Fei et al., 2017).

Similarly, a CRISPR-KO screen using a nuclear protein single-guide RNA (sgRNA) sub-pool library demonstrated that heterozygous deletion of chromosome 17p, observed in up to 63% of metastatic PCa cases, creates a selective dependency on ring-box 1 (RBX1) (Lei et al., 2021). Furthermore, the combined suppression of RNA polymerase II (RNAP2) and RBX1 significantly inhibited castration-resistant prostate cancer (CRPC) growth, thereby enhancing the therapeutic efficacy of RNAP2 inhibitors, such as α -amanitin-conjugated anti-EpCAM antibodies (Lei et al., 2021).

Shalem et al. (2014) performed a detailed experiment in which 33 cancer cell lines and loss of genetic function was analyzed. Expanding on these findings, Yoshiyama et al. (2021) analyzed data from CRISPR-KO screens in PCa cell lines obtained from the Cancer Dependency Map (DepMap), a public repository for CRISPR-KO screenings. They identified a context-specific vulnerability in histone demethylase JMJD1C, particularly in AR-negative cells. Their findings demonstrated that JMJD1C depletion selectively suppresses the growth of AR-negative PCa cells by activating the tumor necrosis factor alpha (TNF- α) network. Consequently, they proposed JMJD1C inhibition as a potential therapeutic strategy for patients with AR-negative PCa who no longer respond to AR inhibitors (Yoshiyama et al., 2021).

Additional research acknowledged “Kinesin Family Member 4A” (KIF4A) and WD Repeat Domain 62 (WDR62) as significant contributors to PCa phenotypes in both in vitro and in vivo models. Based on clinical data, these genes were nominated as PCa driver genes (Jiang et al., 2021). Additionally, a CRISPR-based E3 ligase screening approach in DsRed/EGFP-PDK1 reporter HKT cells conducted by Jiang et al. (2021) identified the Cullin3SPOP E3 ligase as a regulator of PDK1 ubiquitination and degradation. Notably, approximately 15% of PCa cases exhibit SPOP mutations. Mechanistically, the study demonstrated that SPOP recognizes PDK1 through CK1/GSK3 β -mediated phosphorylation and degron-dependent binding. Mutations within PDK1's binding region impair this recognition and ubiquitination process, leading to elevated PDK1 protein levels, enhanced AKT kinase activity, and increased tumor malignancy. These findings suggest that targeting the PDK1-AKT pathway could serve as a promising therapeutic approach for PCa (Jiang et al., 2021).

7.2. Resistance Mechanisms and Synthetic Lethality Targets

Most patients who get ADT for their locally progressed disease have remission. Although most patients who get ADT experience near-certain remissions lasting 1-2 years, CRPC causes cancer cells to progress resistance. The success of medications like abiraterone and enzalutamide demonstrates the critical role AR signaling plays in CRPC. Unfortunately, patients acquire treatment resistance and always end up dying from the illness. Regulators of AR inhibitor sensitivity has been identified using a genome-wide CRISPR screen. It's interesting to note that TLE3 deletion increases the expression of the glucocorticoid receptor (GR), which is consistent with the interaction of TLE3 and AR at the GR locus. Their findings provide new insights into the regulation of the GR locus in the context of AR inhibition in PCa cells, identifying TLE3 as a key regulator of GR-mediated resistance to AR inhibitors (Setton et al., 2021).

The researchers then used a similar strategy to find kinases whose inhibition could increase the effectiveness of enzalutamide in PCa cells in an effort to find genes associated with resistance and potential medication combinations that could overcome enzalutamide resistance. It was demonstrated that in the main activating region of “BRAF” gene, PCa cell hides mutation by suppression, or downstream, MAPK or increased activity of other genes. These findings suggest that the co-inhibition of MAPK and AR pathways in BRAF-mutated PCa may hold therapeutic potential (Qu et al., 2013).

Conclusion

Since “CRISPR screenings” have been conducted across multiple cancer lineages in hundreds of cell lines, including PCa, data portals like

DepMap serve as valuable resources for this research. As noted earlier, analyzing data from other tumors may provide valuable insights for PCa and vice versa. Further studies in PCa patients are needed to examine the role of the examined future to investigate new targets identified in screens presented in this paper. Advancements in genomic research, such as CRISPR screening, will enhance our understanding of the molecular characteristics of CRPC and be translated into clinical practice through increased molecular testing for therapeutic selection and clinical trial eligibility.

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Potential role of Zinc Nanoparticles against Bacterial Leaf Blight of Wheat

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Abstract

Management of plant diseases through conventional agricultural techniques encounters several problems, leading to a serious threat to climate change and toxicity. The development of resistance to biotic stress in plants or by damaging the biochemical potential of pathogens can be possible with the use of Zinc nanoparticles (ZnNPs). This approach is economically feasible and eco-friendly. This chapter reviews the utilization of zinc nanoparticles and their role in plant defense mechanisms and their mechanism of action against the leaf blight pathogen. It was found that ZnNPs play a crucial role in regulating hormonal pathways and also improve the efficiency of various antioxidants to suppress the detrimental effects of bacterial pathogens. Deficiency of zinc makes plants susceptible to various pathogens, while its excess leads to destroying plant defense mechanisms and growth due to toxicity. This chapter discusses the level of zinc necessary for the normal functioning of plants and the role of ZnNPs in boosting the plant defense mechanism against bacterial leaf blight of wheat.

Keywords: Nanotechnology, Bacterial leaf blight, Biotic stress, Wheat, Antibacterial mechanism

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Introduction

On a global level, wheat is regarded as a basic food item and a vital source of food grains for humans. For a large portion of the world's population, particularly in North America, Europe, and Asia, wheat is a staple grain (Erenstein et al., 2022). Wheat is also regarded as a vital source of vitamins and fiber. There might be as much as 11-14% protein in wheat (Iqbal et al., 2022). But it also contains a concentration of lysine and other important amino acids. The production of wheat is reduced by 10 to 40 percent as a result of bacterial infections (Singh et al., 2023). Wheat bacterial infections can cause large yield losses as well as quality issues, such as discoloration, shriveled kernels, decreased grain weight, and poor milling qualities (Mehmood et al., 2023). Significant bacterial infections like *Xanthomonas translucens* pathogens' bacterial leaf streak and black chaff; *Pseudomonas syringae* pathogens' bacterial leaf blight & basal glume rot and diseases of minor importance due to the lack of research on them, like spike blight of wheat, bacterial mosaic of wheat, and gumming disease of spike, caused by genus *Clavibacter* pathogens (Jiang et al., 2022). Multiple aspects of controlling bacterial disease in wheat have been the focus of researchers and scientists, including disease-resistant cultivars, cultural practices, pathogen identification, disease characterization, and biological control techniques (Ayaz et al., 2023).

The management of bacterial disease in wheat has advanced significantly, but there are still a number of issues that need to be resolved, including a lack of integrated management strategies, sustainable disease management practices, extension and farmer education, quick and precise diagnostic tools, and limited disease resistance (Rajendiran & Rethnaraj, 2024). To overcome these obstacles and safeguard the wheat crop against bacterial illnesses, stakeholders must continue their research, work together, and share knowledge. For bacterial illnesses of wheat, this review offers a current, thorough explanation of the symptoms, disease cycle, epidemiology, and management techniques.

Nanotechnology in Agriculture and Managing Bacterial Plant Diseases

Enhancing nutrient utilization for plant development and improving plant disease resistance are the two main goals of nanotechnology in agriculture (Humbal & Pathak, 2023). Nanoparticle technology is crucial for solving plant-pathogen interaction-related agricultural problems and creating novel approaches to product protection. Currently, spraying is used to apply agricultural chemicals to crops; however, in order to be delivered safely, nano agrochemicals need to be designed with certain properties, such as high solubility, stability, efficacy, controlled release mechanisms, improved targeted activities, lower toxicity levels, and effective concentration (Ghorbanpour & Hatami, 2015). Nanoparticles (NPs) have enormous applications in many scientific domains. To combat the increasing risks of crop damage and disease brought on by a

variety of phytopathogens, such as bacteria, fungi, viruses, and some insects, they have significantly improved traditional techniques in the domains of agriculture and food sciences. Food scarcity has become a serious concern as a result of bacterial illnesses that cause widespread agricultural damage by establishing antibiotic resistance (Iqbal et al., 2025; Salam et al., 2023). To solve the problem of antibiotic resistance along with maximizing crop yield and immunity to diseases, several types of nanoparticles with such potential exists in market. NPs made using green synthesis methods have been shown to be more environmentally friendly and effective than those made using chemical processes (Madani et al., 2022). NPs have a variety of important roles in plants, including increased agricultural output, disease prevention, targeted medicine and pesticide delivery within the plant, and pathogen detection biosensors. NPs play important roles in energy transfer, DNA and protein entity modification, reactive oxygen species (ROS) generation, and cellular membrane disruption. They also help plant to cope the biotic and abiotic stress by altering many important mechanisms in plant (Gul et al., 2024).

Antibacterial Role of NPs

Several nanoparticles possess remarkable antibacterial properties, both bactericidal and bacteriostatic. Usability of NPs based on several factors such as their synthesis techniques, their structure and shape, concentration used, and to obtain the best one against bacteria many analyses are underway by the researchers (Slavin et al., 2017). While gram-negative bacteria with an extra outer layer of polysaccharides prevent NPs from entering bacterial cells, gram-positive bacteria with thick peptidoglycan layers create pores and negative charges on the cellular membranes, allowing NPs to enter the bacterial cells efficiently (Fazal et al., 2022). Research has suggested that biosynthesized metals (e.g., AgNPs, AuNPs, CuNPs), metal oxides (e.g., ZnONPs, TiONPs, CuONPs), carbon (e.g., GONPs), and magnetic (e.g., FeONPs) NPs present efficient antibacterial activity against plant bacterial pathogens (Gul et al., 2024). These properties are discussed in Table 1.

Table 1: Utility of nanoparticles in controlling various plant diseases spread by bacterial infection.

Nanoparticles	Bacteria	Crop	Diseases	Reference
ZnNPs	<i>Xanthomonas translucens</i>	<i>Triticum aestivum</i>	Bacterial leaf spot	(Hangamaisho, 2022)
MgONPs				
CuONPs				
ZnONPs	<i>Pseudomonas syringae</i>	<i>Triticum aestivum</i>	Bacterial leaf blight	(Ayisigi et al., 2020)
Nanosized Ag-Silica hybrid Complex (NSSC)	<i>Pseudomonas syringae</i>	<i>Arabidopsis thaliana</i>	Blight diseases	(Chu et al., 2012)
SiO ₂ NPs	<i>Pseudomonas syringae</i>	<i>Arabidopsis thaliana</i>	Blight diseases	(El-Shetehy et al., 2021)
AgNPs	<i>Pseudomonas syringae</i>	<i>Nicotiana benthamiana</i>	Tobacco wildfire	(Jiang et al., 2022)
ZnONPs	<i>Fusarium oxysporum f.sp. lentis</i>	<i>Lens culinaris</i> Medick	Gall formation	(Siddiqui et al., 2018)
	<i>Pseudomonas syringae</i> pv. <i>syringae</i>		Nematode multiplication	
			Bacterial wilt	
			Leaf spot	
ZnONPs	<i>Pantoea ananatis</i>	<i>Zea mays</i>	Maize white spot	(Mamede et al., 2021)
ZnONPs	<i>Xanthomonas translucens</i>	<i>Triticum aestivum</i>	Bacterial leaf streak	(Ocoy et al., 2013)
Calcium Nanocrystals	carbonate <i>Xylella fastidiosa</i>	<i>Olea europaea</i>	Olive quick decline syndrome	(Baldassarre et al., 2020)

Understanding Bacterial Blight in Wheat

Bacterial leaf blight, caused by *Pseudomonas syringae* pv. *Syringae* Van Hall was first identified as an important wheat disease in the early 1970s. The bacterium is found in soil in large quantities and inhabits wheat leaves as a member of the resident bacterial population. Additionally, it is seedborne (Nadeem et al., 2025). The pathogenicity of the strains to wheat varies greatly among the population. According to some theories, the rise in bacterial leaf blight cases could be brought on by a shift in *P. syringae* virulence linked to increased vulnerability of more recent cultivars (Lamichhane et al., 2015). Certain environmental factors can cause leaf blight. These are times of rainy weather, particularly driving rain, which could help the virus enter the leaf, and temperatures ranging from 15 to 25°C. Initially appearing as tiny, wet patches, symptoms gradually get bigger (Nadeem & Batool). Over a few days to develop bleached white necrotic patches and uneven tanning as well as streaks. Even though none were noticeable previously, symptoms frequently start to show up abruptly around the onset stage. Due to the fact that virulent strains live on the leaf surface, symptoms may appear quickly on every leaf when the environment supports the bacterium's growth and spread (Rajput et al., 2024).

Many plant diseases, notably wheat leaf blight, are caused by *P. syringae*. *P. syringae* is a very diverse group that is a member of *Pseudomonas*' RNA homology group I, which is a subclass g. from the Proteobacteria class. This species exhibits genetic diversity and the DNA homology of its pathogens ranges from 40 to 100%, while that of strains of one specific *P. syringae* strains were characterized using a variety of molecular approaches as mentioned in Table 2, which revealed that there was significant genetic variability in the various strains, such as those that were separated from the identical host (Khezri & Mohammadi, 2018).

Classification and Features

Gammaproteobacteria is the class to which *P. syringae* belongs. There is still much disagreement regarding the species' precise categorization. According to Young and associates, all fluorescent and plant-pathogenic oxidase-negative *Pseudomonas* isolates should be grouped into a single species, *P. syringae*, which will then be further subdivided into pathovars (Young et al., 1978). Large genetic variation

among the groupings has been revealed by several DNA hybridization investigations; nonetheless, biochemical traits, with a few exceptions, prevented those groups from being elevated into different species (Dudnik & Dudler, 2013).

Table 2: *Pseudomonas syringae* pv. *Syringae* strains studied in wheat.

Strain	Host	Stage of isolation	Location	References
PW1	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Roodbar	(Dariush et al., 2012)
PW2	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Roodbar	(Dariush et al., 2012)
PW3	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Roodbar	(Khezri & Mohammadi, 2018)
PW4	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Siahkal	(Khezri & Mohammadi, 2018)
PW5	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Siahkal	(Gul et al., 2024)
PW6	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Roobar	(Gul et al., 2024)
PW7	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Amlash	(Gul et al., 2024)
PW8	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Amlash	(Gul et al., 2024)
PW9	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Talesh	(Gul et al., 2024)
PW10	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Talesh	(Dariush et al., 2012)
PW11	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Astara	(Dariush et al., 2012)
PW12	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Astara	(Dariush et al., 2012)
PW14	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Astara	(Dariush et al., 2012)
PW15	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Roodbar	(Dariush et al., 2012)
PW16	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Roodbar	(Ayisigi et al., 2020)
PW17	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Siahkal	(Ayisigi et al., 2020)
PW18	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Siahkal	(Ayisigi et al., 2020)
PW19	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Amlash	(Ayisigi et al., 2020)
PW20	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Roodbar	(Ayisigi et al., 2020)
PW21	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Roodbar	(Ayisigi et al., 2020)
PW22	WHEAT (<i>Triticum aestivum</i>)	<i>In vivo</i>	Roodbar	(Ayisigi et al., 2020)

PW=*Pseudomonas* wheat

Challenges in Controlling Bacterial Leaf Blight

Certain meteorological variables determine the disease's significance for wheat. Several days with high humidity, low temperatures (15–25°C), and a lot of rain are when the disease is most frequently seen (Von Kietzell & Rudolph, 1997), and plants are more susceptible at the boot stage. Otta (1974) revealed significant output losses in South Dakota, where areas with 75% or more necrotic leaves experienced extremely high infection severity due to an epidemic outbreak. Additionally, growing sensitive cultivars like Chris, Era, Scout 66, and Winoka resulted in large yield losses in North America. Since resistant wheat varieties have supplanted these susceptible ones, the disease is now sometimes found in North America. For the bacterial leaf blight disease brought on by *P. syringae* pv. *Syringae*, there are no conventional control techniques. However, planting very susceptible varieties is discouraged.

Zinc Nanoparticles (ZnNPs) Synthesis

Zinc nanoparticle (Zn NP) eco-friendly synthesis techniques have drawn interest because they have less adverse effect on the environment than conventional chemical synthesis techniques. Biological resources like plant extracts, microbes, and biopolymers are frequently used as reducing and stabilizing agents in these "green synthesis" techniques (Alsaiani et al., 2023). Because of its simplicity, affordability, and capacity to generate zinc nanoparticles without producing any toxic byproducts, plant-based synthesis is especially preferred (Ehsan et al., 2022). Commonly utilized plant extracts include those from *Azadirachta indica* (neem) and *Cassia fistula* (golden shower); these extracts contain bioactive substances such as flavonoids, tannins, and alkaloids that help reduce zinc ions into nanoparticles (Agarwal et al., 2017). The most widely used technique for the straightforward synthesis of ZnONPs from leaves or flowers involves thoroughly washing the plant portion under running water and sterilizing it with double-distilled water (some people disinfect it with Tween 20) (Dejene & Geletaw, 2024). The plant portion is then allowed to dry at room temperature before being weighed and crushed with a crusher and pestle. Using a magnetic stirrer, the mixture is continuously stirred while Milli-Q H₂O is introduced to the plant portion in accordance with the desired concentration (Rajeshkumar et al., 2016). Whatman filter paper is used to filter the solution, and the clear solution that is produced is used as a plant extract (sample). To ensure effective mixing, a certain volume of the extract is combined with 0.5mm of hydrated zinc nitrate, oxide, or sulfate, and the combination is cooked at the appropriate temperature and duration (Ochieng et al., 2015).

At this stage, some people optimize by varying the temperature, pH, extract concentration, and time. The mixture turns yellow during the incubation phase, providing visual proof of the produced NPs (Rajeshkumar et al., 2016). The synthesis of NPs is next verified by UV-Vis spectrophotometry, then the mixture is centrifuged, and the pellet is dried in a hot air oven to obtain the crystal NPS (Yasmin et al., 2014). Moreover, X-ray diffractometers (XRD), energy dispersion analysis of X-rays (EDAX), Fourier transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), transmission electron microscopy (TEM), *in vivo* emission scanning electron microscopy (FE-SEM), atomic force microscopy (AFM), thermal-gravimetric differential thermal analysis (TG-DTA), photoluminescence analysis (PL), X-ray photoelectron microscopy (XPS), Raman spectroscopy, attenuated total reflection (ATR), UV-visible diffuse reflectance spectroscopy (UV-DRS), and dynamic light scattering (DLS) are used to further characterize synthesized nanoparticles (Ali et al., 2014).

Physicochemical Properties

Nanoscale size increases their specific contact area, which, in turn, increases reactivity and allows for better interactions with bacterial membranes (KhokharVoytas et al., 2023). Some of the unique physicochemical characteristics of ZnNPs include high surface area, individual size of particles, and structural stability that make them more effective antibacterials (Gohar et al., 2024). In addition, their shape, which is often spherical or rod-shaped, breaks bacterial cells by affecting particle stability and promoting interactions through membrane adsorption (Sirelkhatim et al., 2015). ZnNPs' antimicrobial properties comprise the capacity to penetrate biofilms and bear environmental conditions, making them more resilient and ideal to apply in antibacterial coatings as well as in medical devices. They also have the ability in them to produce reactive oxygen species (ROS) when exposed to light. Even in the presence of different environmental stressors, a persistent and effective antimicrobial action against diverse pathogenic microorganisms is ensured by the retention of high reactivity coupled with structural integrity (Regiel-Futyra et al., 2017).

Antibacterial Mechanism of Zn NPs

Production of Reactive Oxygen Species (ROS)

Upon UV or visible light exposure, zinc nanoparticles (Zn NPs) can produce reactive oxygen species such as hydrogen peroxide (H_2O_2), hydroxyl radicals ($OH\cdot$), and superoxide anions (O_2^-). Oxidative stress induced by these highly reactive ROS degrades critical cellular components such as proteins, lipids, and DNA in bacterial cells, as indicated by Figure 1. Bacterial viability is disrupted by this oxidative stress, which disrupts biological activity. Zn NPs are versatile for applications over a spectrum because they can generate ROS even without light, which means they should also be efficient in dark environments (Ali et al., 2018). As earlier stated, internalization of ZnONPs within the bacterial cell is not always required for their toxicity. Environmental alterations close to the bacterium, like the release of ROS or enhancement of ZnONP solubility, can lead to cell damage (Hajipour et al., 2012).

Disruption of Cell Membrane

Nanoparticles also have great usefulness due to their specific interaction with the bacterial cell membrane. ZnNPs have positive charge on them that allows them to bind with the negatively charged bacterial cell membrane, leading to membrane instability (AlQurashi et al., 2025). Increased membrane permeability due to this interaction can lead to the release of ions, proteins, and DNA, which ends up in cell lysis and death. Zinc nanoparticles (ZnNPs) are shown by studies to be excellent at entering and lysing bacterial membranes due to their small size and positive surface charge (Lallo da Silva et al., 2019).

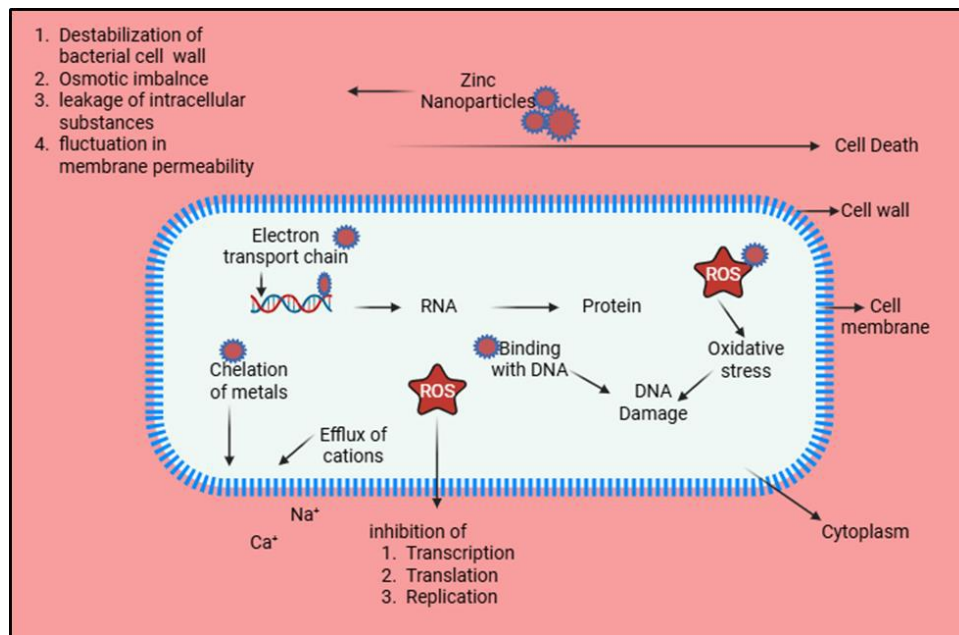


Fig. 1: Mechanism of action of Zn nanoparticles in generating ROS and cell membrane disruption, which leads to bacterial cell death.

Nutrient Deprivation

ZnNPs bind with the bacterial membrane more strongly as compared to other required nutrients for growth and development of bacteria, and when these nutrients are blocked to get entry into the cell, cell may damage and death can occur of such cells (Sirelkhatim et al., 2015). Research indicates that this inhibition can lead to a significant reduction in the uptake of essential nutrients, thereby affecting the growth and viability of bacteria (Mustafa et al., 2024). In addition, ZnNPs can induce conformational alterations in transport proteins, which further inhibits their activity. These conformational changes can be caused by contact of ZnNPs with the lipid bilayer of the membrane, potentially destabilizing the membrane-anchored transport proteins (Altunbek et al., 2018).

Consequently, the metabolic activities on which bacteria rely for energy and reproduction are disrupted, and nutrient uptake efficiency decreases. Production of ROS by ZnNPs may also be responsible for interference with nutrient transport. Membrane lipids and transport proteins are some of the cellular structures which ROS can damage, further interfering with the mechanisms through which nutrients are absorbed (Ozougwu, 2016). This oxidative stress might overwhelm the protective mechanisms of the bacteria and further inhibit their capacity

to sustain homeostasis as well as absorb vital nutrients. Furthermore, it has been proved through research that Zn NPs can affect the proton motive force (PMF), necessary for most bacterial species' active uptake of nutrients. A number of transport processes rely on the PMF to operate, and ZnNPs can interfere with it, resulting in a domino effect on nutrient uptake (Wang et al., 2024).

Application Methods and *In vivo* Efficacy of ZnNPs

ZnNPs for Seed Nano-Priming

Seed priming when done with ZnNPs they boost the growth, nutrient uptake and also able plant to be tolerant against stresses. Due to small size of NPs they can easily move inside the plant tissues through cell wall and promotes the activities of various important pathways of cell. For instance, research on rice has shown that ZnNP priming results in taller plants, stronger root systems, and higher yields. In drought situations, where nano-primed seeds exhibit improved root development, water uptake, and enzyme activity, this technique has been proven to be very successful in helping the plant adapt to stress (Nile et al., 2022).

Foliar Application

ZnNPs can also be applied to plants through foliar spray of it after making their liquid solution of certain concentrations. Foliar application facilitates rapid absorption of zinc nanoparticles (ZnNPs) through leaf pores, making them instantly available for physiological activities. ZnNPs promote improved plant growth and biomass accumulation by increasing chlorophyll production and photosynthetic efficiency. Because Zn NPs may break down bacterial cell walls and stop infections like bacterial leaf blight, foliar sprays are also very helpful in reducing pathogen attacks and enhancing plant health (Hong et al., 2021).

Environmental and Health Considerations

Numerous creatures, especially aquatic ones, have been demonstrated to be toxicologically affected by zinc nanoparticles. For example, research shows that zinc nanoparticles (ZnNPs) can build up in aquatic creatures, which can result in bioaccumulation and even biomagnification in food webs. Significant acute toxicity was noted in tests employing models such as *Artemia salina* and zebrafish, with deadly dosages resulting in physical deformities and impairing general health. This emphasizes how crucial it is to assess the amounts at which these nanoparticles endanger aquatic environments (Sibiya et al., 2022). Since biological/green methods are made from plants, beneficial bacteria, algae, and other sources, they are safe, economical, biocompatible, and environmentally friendly, making them less harmful to the ecosystem than physical and chemical approaches. As plant extracts consist of large amount of useful phytochemicals and also easily available and environmentally friendly approach, has gained attention for the manufacturing and synthesis of NPs. Beyond plants, microorganisms can also be used to synthesize NPs as their extract also enriched with many important nutrients and vitamins (Rajeshkumar, 2016). Microorganisms that are the beauty of nature and also play crucial role in the cycling of nutrients and the health of ecosystems, can be impacted by these nanoparticles and change the chemistry of the soil. Research has shown that ZnNPs might alter soil microbial activity, which could upset the equilibrium of soil ecosystems (Chan & Dudeney, 2008).

Challenges in *In Vivo* Application

In Vivo applications of NPs are not yet gained much attention by the small scale farmers as their resources are much limited and they are reluctant to use or implement new technologies rather they preferred traditional practices more to gain benefit immediately (Vamuloh et al., 2020). Another problem that reduce their *In Vivo* application is scalability issues as they can be produced in laboratory settings but scaling up these NPs to meet the agricultural requirements need much attention. Homogeneity in their size, quality and manufacturing procedures is necessary to make nanoparticles more effective. The methods employed must also be economically viable and sustainable in order to promote widespread adoption in agricultural operations (Ur Rahim et al., 2021). Regulatory limitations are a significant barrier to the application of ZnNPs in agriculture. The long-term effects on ecosystems and the potential toxicity of zinc nanoparticles on non-target animals need to be thoroughly examined. Due to no strict check and balance and regulations of NPs farmers also hesitate to employ these NPs in agriculture settings (Mishra et al., 2022).

Future Prospects and Challenges

Green synthesis of NPs is the demand of the time due to reason that they are synthesized from renewable sources and research institutions are trying their best to shift their synthesis to green method in place of metallic synthesis of NPs. Along with their synthesis methods researchers are also focus to maximize their efficacy and their potential to tackle the problems for which they are used. In addition, novel methods for surface modification are being investigated to enhance ZnNPs' antibacterial activities. Such modification increases the antibacterial activity of nanoparticles by increasing their interaction with microbial cells. As ZnNPs and other therapeutic agents can be employed synergistically in order to overcome microbial resistance, nanocarrier systems comprising them are very interesting as well. Not only does this holistic approach enhance overall treatment effectiveness but also reduce the chances of infection resistance. Exploring new applications, including the addition of zinc nanoparticles to agricultural applications, is also becoming more popular. To enhance plant health and disease resistance, they can be incorporated in foliar sprays and seed treatments. This can increase agricultural output and lower the demand for chemical pesticides.

Conclusion

Traditional farming techniques of disease management have several setbacks, which present a significant hazard to toxicity and climate change. One of the possible, sustainable, and economically viable ways of controlling bacterial leaf blight of wheat through a multitude of ways

is employing specific nanoparticles, particularly zinc nanoparticles. They modify signal transduction pathways, enhance antioxidant activity, and destroy the infections' several crucial metabolic processes. ZnNPs' environmental safety is also aided by green synthesis methods, making them suitable for sustainable agriculture. A delicate balance between zinc's effectiveness and toxicity, though, must be achieved to optimize plant health and production for optimal outcomes.

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Improving One Health using Biotechnology and Nanotechnology

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Abstract

Biotechnology and Nanotechnology are two fields in an advanced era that are being used in improving One Health. Biotechnology has transformed our lives by creating vaccines, antibiotics, and diagnostic tools. The cutting-edge technologies, such as CRISPR-CAS9, are used to edit genes to acquire desired traits. GMOs are being produced at a higher rate to feed crops and animals for human consumption. Nanotechnology includes the manipulation of atoms and the evolution of systems, which provide targeted therapies for the betterment of health. These branches of science led us to advancements in human, animal, and plant health by using nanoparticles or microorganisms. Tissue regeneration, boosting sperm viability, nano vaccines, and disulfiram nano capsules for anticancer activity are advanced techniques for a better future. In this chapter, tools and techniques regarding biotechnology and nanotechnology are discussed that provide a promising solution for health-related challenges among living organisms.

Keywords: Tissue regeneration, GMOs, Disulfiram capsule, Antibiotics, CRISPR-Cas9, Genes, Targeted therapies

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Introduction

Biotechnology is an interdisciplinary field that employs biological systems, living organisms, or their cellular components to create practical solutions and cutting-edge technologies in healthcare, agriculture, industry, and environmental conservation (Anyanwu et al., 2024). It brings together insights from molecular biology, genetics, engineering, and computational sciences to precisely modify biological processes in order to address real-world problems, improve quality of life, and promote sustainable development (El Dosary, 2023). Biotechnology plays a crucial role across various sectors, such as medicine, industry, farming, and environmental conservation. It has transformed how we prevent and treat diseases by creating vaccines, pharmaceuticals, and diagnostic tools. By combining technology and biological sciences, biotechnology promises continuous innovation, and it also plays an important role in global health advances (Gupta et al., 2017).

The history of biotechnology starts from different ancient techniques, such as fermentation, but the scientific evolution of biotechnology began in the 19th century. The experiment of Louis Pasteur showing that microorganisms not only cause illness and disease but can also be used in other ways that are beneficial in many ways was a significant breakthrough. Modern genetics that we know today is the result of Watson and Crick's 1953 discovery of DNA's double helix (Verma et al., 2011; Anyanwu et al., 2024).

Biochar is a carbon-rich product produced by the process of pyrolysis from crop residues, wood, and agricultural wastes. In a recent study, it was revealed that biochar increases the availability of nutrients in soil, enhancing its quality as a soil supplement in arable territories. Biochar has also been observed to minimize environmental pollution, enhancing soil health. Microalgae are a green technology providing an eco-friendly solution for converting CO₂ into valuable biomass (Osorio-Reyes et al., 2023). Microalgae as bio fertilizers enrich soil in micronutrients, macronutrients, and phytohormones (plant hormones that regulate physiological processes in plants). They foster beneficial interactions between crops and the soil microbiome. Microalgae can also enhance nitrogen fixation and maximize growth. Some prokaryotic organisms, i.e., cyanobacteria and *Bacillus*, are known for their nitrogen-fixing abilities. Mitigation of phosphorus contamination in water bodies can also be carried out by microalgae by absorbing excess phosphorus (Yadav et al., 2023).

Transforming Agriculture through Biotechnology to Improve One Health

The first agricultural communities were formed about some 10,000 years ago by people in order to improve their quality of life by harnessing the biological processes in sight at that time (Das et al., 2023). Approximately 6,000 years ago, humans began to harness the biological processes of microorganisms to produce bread, cheese, and alcoholic beverages, and to preserve dairy products. But such processes are not how biotechnology is perceived today, a term first widely perceived as the molecular and cellular technologies that started to emerge in the late 1960s to mid70s (Verma et al., 2011). Genentech was established to commercialize recombinant DNA technology in 1976 by Robert A. Swanson and Herbert W. Boyer. This initiative catalyzed the modern definition of biotechnology as the exploitation of biological processes

for the benefit of mankind, which includes the use of microorganisms, manipulation of genes, and use of other such advanced techniques for the production of antibiotics and hormones.

In agriculture settings, biotechnology significantly influences modern farming by supporting innovations that make crops more resistant and adaptable to threats like pests, diseases, and extreme climate conditions (Das et al., 2023). Crops that are engineered to have essential nutrients, like golden rice, that have vitamin A added, are used in backward areas to help deficiencies and solve health issues in those areas. These crops also dramatically decrease the need and use of chemical pesticides, which leads to lower health risks. This leads to food systems that are safe and environment friendly. If we look into our past, enhancement in our livestock depended on traditional techniques like selective breeding. These techniques improved traits like fertility, resistance to diseases, and growth. (Funahashi et al., 2020; El Dosary, 2023).

PLF, also known as precision livestock farming, is the technique in which we use modern technologies for managing, monitoring, and improving the overall health of livestock animals in real time. Modern technology, like biosensors in cattle industries, has given us the ability to monitor animal issues beforehand. This helps in treatment before the condition gets worse or severe (Neethirajan et al., 2021). The role of genetically engineered crops is shown in Figure 1. Veterinary biotechnology is an emerging field in the discipline of biotechnology. Cancer in animals is a major concern in this field. Veterinary oncology is determined to identify, manage, and treat cancer in animals (Prasad et al., 2023).

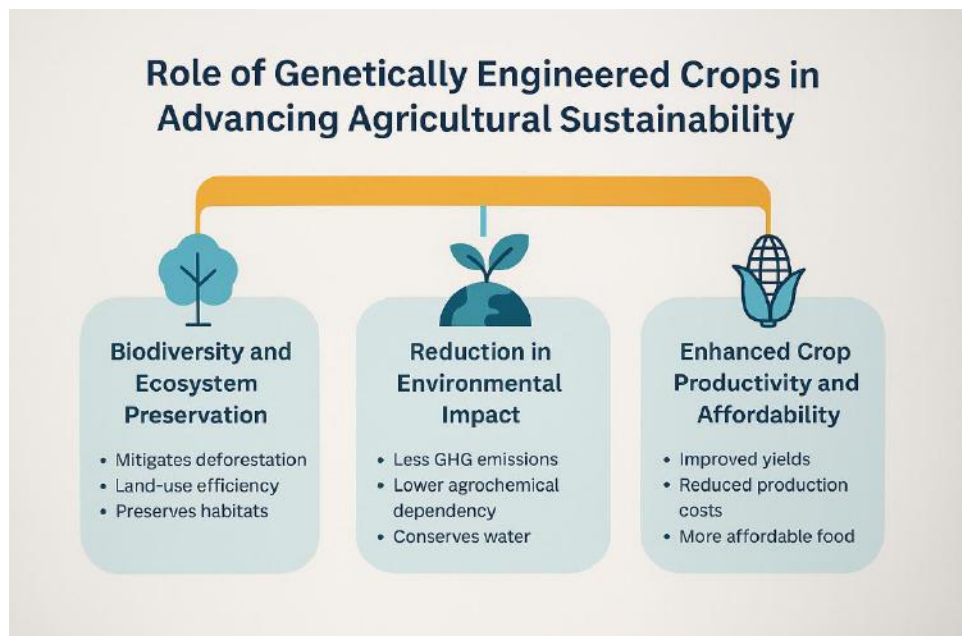


Fig. 1: Contribution of genetically engineered crops to sustainability

Through transgenic technology, foreign gene expression has resulted in the large-scale production of valuable products. Genetically modified crop (GMC) is the world's fastest-growing agricultural technology. Utilizing new breeding techniques can ensure food security, sustainability, and a broader range of desirable food products (Sharma et al., 2022)

Biostimulants have emerged as an essential supplement in agricultural practices, boosting plant growth, development, and stress resilience (Hamid et al. 2021). EPHs- Enhanced Plant Holobionts represent an innovative strategy for sustainable agriculture, employing beneficial plant-microbe interactions to improve crop resilience, accelerate productivity, and enhance environmental health. On the other hand, it also highlighted the use of several species and strains of *Bacillus* spp. as biofertilizers, biopesticides, and other biotechnological tools (Ortiz & Sansinenea, 2022).

Genetically engineered animals, such as transgenic goats that produce human insulin in their milk and genetically modified pigs resistant to porcine reproductive and respiratory syndrome (PRRS), offer groundbreaking solutions for medical treatment and improve livestock health (Whitworth et al., 2016). Gene-editing technologies such as CRISPR have given us humans the ability to create livestock of our own choice with desired specific traits such as enhanced disease resistance (Golovan et al., 2001).

MAS systems (Marker-Associated Selection) link desired traits to specific genetic markers. This system has revolutionized the way we breed traditional animals. Moreover, MAS has allowed us to specifically bind our desired traits to different genes (Bishop et al., 2014). These achievements have laid the foundation for future inventions and discoveries that will ultimately have a world impact. In the upcoming section, we will explore recent developments and other recent approaches in humans, animals, and the environment.

Transforming Healthcare through Biotechnology to Improve One Health

A state of complete physical, mental, and social well-being is defined as human health and not merely the absence of disease or infirmity alone (World Health Organization, 1946). The social determinants of health (SDOH) are grouped into five categories: economic stability, education, social context, neighborhood environment, and healthcare access. As the population diversifies, increasing evidence highlights the profound influence of SDOH on healthcare outcomes, including mortality, morbidity, life expectancy, healthcare costs, health status, and functional limitations (Agnikula et al., 2021). According to the World Health Organization (WHO), nearly 71% of global mortality is caused due to the surge in lifestyle diseases that have been precipitated as a result of rapid globalization and economic development. This has emerged as

a major global public health crisis and a leading concern in the past few decades. These conditions are preventable and can be controlled by regulating various controllable factors.

Cell-replacement therapies could have a favorable outcome in treating Alzheimer's disease. Such therapies involve induced pluripotent stem cells (iPSCs) or human embryonic stem cells (ESCs)-derived neural cells (Rahman et al., 2022). The stem cell's pluripotent properties, the unique property of stem cells to differentiate into various cell types, can be utilized to repair or replace neuronal loss. Mesenchymal stem cell (MSCs) is a form of stem cell therapy that is a clinically promising approach to treat chronic liver failure and liver cirrhosis (Li et al., 2022)

Recently, neutrophil-derived exosomes have been found to have antitumor properties. Zhang et al. (2022) generated a xenograft of BALB/c nude mice that was injected with HGC27 cells to evaluate the antitumor efficacy of N-Ex. His work not only demonstrated the role of exosomes as anticancer agents of neutrophils but also found it as a drug delivery nanoplatform. Bioinspired exosome mimetic nanovesicles (NVs) are artificial nanoparticles that mimic the structure and function of natural exosomes, have been developed to deliver chemotherapeutic drugs for cancer treatment. Also, monoclonal antibodies can be used for targeted chemotherapy (Mitra et al., 2021). Advancements in biotechnology have revolutionized healthcare by integrating artificial intelligence (AI) for sophisticated data analysis. These innovations have collectively transformed into a healthcare paradigm that is more precise, effective, and tailored to individual needs (Biswas et al., 2023).

Nanotechnology and One Health

The branch of science and technology that employs systems with at least one dimension on the nanoscale (one-billionth of a meter) at the cellular level is known as Nanotechnology. It consists of the manipulation of particles at the molecular, atomic, and sub-atomic levels. Nanoparticles are tiny particles that range from 1 to 100 nanometers in scale (Silva et al., 2004). It works depending on molecular size; particle properties and behavior change dynamically. The materialistic and systematic properties are affected by molecular composition and interactions at the molecular scale, which may alter and affect at macroscopic level. Nanotechnology allows the evolution of systems and devices that interact with the body at the microscopic level, which ensures high specificity and precision (Roco et al., 2003)

The development of novel engineered particles and materials for medicine over the past few years, especially nanomaterials, has ramped up rapidly. Nanotechnology has been playing a key role in human health and research, especially in nanomedicine, as in the first nano-based treatments, i.e., vaccines, drugs, and diagnostic devices (Ambrose et al., 2025). Nanomaterials have specific properties unlocking great potential in disease detection that enable targeted manipulation, as in biomarkers at the nanometer scale, which execute targeted drug-based delivery to the cells. Additionally, the Nanoparticles are used broadly, involving both the organic (e.g., liposomes, biopolymers) and inorganic materials like silver, iron oxide (Contera et al., 2020).

Nanotechnology and Healthy Ecosystem

For centuries, scientists have been rearranging the patterns of atoms by using diverse types of techniques, such as heating the atoms, mixing, or even pounding them to get firsthand control over the structure of matter, and this has significantly advanced both animal and human health sectors. Nanomaterials have been used in procedures like therapeutic techniques and targeted drug delivery (Rizvi et al., 2018).

Most of the work on nanotechnology remains under research in laboratories. By homogenizing nano- and biotechnology, major breakthroughs in the fields of medicine have been derived that have helped us in techniques like regenerative medicine and targeted drug delivery (Contera et al., 2020). Recent research in nanotechnology has led to several revolutionary discoveries. This revolution of nanoscale science is evidence that, in the near future, nanotechnology will be integrated into almost every field of research and development (Malik et al., 2023). The ability to regulate matter at the nanoscale has facilitated revolutionary advancements, innovations in diagnostics, clinical interventions, and overall patient care (Ma et al., 2024).

Transforming Agriculture through Nanotechnology to Improve One Health

The latest research in nanotechnology has been focused on its applications in sustainable agriculture and nutrition science. Scientists have been investigating uses of nanotechnology in agricultural fields in order to enhance the growth of crops and their yields, reduce the use of chemical growth enhancers like fertilizers, and to get rid of the use of pesticides. Newer research has found that nanoformulations like nanogels, nanosuspensions, and nanoemulsions are a very useful alternative to pesticides. These are called nano-pesticides that enhance plant productivity without harming the crop or the soil in any way (Munir et al., 2023).

Types of Nanoparticles Used in Improving Soil Health

Titanium Dioxide Nanoparticles:

Plant growth and disease management have been greatly improved by using titanium dioxide nanoparticles. TDNs have properties like photocatalysis, which are effective against plant pathogens. The combination of nanotechnological particles like TDNs in the field of agriculture has positively impacted agriculture and has changed the way we approach agriculture. This has led us to better and more sustainable food productivity systems. (Malik et al., 2023). Nanotechnology offers sustainable solutions for plant nutrition by replacing bulk fertilizers with different nanoparticles like TDNs. It helps in improving the availability of nutrients, mineral uptake, and crop yield while limiting the use of fertilizers. These nanoparticles or nano-fertilizers are applied through soil routes or foliar systems. (Gauri et al., 2018).

Nanotechnology for Animal Health

Use of nanotechnology in veterinary and animal sciences is being increased due to its potential benefits, with very low to no harmful effects. It helps in advanced techniques such as specific drug delivery systems to treat diseases like trypanosomiasis. Nanotechnology is also being used to create biological sensors that detect changes natural body changes or germ-caused changes in the body. Also, metallic nanoparticles help in maintaining, controlling, and enhancing the fertility of animals. PCNs (protein cage nanoparticles) are being widely used in virus removal in models of flu and SARS, and it has shown success in improving the survival of the animal, which improves how the body

reacts to disease and creates strong antibody responses (Malik et al., 2023). Moreover, sperm and embryos are safely preserved by cryopreservation using nanotechnology. Nanotechnology has also allowed us to create slow-release systems for active substances such as hormones. These efforts in nanotechnology are being done due to its cost-effectiveness and its ability to control matter at the nanoscale, which causes no harmful side effects and is eco-friendly for animal health and reproduction (Mukhtar et al., 2015).

Researchers have also found out that nano-particles carry reproductive hormones that have very less side effects and they boost fertility greatly as compared to other modes of enhancing fertility. Use of nanotechnology in fertility follows ethical and moral rules and also ensures good reproduction (Hashem et al., 2021)

While nano-diagnostics have been the center of attention due to their application in early detection of diseases using tiny materials called “Nanobots,” which can detect diseases like tumors and cancers by working as markers at early stages with very high accuracy. Nano-particles are integrated with other binding molecules (aptamers) to detect germs like “*Mycobacterium Tuberculosis*” in farm animals for early diagnosis (Singh et al., 2018)

Tissue Regeneration and Wound Healing

The antimicrobial nature of some nanoparticles helps in the treatment of open wounds, thus promoting wound healing. AgNPs (Silver Nanoparticles) help in boosting tissue regeneration and promoting the wound healing process. Due to this natural and unique antimicrobial property, AgNPs are also used in dressings that are used to cover the wound in order to reduce or completely stop inflammation and help in the healing process. Some of the medical-grade bandages are also coated and fused with silver nanoparticles that are used in post-surgical practices to promote tissue regeneration and boost healing in livestock or pets. (Ghosh et al., 2014). Biodegradable polymers such as Polylactic acid (PLA) or Polycaprolactone (PCL) are used to construct materials called “Nano-Fibers”. Damaged tissues or traumatic injuries in livestock are treated and repaired with the help of these nano-fibers. When these nano-fibers are attached to the affected areas, they attach to the surface of the wound and instantly start cell division and cell migration, which leads to faster tissue regeneration and healing (Zhang et al., 2016)

Hydrogels are combined with different nanomaterials, which creates a unique material known as “nanocomposites”. This unique material is used in drug delivery systems for more controlled delivery of drugs and is also used in tissue regeneration. The quantity of water that hydrogels contain develops a very moist environment, which induces healing of tissues at a greater speed. Carbon Nanotubes (CNTs) and graphene oxides are combined together and then fused with hydrogels to improve healing time and effectiveness. These nanocomposite materials are widely used in burn wounds of animals to accelerate tissue repair and skin regeneration (Li et al., 2015).

Boosting Sperm Viability

Nanotechnology has been embedded within *in vitro* reproductive techniques to ensure that these techniques will surely serve the purpose and to improve the effectiveness of these techniques, such as artificial insemination, in vitro fertilization, and embryo transfer. This combination of nanotechnology with reproductive techniques has boosted the success rate of reproduction in animals. This collaboration has changed animal breeding, which is leading to more sustainable livestock production in tough environments, which ultimately leads to more genetic diversity. When the sperm cells are added to semen extenders, zinc oxides and Selenium nanoparticles are added to ensure the survival of sperm cells and to improve their longevity. Moreover, magnetic nanoparticles (MNPs) are also added to the extenders in order to get more genetic diversity and desired phenotypes (Kandil et al., 2019; Martins et al., 2020).

Nano-Vaccines

The focal point of scientists from all over the world has been redirected from traditional vaccines due to their low effectiveness. As medicine excels towards modernization and biotechnology progresses, scientists have developed newer techniques using nanoparticles to produce new types of vaccines called “Nano-Vaccines”. These vaccines mainly use lipid nanoparticles (LNP’s) and virus-like nanoparticles (VNP’s). As of now, these vaccines are being used to cure animal diseases relating to FMD (Foot and Mouth Disease). These vaccines have also shown effectiveness against Influenza and PRRSV (porcine reproductive and respiratory syndrome) (Zhang et al., 2016; Zhao et al., 2023).

Transforming Healthcare through Nanotechnology to Improve One Health

Groundbreaking revolutionary breakthroughs in diagnostics, treatment modalities, patient care, targeted drug delivery, etc. have been achieved so far by manipulating matter at the nanoscale, ensuring more promising advancements in the future. Nanotechnology holds immense promise in revolutionizing our daily lifestyle, such as healthcare, offering record-breaking breakthroughs in diagnostics, drug delivery, cancer therapy, and combating infections and diseases in the modern era and in the future (Ma et al., 2024).

Nanotechnology has been greatly involved in the transformation of healthcare diagnostics, offering precision accuracy in disease detection and management at the cellular level. Nano devices have been enabling early disease detection and providing vigilant medical contributions. Nanoparticle-enhanced diagnostic imaging has increased the accuracy of disease detection, such as in magnetic resonance imaging (MRI), computerized tomography (CT), and positron emission tomography (PET) (Malik et al., 2023).

Disulfiram Containing Polymeric Nano-capsules with Anticancer Activity

Disulfiram-loaded polymeric nano capsules exhibit potent anticancer activity by obstructing aldehyde dehydrogenase enzymes and proteasome function. It leads to the accumulation of defective proteins in cancerous cells, causing oxidative stress, which leads to cellular death (Ambrose et al., 2025). They also target cancer stem cells, which are implicated in relapse, offering a promising strategy for preventing relapse. It is effective against breast, lung, and colorectal cancers. The nano capsules enhance solubility, enable targeted delivery, and overcome the limitations of poor water solubility. It provides controlled release of the drug where needed. These Nano capsules combine with liposomes to facilitate disulfiram delivery, ensuring stability in the bloodstream and promoting efficient cellular uptake within tumor tissues (Filipczak et al., 2025).

Nanotechnology in Drug Delivery

Observing, fabrication, overhauling, and controlling of human biological systems at the nano level by engineering nano devices and structures at the nanometer scale is known as nanomedicine. During the past 10 years, researchers and scientists have been understanding the drug delivery of different yet especially important drugs for human health. Decreasing the frequency of drug dispensing and enhancing the comfort level for the patients is the main goal of targeted drug delivery (Sahoo et al., 2017). Nanotechnology has been used in nanomedicine, where nanoparticles are crafted in such a way that they transport drugs directly to the point of disease. This has greatly reduced the side effects and has revamped therapeutic efficiency (Ambrose et al., 2025).

Lipid vesicles that were depicted in the 60s are known as the first nanotechnological drug delivery systems that later became the term “liposomes”. On the other hand, in 1976, the first controlled release polymer system for the delivery of macromolecules was presented. As the years more efficient systems of drug delivery were developed that were competent enough to respond to changes like pH that triggered drug release. “Stealth Liposomes” were the first long-circulating liposomes that were characterized in 1987. The circulation time for the liposomes was significantly enhanced by using “polyethylene glycol” (PEG) in 1990. Furthermore, AIDS-associated Kaposi’s sarcoma was treated by using “Doxorubicin Liposome,” also known as Doxil (Farokhzad et al., 2009).

Nanotechnology and Stem Cell

The incorporation of nanotechnology with stem cells has opened various pathways to increase the efficacy of stem cell therapy by improving the delivery and differentiation of stem cells (Ding et al., 2021). Stem cells are cells that differentiate into other cells according to the needs of the body. Stem cells are produced in bone marrow and then differentiate into other cells in organs like the lymph nodes, etc. Table 1 gives us information on the different sizes in nanometers of various important objects used in nanotechnology.

Table 1: Some size ranges are connected to stem cell therapy

Object	Size (Nanometer)
Ions	0.1-0.5
Proteins	1-5
Quantum Dots	10-20
Liposomes	40-500
Carbon Nanotubes (CNTs)	100
Stem Cells	5,000-50,000
Metallic Nanoparticles	19-25
Gold nanoparticles (AuNPs)	1-100
Dendrimers	1-10
Silica nanoparticles	10-100

Stem cells have the capacity for self-renewal and play a critical role in regenerative medicine. They replace the damaged tissue and restore its normal function (Luo et al., 2022). Stem cells such as induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs) are studied for their ability in organ repair and tissue engineering, thus helping in stem cell therapy (Patra et al., 2021).

Metallic nanoparticles such as gold and silver nanoparticles have been investigated to steer MSC differentiation into neurogenic lineages because of their distinctive physicochemical properties (Kim et al., 2021). With the integration of nanotechnology into medicine and surgical techniques, we can treat some really difficult-to-treat injuries, such as spinal cord injuries. “Carbon nanotubes” are nanostructures that were found to facilitate neural stem cell differentiation and axonal regeneration in the damaged areas of

the spinal cord (Shao et al., 2020). Calcium phosphate nanoparticles have helped in bone healing by promoting osteogenic differentiation of MSCs (Bose et al., 2018).

Recent research in nanotechnology has yielded promising results, but has also created doubts regarding its impact on human health. Nanomedicine is a wide-ranging field of science and technology that unifies multiple streams of medical applications such as disease treatment and diagnosis, disease prevention, analgesic innovations, health-enhancing medications, nanoscale technology against traumatic injury, and healing approaches (Malik et al., 2023).

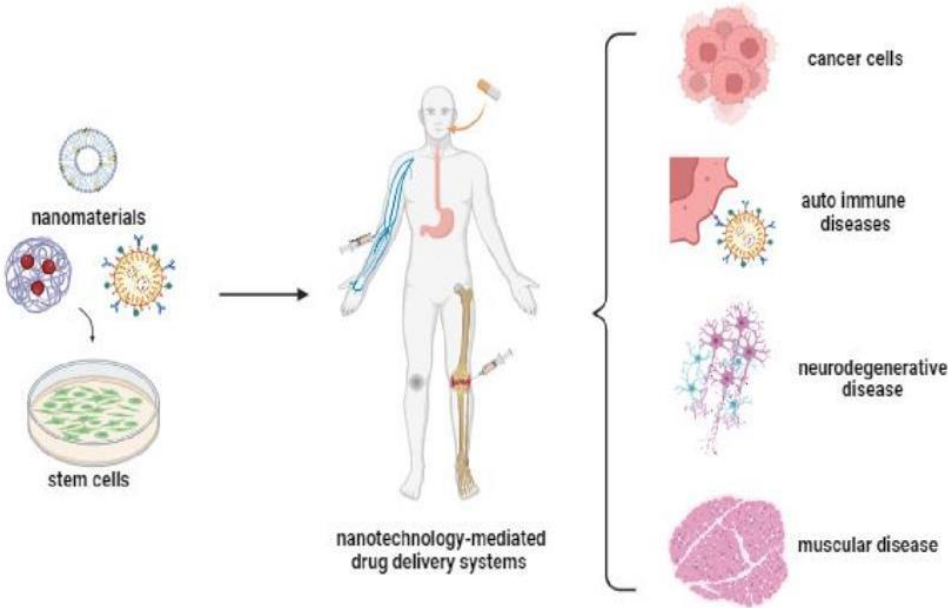


Fig. 2: Nanoparticles and stem cell integration for various treatments

In diagnosis, nanotechnology enables the development of imaging agents, biosensors, and lab-on-a-chip devices. In treatment, nanotechnology includes targeted therapy, drug delivery, and gene therapy as shown in Figure 2.

Nanotechnology provides simultaneous diagnosis and treatment of cancer using nanoscale theragnostic agents that facilitate early detection and targeted elimination of cancer cells. (Dessale et al., 2022). Silver-based therapies have been used in wound healing as they contain toxicity, bacterial resistance, which have limited their use. Now, silver nanoparticles (AgNPs) have shown the potential to avoid the limitations associated with conventional silver-based therapies (Nqakala et al., 2021).

Future Aspects

As these technologies continue to advance, they ensure more promising solutions for health-related challenges among living organisms. The major concern of biotechnology is to provide mankind with miraculous cures and solutions only with the application and manipulation of microorganisms. Along with generating such solutions, ethical concerns still need to be considered to ensure authenticity. Some cutting-edge genome editing tools like CRISPR/Cas9 are one of the most exciting frontiers in biotechnology.

Artificial intelligence (AI) and machine learning (ML) offer great prospects in advancing agricultural practices from predictive breeding to automated phenotyping. Firms of biotechnology are leveraging AI and ML solutions to carry out agricultural tasks such as harvesting crops at a faster pace than humans. Optimized product efficiency can be achieved by the combined use of tissue culture with AI and other optimization algorithms.

Conclusion

Biotechnology and Nanotechnology are reshaping the chemical processes, providing vaccines and biopharming, improving our environment, including soil health, air quality, animal, and ultimately human health. Extensive efforts are required in research and development to improve One Health and to control the escalating pollution. Green processes, biopesticides, and vaccines for emerging viruses are crucial to improve animal-, human health and to achieve a healthy and sustainable future. Biotechnology and nanotechnology are revolutionizing health, agriculture, and environmental sustainability through innovative tools like CRISPR, nano-vaccines, and regenerative therapies. Their integration offers targeted solutions for disease management, enhanced food security, and improved animal and plant health. With advances in AI and precision techniques, these fields promise transformative impacts across One Health. Continued ethical oversight and interdisciplinary collaboration are vital to ensure responsible innovation and long-term benefits for all living organisms.

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Regenerative Therapies in Elite Equine Athletes: Optimizing Recovery and Performance in Sport Horses by PRP and Stem Cell Therapy

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Abstract

Elite equine athletes always remain under massive physical stress, which results in a high prevalence of musculoskeletal injuries affecting their joints, tendons, ligaments, and bones. Traditional treatments like anti-inflammatory drugs and surgeries fall short in complete recovery from these intense injuries, so it is necessary to develop advanced therapeutic strategies. Regenerative therapies, especially platelet-rich plasma (PRP) and stem cell treatments (SCTs), offer an innovative approach by healing damaged tissues at the cellular and molecular levels. They help in enhancing the body's innate healing capabilities. PRP therapy uses concentrated platelets to release growth factors that facilitate in reduction of inflammation, provide stimulation to tissue regeneration, and speed up recovery. Stem cell therapy, mostly used mesenchymal stem cells (MSCs), supports tissue repair via direct differentiation into damaged cells, promoting new blood vessel formation, immunomodulation, and extracellular matrix production. Techniques for preparation, administration, and mechanisms of action for these therapies are continually being refined to improve results. Future directions point toward cell-free regenerative approaches, genetically enhanced stem cells, and the integration of bioengineered supports to further augment healing. As research advances, regenerative therapies are poised to become the cornerstone of equine sports medicine, improving performance longevity and welfare of athletic horses while reshaping the standard of care.

Keywords: Equines, Injuries, Chemical Drugs, Surgeries, Alternatives, Regenerative therapies

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Introduction

Equines, especially horses, play an important role in the economy of the nation. Athlete Horses, like human athletes, put too much physical stress on their bodies, especially on joints, bones, tendons, and ligaments (Bartolomé & Cockram, 2016). The possibilities of acute and chronic injuries are also extreme in athletes. Rigorous training and continuous movement make the recovery very difficult.

Conventional medicines like anti-inflammatory medicines and surgeries have constraints in complete recovery (Paoloni et al., 2009). Retrieval from these injuries is very significant not only for the welfare of horses but also for the restoration of competitive potential. These horses have superior genetics and the best stamina in their sport, but injuries can ruin their capability. Traditional medicines are mostly used for symptomatic relief, but they work at the cellular level, remold the repair processes at the molecular level, and restore the exact structure of the cell or tissue for fully functional working by introducing bioagents like growth factors, platelets, and stem cells (Mahla, 2016).

So, it is foremost to figure out modern techniques that can help them to recover completely (Upadhyay, 2015). Regenerative therapies are procedures that are used to reinstate or restore the damaged cells or tissue of the body (Sánchez et al., 2012). They pace up recovery by restoring the damaged tissue or cell via using the normal healing process of the body (Upadhyay, 2015). They increase the capacity of body to heal quickly. This chapter explores various modern therapies that are being used for the welfare of equines to enhance their efficiency and make their muscles and bones strong.

Key Regenerative Therapies in Equine Practice

Platelet-Rich Plasma (PRP)

PRP was developed only for the use of humans in the 1970s (Alves & Grimalt, 2018), in which only platelets are transfused to those patients with low platelet numbers, but with further progressions, it was used as a regenerative therapy agent in the 1990s, initially in maxillofacial and dental surgery. The transition to veterinary medicine ensued in the 2000s, especially used in equine orthopedic (Camargo Garbin et al., 2021).

Doctor Alan Nixon and the team were pioneers of equine PRP at Cornell University College of Veterinary Medicine. They were first used for the tendon and ligament repair, which showed wonderful results. They work on evaluating the ability of PRP for the reduction of inflammation, enhancing cellular proliferation, and stimulating collagen synthesis in damaged tendons, especially in the superficial digital flexor tendon (Schnabel 2023). Through in vitro (lab-based) and in vivo (live animal) research models, Nixon's team demonstrated the benefits of PRP in equine rehabilitation therapies as compared to traditional medicines. This research recognized the credibility of PRP, which leads towards the practice of PRP to treat soft tissue injury in sport horses (Specchio, 2013; Schnabel, 2023). PRP is an autologous concentration of platelets in a small volume of plasma. It is prepared by the centrifugation of the horse's own blood to isolate the platelets (Miranda et al., 2019). It is categorized into three types: pure PRP in which low leukocyte contents are present with minimal RBCs (Yin et al., 2016), leukocyte PRP which has higher leukocyte number and inflammatory cytokines (Di Martino et al., 2022), and platelet-rich fibrin (PRF) is prepared without anticoagulants and forms a gel matrix (Singh et al., 2012).

Preparation of PRP is a crucial procedure in which whole blood (50-60 ml) is collected from the jugular vein of the horse by sterile methods in a syringe or collection tube (ACD-A) for the prevention of clotting during the process. Strict aseptic techniques are mandatory to avoid contamination because PRP will be injected directly into sterile organs like tendons and joints (Dashore et al., 2021; Segabinazzi et al., 2021). After collecting, the next process is centrifugation, in which two spin centrifugation protocol is applied. First spin is a soft spin at the slow speed of 1000-1500rpm for 10-15 minutes. After the first spin, the blood divided into three layers. The top layer is plasma, the middle layer is a buffy coat, which is rich in platelets and white blood cells, and the bottom layer is RBCs. This spin separates the plasma and buffy coat from heavy red blood cells (Fukuda et al., 2020; Xue et al., 2025).

The second spin is called hard spin, in which the centrifugation happens at 3000- 3500 rpm for 10-15 minutes. Platelets are forced to the bottom to form pellets. The top portion is removed while plasma and pellets are mixed to form platelet-rich plasma (Seidel et al., 2019; Fantini et al., 2021). Then this platelet-rich portion is carefully extracted by using a syringe or a pipette. Commercial PRP kits are generally used to standardize the preparation of PRP, such as ACP, Equine Pure PRP, or GPS III (Xue et al., 2025).

Mechanism of Action

If an immediate application is necessary, then use it in natural form, but it can be enhanced into activated form by adding Calcium chloride, thrombin, etc. This activation leads toward degranulation of platelets, forming a fibrin shell and releasing growth factor (Camargo Garbin et al., 2021). Growth factors, including PDGF, TGF- β , VEGF, and IGF-1, are released for various functions (Roberts & Halper, 2021). Platelet-derived growth factor (PDGF) stimulates fibroblast and smooth muscle cell proliferation (Sánchez et al., 2025). Transforming growth factor (TGF- β) promotes the synthesis of collagen and tissue regeneration (Huang et al., 2024). Vascular Endothelial growth factor (VEGF) enhances angiogenesis (process of forming new blood vessels) (Chávez et al., 2025). Insulin-like growth factor 1 (IGF-1) promotes tissue remodeling and cell differentiation (Zhang et al., 2024).

PRP also has anti-inflammatory effects (Oneto & Etulain, 2021). Leukocyte-rich PRP contains IL- β , IL-6, and TNF- α , which are inflammatory cytokines, and can have pro- and anti-inflammatory effects according to the environment (Tramés et al., 2022). Timely administration can reduce the inflammation of tendons due to injuries. PRP provides chemotactic stimulation, which supports tenocytes proliferation, ligament fibroblasts, and recruits progenitor cells that help in tissue repair and scar formation (Tramés et al., 2022). The route of administration for PRP is very important. The following are some routes for PRP in equine medicine.

Intralesional injection is generally used in tendon and ligament injury, especially injuries of the superficial digital flexor and suspensory ligaments. It is performed under an ultrasound guide for exact placement at the injury. A 22G or 20G needle is used to inject PRP under sedation or limb restraint. Volume of PRP varies with the size of the lesion, usually injected between 2- 5 mL. Sometimes this is repeated after several weeks if needed. It helps to remodel collagen in the lesion (Hijazi et al., 2022).

Intra-articular injection is used to inject directly into the joint space in the condition of joint inflammation or mild osteoarthritis. For this type of PRP joint is aseptically prepared, and PRP is injected into the landmark under sedation. 3- 6 mL PRP is injected according to joint size. It helps in modulating inflammation and promoting cartilage repair (Rodríguez-Merchán, 2022a). Subcutaneous or perilesional injection is used for the soft tissue swelling around the tendons, as mentioned in Table 1. PRP is injected around the injury site rather than directly into it. Its result becomes best by adding fibrin matrix or PRP gel. It helps in stimulating local healing and reducing external inflammation (Rani et al., 2023).

Intradermal or topical application of PRP is used to heal chronic wounds in horses. PRP is applied directly to the wound or injected into the wound margin. It may be used with bandages or dressings. It helps in improving granulation tissue and reducing infection (Abd Elraouf et al., 2023).

Stem Cell Therapy in Horses

Stem cell Therapy is a revolutionary regenerative therapy used in equine sports medicine, particularly in the cure of musculoskeletal injuries that are common in sports horses (Cequier et al., 2021). This therapy benefits from augmenting tissue regeneration, reducing reinjury rates, and promoting faster recovery as compared to traditional medicines. Stem cells are the undifferentiated cells with the ability to self-renew and differentiate into specific and specialized cell types, e.g. tendons cells, cartilage cells, bone cells (Chowdhury et al., 2021). Their regenerative potential makes them highly desirable for the treatment of injuries that heal poorly in normal conditions (Zeng, 2023).

Several types of stem cells have been isolated in equines: mesenchymal Stem Cells (MSCs) are the specialized type of adult stem cell that originates from the mesodermal layer during embryonic development. They are multipotent, meaning they can be differentiated into various cells, particularly those forming connective tissues, including osteocytes, chondrocytes, tenocytes, fibroblasts, and myocytes (Zhang et al., 2024). Due to these properties, they are highly able to treat musculoskeletal injuries in horses. In horses these stem cells are harvested from bone marrow and adipose near tailhead or cutaneous fat stores (Yildirim et al., 2020).

Table 1: Mechanism of PRP action and immune modulation based on origin and activation

Step	Key Elements	Biological Effects	References
Bone Marrow	Hematopoietic stem cells	Differentiate into megakaryocytes	(Stone et al., 2022)
Megakaryocytes	Platelet production	Platelets enter blood circulation.	(Carminita et al., 2024)
Platelets (Resting)	Platelet production	Inactive until activated by stimulants.	(Veninga et al., 2022)
Activation Stimuli	Thrombin / Calcium chloride (CaCl ₂)	Converts resting platelets into an active form in PRP.	(Ahmed, 2023)
Activated Platelets in PRP	Release - PDGF (Platelet-Derived Growth Factor) - HGF (Hepatocyte Growth Factor) - FGF (Fibroblast Growth Factor) - Histamine	of: Promote angiogenesis, endothelial migration, and proliferation.	(Cecerska-Heryć et al., 2022)
Inflammatory Signaling	Release RANTES, IL-8, Platelet microparticles	of: Recruit immune cells, then monocyte polarization. and trigger cytokine and chemokine production	(Scopelliti et al., 2022)
Response of Immune Cell	Influx of immune cells	Improves healing, reduces inflammation	(Caballero-Sánchez et al., 2024)
Interaction with MSC (Mesenchymal Stem Cell)	Stimulated by PRP factors (e.g., SDF-1, HGF)	Promote stromal cell proliferation, cytokine production, and angiogenesis.	(Bouland et al., 2021)
Tissue Anabolism	Growth factors (IGF, TGF- β , MMP)	Supports extracellular matrix production and tissue regeneration.	(Klein, 2022)

Embryonic Stem Cells (ESCs) are pluripotent cells taken from the inner cell mass of blastocyte which is an early stage of preimplantation embryo about 6-7 days post fertilization in mammals (Irie et al., 2020). They can differentiate into three germ layers (ectoderm, mesoderm and endoderm) which can make any cell type in the body. Their self-renewing ability can proliferate in dedifferentiation states under proper culture conditions by which large number of cells can be made (Efthymiou et al., 2014). These properties make ESCs extremely powerful for regenerative medication, at least in theory. They are garnered from early embryos via breeding programs e.g. embryo flushing (Kingham & Oreffo, 2013). Then isolate the inner cells mass under sterile laboratory conditions, culture the isolated cells in specific media that preserve their pluripotent state. However, this process is rare in equine compared to human and mice but has extensive ability to use in regeneration therapies. This therapy is very beneficial because they can be used to treat any type of injury including tendon, bone and nerve injury. Their growing ability in culture media makes it more favorable without losing their characteristics (Górska et al., 2024). But they are used rarely in horses because it is unethical to destroy the early embryo. Moreover, the risk of tumor formation is higher in these ESCs than in other stem cells, and they can form teratomas if injected without proper differentiation.

Mechanism of Action

In the initial study, scientists believe that stem cells directly replace the damaged tissue by differentiating into specific cells. But with modern research, a different mechanism has been found. The stem cells create the paracrine effect by releasing growth factors and cytokines that help in the reduction of inflammation, as shown in Figure 1 (Smith et al., 2024). They stimulate resident cells to proliferate and repair the damaged tissues, promote the new blood vessels (Angiogenesis), and modulate the immune response as mentioned in Table 2. They act as biological stimulators for healing rather than simple building blocks (Reis et al., 2024). In the case of MSCs, they can act as building blocks by differentiating into specific cell types and replacing the damaged cells when they get signals from certain environments (Salsbury). In injury, they can detect local biological signals like growth factors and cytokines. As the right conditions arrive, they differentiate to replace damaged cells, like as tenocytes in case of tendon injury or into chondrocytes in case of damaged joints (Augustin et al., 2024). Beyond simply replacing damaged cells, MSCs apply immunomodulatory effects that make them precious in mastering inflammatory and immune-mediated conditions in horses (Feng et al., 2025).

Collection, Culture and Administration

Stem cells used in equine regenerative therapies are mostly mesenchymal stem cells (MSCs). They are collected from two main sources: Bone marrow or adipose tissue (Siddiqui et al., 2024). Bone marrow-derived MSCs are obtained from the sternum or the tuber coxae. For this process, horses are sedated, and local anesthesia is administered. A sterile bone marrow biopsy needle is injected into the bone marrow space. 10-30 mL of bone marrow aspirated is removed into a heparinized syringe, which prevents clotting (Ferris et al., 2014; Al Naem et al., 2020).

Adipose-derived MSCs are collected from the tail head or abdominal fat of the horse. Under sedation and local anesthesia small incision is made to collect 10-20g subcutaneous fat (Cequier et al., 2021).

Strict aseptic techniques are crucial to avoid contamination, which can lead to severe infection in the body of horse. After collection, bone marrow or adipose fat is processed to isolate and expand the MSCs (Al Naem et al., 2020). For isolation density gradient centrifuge is used to separate MSCs from RBCs and other unwanted components (Al Naem et al., 2020). Cells are then plated into a cell culture flask with media such as DMEM or alpha-MEM supplements with antibiotics and fetal bovine serum (Pezzanite et al., 2021). Then, cells are cultured in an incubator with a temperature of 37°C, 5 % CO₂, and high humidity. MSCs stick to the plastic surface and start forming colonies. Media should change every 2-3 days to remove non-sticky cells (Espina et al., 2016). As confluency reached 80-90%, cells were passaged to new flasks to

continue the expansion. Expansion takes around 2-4 weeks, depending on the source and horse-specific cell growth rate. MSCs makers are confirmed by using a flow cytometer, while trilineage differentiation assays are performed to confirm multipotency (De Schauwer et al., 2011).

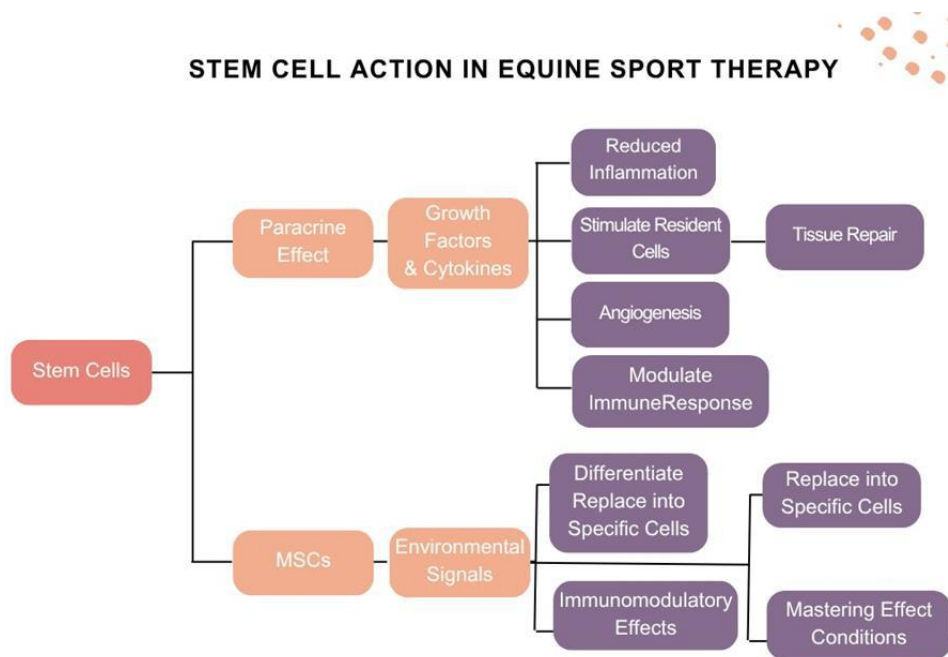
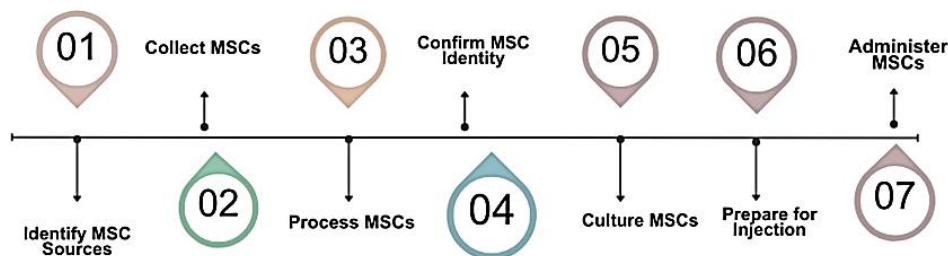


Fig. 1: Mechanism of action of stem cells in equine sport therapy

Equine Stem Cell Therapy Process

Fig. 2: The process of equine stem cell therapy



As a large enough number of MSCs is obtained, the cells are prepared to be injected into the body. They are harvested by using enzymes that detach them from plates. After detachment, cells are washed and resuspended in saline or plasma for injection, as shown in the therapy process, Figure 2. The final product contains 10-50 million MSCs (Broeckx et al., 2019). Several routes are adapted for the administration of stem cells according to the injury site: Intralesional injections are used to inject directly into the lesion site under ultrasound guidance. About 1- 5 mL volume stem cells is injected. This administration is used in case of tendon or ligament injury (Geburek et al., 2016; Geburek et al., 2017). Intra-articular injections are directly injected into the joint space in case of joint injury or osteoarthritis at a dose of 3-6 million MSCs per joint (Joswig et al., 2017; Magri et al., 2019). Intravenous routes are rare, but they are used in cases of systemic inflammatory conditions. MSCs are administered intravenously for generalized actions (Broeckx et al., 2014). The perilesional route of administration is used if intralesional injection is not possible. MSCs are injected around the damaged structure (Wilke et al., 2007; Barrachina et al., 2018).

Future Directions of Regenerative Therapies

The field of regenerative therapy is expanding steadily with the progression of medical science. In the future, it will be the most used veterinary practice to treat the acute and chronic injuries of sport horses and other animals. The regenerative therapies that we are using nowadays are at their first stage, studies are paving their way to enhance the therapeutic uses of these procedures. Advancements in genetic and molecular biology are thriving on gene therapy, which is a futuristic approach to personalized therapies according to a horse's genetic makeup and characteristics of injury. This technique helps in healing injuries and other problems at the gene and molecular levels. In regenerative medicines, researchers are using whole cells like stem cells and plates, but there is raised curiosity in using secretory components

besides whole cells, such as exosomes, micro vesicles, and growth factors. These cell-free therapies reduce the risk of immune response, formation of tumors, and regulatory complications, although they still give regenerative benefits.

Table 2: Mechanism of Stem Cell Therapy in Equine Medicine

Step	Key Elements	Biological Effects	References
Stem Cell Origin	Mesenchymal Stem Cells (MSCs)	Bone marrow, adipose tissue multipotent	(Soliman et al., 2021)
Isolation	and Collection by bone marrow aspiration or fat harvest	Increase the number of viable	(Pakzad et al., 2022)
Expansion	lab expansion under sterile conditions	therapeutic cells before injection.	
Delivery to Target Site	Injection into injured tendon, ligament, or joint (intralesional or Intra-articular routes)	MSCs are home to the injury site	(Rodríguez-Merchán, 2022b)
Cellular Action	Direct differentiation into local cell types (e.g., tenocytes, chondrocytes)	Replace damaged cells and regenerate tissue structure.	(Donderwinkel et al., 2022)
Paracrine Action	Secretion of: Stimulate local progenitor cells, enhance growth factors (e.g., TGF- β , IGF-1) cytokines exosomes	tissue repair, and modulate immune response	(Xue et al., 2024)
Immunomodulation	Suppression of T-cells, B-cells, and macrophages Reduction of pro-inflammatory cytokines	Reduces chronic inflammation and supports tissue healing (e.g., in osteoarthritis).	(Babu et al., 2021)
Tissue Regeneration	ECM (extracellular matrix) production, angiogenesis reduced fibrosis	Enhances biomechanical strength and functional recovery	(Potekaev et al., 2021)

In mesenchymal stem cells therapy, we use native cells that we extract from the body, but researchers are investigating the modification of MSCs for the extra extraction of beneficial proteins like growth factors. The modified MSCs have more potential to repair the targeted injured tissue with more precision and faster as compared to native cells. Many futuristic materials can be combined with stem cells and PRP to enhance their abilities, such as hydrogel, fibrin matrices and nanoparticles, which lead to tissue support and promote healing of joints, tendons, and ligaments. One of the future goals is to establish a standardized protocol for the preparation and use of PRP and stem cell therapy. This can lead to improving the treatment strategies, research facilities, and increasing clinical confidence in regenerative therapies. Regenerative therapies should be used on a regular basis as sophisticated equine sport therapies to enhance the healing process and prevent reinjuries. This will increase the confidence of the veterinarians, and they will do more research on it to enhance its benefits.

Conclusion

Equines, especially horses, play an important role in the economy of the nation. Athlete Horses, like human athletes, put too much physical stress on their bodies, especially on joints, bones, tendons, and ligaments. Various traditional drugs and surgeries were used, but they may cause complications. Regenerative medicine has opened new ways for treating musculoskeletal injuries in horses, especially elite equine athletes. The benefits of PRP and Stem cell therapy are undeniable. They help in promoting natural healing as well as stopping reinjuries. Due to working at the cellular level, healing becomes fast and precise, helping equines a lot in returning to their peak performance. Progress can be made in this therapy by continuous research and clinical use of these therapies. They promise care and a long career to athletic horses.

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Biosensors and Nanotechnology: Tools for Advanced Diagnostics

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Abstract

Incorporating nanotechnology into biosensors has resulted in more accurate diagnostics, faster test outcomes and lower costs. Many research studies showed that the presence of gold nanoparticles, carbon nanotubes and quantum dots in biosensors increased both how sensitive they were and how small the amounts they could detect. Using nanoparticles in their sensors allowed researchers to find both viral and bacterial pathogens in the body before most other methods could detect them. Using graphene and polymer-based nanomaterials, sensors could measure glucose, lactate and electrolytes in the body continuously and accurately. With the use of nanostructured biosensors, early detection and improved judgment of prognosis became possible for PSA, CEA and HER2, whose amounts were measured in such small units. With multiplexed nanosensors, researchers could detect different analytes from one sample which cut down the testing time and improved how many results could be processed in the same run. Implanted biosensors produced from biodegradable nanostructures remained secure and did not show any significant change in response from the nearby tissues for a prolonged time. While these improvements were achieved, differences in performance resulting from the environment and the short lifespan of a few nano-sensors were observed. However, the results prove that nanotechnology-based biosensors can offer fast, sensitive and accurate diagnostics for different purposes.

Keywords: Nanobiosensors, Medical Diagnostics, Wearable Sensors, Personalized Medicine

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Introduction

The quick development of healthcare and diagnostics has led to a strong need for technology that is accurate, efficient, lightweight, movable and usable in different situations. Because people are now living longer, the healthcare sector must meet the demands for efficient detection, continuous monitoring and personal treatment measures. As more chronic diseases, outbreaks and health risks appear, it is more important than ever to use new diagnostic techniques that provide accurate and helpful findings. Using the standard approaches may be effective, but they generally do not work well with the many demands we face today. Integrating biosensors and nanotechnology is now considered a groundbreaking solution for dealing with the challenges mentioned above (Nakhjavani et al., 2024).

New medical technology has revolutionized the way diseases are spotted and looked after. Biosensors and nanotechnology are now important tools in advanced diagnostics. A biosensor detects biological signals by converting them into quantities, giving more precise and sensitive output when looking for different biomarkers (Kaya et al., 2022). Nanotechnology helps achieve improvements in biosensors by allowing for superior sensitivity, a smaller size and continual detection. A biosensor includes a bioreceptor that recognizes certain molecules, along with a transducer that changes these interactions into signals in optical or electrochemical form. Since the first introduction of biosensors in 1962 to detect oxygen with enzymes, they have been developed into their modern sophisticated forms. As a result of their high sensitivity, selectivity, affordable cost and easy miniature design, they are often used today for drug analysis as well as for detecting heavy metals and environmental pollutants (Malik et al., 2023).

Basically, biosensors detect substances by the combined action of a bioreceptor and analyte which is then converted by a transducer using electrochemical, optical, magnetic or electrical methods. Such biosensors are grouped by their recognition components as immunosensors, apt sensors and Geno sensors, while other groups define biosensors by function as affinity, chemical and catalytic types (Nakhjavani et al., 2024). Moreover, scientists are investigating new ways like wearable biosensors which promise to make it possible to diagnose testing results instantly on site. Nanotechnology is important for enhancing biosensors because it uses the unique features of nanomaterials, for example their high ratio of surfaces to volume, quick reaction rate and electronically and optically changeable qualities. With these features, it becomes possible to develop modern tools for diagnostics that are easier to carry and more accurate. Nanotechnology

linked to biosensors has made possible new systems in healthcare such as wearable, multipurpose and implanted biosensors for use in infection control, cancer monitoring and monitoring food safety (Hammond et al., 2016).

The chapter covers in detail biosensors, applications of nanotechnology in diagnostics and their use in advanced medicine. It demonstrates how examining different principles and real-life uses shows how these technologies are advancing personalized medicine and healthcare, coping with worldwide health problems and driving important changes in diagnostics.

2. The Role of Nanotechnology in Advancing Biosensor Design and Performance

Developments in nanotechnology have enabled the creation of nanodevices that directly interact with the biomolecules or analytes for which the biosensors used. These new biosensors are unique in that they have their own magnetic, electrical and optical qualities, greater conductivity, and more sensitivity and respond much faster than traditional biosensors. As a result, these types of biosensors have roles in drug delivery applications (Mao et al., 2018). There is evidence that nanotechnology has a strong impact on the medical field when it comes to finding diseases by using resonance, electrochemical, magnetic and electromechanical methods (Karikalan et al., 2016).

Biosensors have seen big progress recently due to important developments in transducers, nanotechnology and ways to amplify signals. Even so, biosensors typically experience irregular signal noise. A number of biosensors need to depend on aptamers or antibodies as bioreceptors which shortens their shelf-life and leads to unstable sensing over time. Generally, commercial development of biosensors is limited by how accurate and reliable they are (Chandra et al., 2017). In many possible ways, researchers are devoting great effort to improving the performance of biosensors. There have been a number of studies that examine machine learning (ML) techniques for looking at sensing data. ML makes it possible for biosensors to address current issues by changing standard biosensors into smart ones which can anticipate what type or quantity of analyte they detect using an algorithm (Bhaiyya et al., 2024). Other research teams have centered chemometrics on the analysis of how a biosensor responds. Chemometrics is a popular method for chemical analysis that uses math or statistics to get the most from chemical data and improve the design of experiments (Banerjee et al., 2021; Cui et al., 2020; Deepa et al., 2022).

Fabrication includes nanoparticles and the resulting devices are recognized as nano-biosensors. Nanomaterials are especially important in bioanalytical sciences due to the many bio-imaging, diagnostic, medication and treatment activities they support (Munawar et al., 2019; Tran et al., 2015). Amperometric devices are applied to investigate enzyme reactions, but fluorescent QD devices are preferred for testing the binding ability and use of conjugated nanoparticles in immunolabeling and analyzing interactions between different biomolecules. Nanoparticles are promising for biosensing because they naturally have optical qualities and can be joined to fluorescent markers. By using electro/chemiluminescent, fluorescent and bio-FET tests, nanomaterials like CNTs or rGO, graphene and graphene sheets can be produced. Fluorescent detectors rely on quenching properties of graphene in fluorescent-based assays (Rasheed et al., 2019; Singh et al., 2016) and different measurement methods make carbon nanomaterials adopt several forms (Ramesh et al., 2022).

3. Types of Biosensors

3.1 Electrochemical Biosensors

These sensors measure the amount of an analyte by reacting with it and producing an electrical signal that represents that amount. The structure of a typical electrochemical sensor has a working electrode as the sensing element and a reference electrode in contact with an electrolyte. Most of the time, a three-electrode system is chosen, where the reference connects to a high-impedance potentiometer and the counter electrode finishes the circuit for charge flow. Many applications in biosensing use electrochemical tools, including potentiometric (by measuring the open circuit potential changes and biological field-effect transistors), amperometry (by monitoring reduction/oxidation reactions through current measurements) and impedimetric (by detecting changes in system impedance when biolayers are added to the electrode surface). Although other electrochemical techniques can be applied to biosensing, their significance is not as high. A main benefit of electrochemical biosensors comes from their basic design. Electrodes with low cost allow sensors to be built simply and used quickly in small, portable systems. Detecting the amount of an analyte inside a complex sample at the point-of-care in near real-time is highly useful for medicine, handling current diseases and monitoring the environment. In particular, amperometry biosensors are common in helping people with diabetes quickly and accurately test their glucose levels from only a small drop of blood taken by a prick of a finger. The introduction of carbon nanotubes and graphene into electrochemical biosensors is lowering LOD values much further than before which helps drive the development of creative biosensing solutions (Hammond et al., 2016). Table 1 provides an overview of different types of biosensors and their integration with nanoparticles. It categorizes biosensors based on their biorecognition elements, such as antibodies in immunosensors, aptamers in apt sensors, and DNA/RNA in Geno sensors. It highlights the role of nanoparticles in enhancing the performance of these biosensors by improving sensitivity, amplifying signals, and enabling miniaturization. For instance, nanoparticles help in the rapid detection of pathogens and biomarkers, increasing the efficiency of diagnostics. Additionally, other biosensor types like paper-based, microfabricated, and capacitive sensors benefit from nanoparticle incorporation, offering advancements in low-cost, portable, and multiplexed detection systems.

3.2 Optical Biosensors

Optical biosensors make it possible to detect many biological and chemical materials directly, in real time and without using labels which is more advantageous than conventional techniques. Advantages of these methods are their great accuracy, sensitivity, small size and low cost. Various modern methods from engineering and biology including microelectronics, MEMSs, micro/nano-technologies, molecular biology, biotechnology and chemistry are used to develop new optical biosensors. Over the last decade, there has been fast growth in research and development of optical biosensors. Most efforts in optical biosensor research and development have been put into healthcare, environmental fields and biotechnology. Biosensors find many uses in medicine, the environment and biotechnology and each of these fields has specific requirements for the analytes measured, required accuracy, sample concentration, reaction period, recycling time and how to clean the biosensor (Dey & Goswami, 2011).

Table 1: Types of Biosensors and use of Nanoparticles

Biosensor Type	Biorecognition Element	Use of Nanoparticles	Examples/Applications	References
Immunosensors	Antibodies	Nanoparticles enhance binding efficiency, signal amplification, and sensitivity.	Pathogen detection, biomarker identification.	(Chen et al., 2023)
Apt sensors	Aptamers	Nanomaterials improve sensor performance by increasing surface area and reaction sites.	Cancer biomarker detection, nucleic acid analysis.	(Hosseinzadeh & Mazloum-Ardakani, 2020)
Geno sensors	DNA/RNA	Nanoparticles can improve the sensitivity of nucleic acid detection by increasing conductivity or optical properties.	Genetic disease diagnosis, pathogen identification.	(Babaei et al., 2022)
Paper-based Biosensors	Various biological recognition elements	Nanoparticles enable low-cost and portable diagnostic tests with enhanced sensitivity.	Point-of-care diagnostics, rapid tests for infections.	(Nguyen & Kim, 2020)
Microfabricated Biosensors	Varied bioreceptors (enzymes, antibodies)	Nanoparticles facilitate miniaturization, signal amplification, and multi-analyte detection.	Lab-on-a-chip applications, multiplexed detection.	(Blair & Corrigan, 2019)
Capacitive Biosensors	Surface-bound bioreceptors	Nanoparticles improve the sensitivity and increase the capacitance of the sensor.	Real-time monitoring of pathogens and biomarkers.	(Canfarotta et al., 2018)

The optical class of biosensors is the one reported most frequently. By exploiting interactions between the optical field and biorecognition elements, we can detect biological changes. Optical biosensing is generally split into two main ways: label-free and label-based. Without a label, the detector measures the signal that comes up as the focused molecule contacts the transducer. With label-based sensing, labels are attached and then the optical signal forms due to colorimetric, fluorescent or luminescent approaches. Label-free sensing can detect glucose using enzymes during an oxidative reaction. Biosensors have found their biggest success yet in the developing type of device for checking blood glucose, used by diabetics. Yet, in a few cases, for example, when an antibody and antigen interact and one of the bio reactants carries a tag, labeling may affect binding and introduce unwanted mistakes into the analysis (Damborský et al., 2016).

3.3 Magnetic Biosensors

Modern bioanalytical tools and biomedical care depend on particles, from nanometers to micrometers in size, made of magnetic materials. Many diagnostic and therapeutic procedures in healthcare, environmental science and biotechnology use their diverse functions and special magnetic properties. Magnetic detection is distinguished by low background noise relative to the usual problems of signal noise and contamination from the environment seen with optical and electrical detection. As a result, magnetic methods are highly appealing for producing assays that are both highly sensitive and specific (Lee et al., 2015).

Due to their ability to adapt and work easily, different types of magnetic particles are developed as signal markers, separation platforms, force gauges and sensors. Many diagnostic tests use magnetic particles to isolate particular proteins, nucleic acids or cells from complex body fluids. With magnetic separation, testing miniaturized devices such as microfluidics becomes both more accurate and efficient (Chircov et al., 2019). It is also possible to use magnetic particles as labels in bioassays and by measuring them with a magnet, results can be quickly and precisely determined without using bulky optical devices. Apart from diagnosis and labeling, magnetic particles are used for various purposes in imaging and medical therapies. Many doctors use SPIONs as contrast agents in MRI to help see tissues clearly and spot small abnormalities accurately. In addition, particles in a magnetic field heat up which is the basis for magnetic hyperthermia, used to kill specific cancer cells while nearby healthy tissue remains unharmed (Yang et al., 2022). Magnetic particles are also finding their way into new drug delivery systems. After adding targeting molecules and drugs to their surface, they can be driven to chosen parts of the body with the help of external magnets, delivering treatment without a surgical procedure. Magnetic particles are used creatively to study the interactions of biomolecules. Hooking a magnetic tag to a biomolecular combination, like an antibody-antigen or DNA-protein set, enables investigators to see its binding response in different circumstances. Molecular dynamics help researchers create better tools for diagnosis and treatment. Now, these tools can detect biomarkers for diseases like sepsis and influenza in a simple, reliable way at the patient's bedside (Haghighayegh et al., 2024). In addition, test kits using magnetic particles are being used for environmental surveillance. They support the discovery and estimation of heavy metals and toxins within water samples, making the process simpler, more convenient and more sensitive (Chen et al., 2017).

3.4 Piezoelectric Biosensors

Piezoelectric materials are found in a wide range of technology and are typically part of many electronic devices. Oscillators on a piezoelectric system, piezoelectric materials respond by motion whenever a surface flows across them and are thus highly suitable for measuring affinity between particles in biosensors (Pan et al., 2024). A great number of anisotropic materials can generate a piezoelectric effect. Both inorganic and organic substances, as well as nucleic acid, exhibit electric charge under mechanical stress. On the other hand, biosensors are built with only a limited number of materials and quartz crystal is the most typically used due to its dependability. In the future, even more changes are expected because of progress in chemical synthesis and nanomaterials development. The best way to take advantage of piezoelectric biosensors is to make direct measurements with the analyte without needing any labels. For this reason, antibodies and antigens promise to work seamlessly with a piezoelectric sensor (Pohanka, 2017).

4. Nanotechnology in Diagnostics

The multidisciplinary technique of nanotechnology works by applying molecules made on a nanoscale. Nanotechnology is considered a pioneering and fast developing field where objects are manufactured, processed and applied using control over features smaller than a

nanometer. From the Greek word nano, we get the term nanotechnology which means dwarf technology. Objects called nano-particles are considered single, with dimensions that do not exceed 100 nm (Prasad et al., 2021). Specific characteristics of nano-particles are due to their small size and their chemical and physical features. When materials are altered, the resulting products gain versatility and effectiveness which makes them desirable for both industrial and medical fields. These nanotechnologies and nano-materials are used so widely that their particles end up in the environment (Ahmeda et al., 2017).

Types of Nanomaterials Used in Diagnostics

Over the last few years, the development and testing of nanoparticles has increased and their possible uses for diagnosis and therapy have become very popular. Even though diagnostic nanoparticles are being suggested, only iron oxide nanoparticles have been used in routine clinics at present. This problem arises mainly because it is hard to obtain appropriate pharmacokinetic qualities and to manufacture uniform nanoparticles every time. People are also concerned about their ability to be broken down, eliminated and their toxicity. The greatest number of nanomedicines currently used in the clinic are meant for therapeutic action. Through using these modified nanoparticles, researchers aim to bring the (chemo-) therapy drug directly to the diseased site while protecting healthy organs and tissues, usually by counting on the enhanced permeability and retention (EPR) effect. Additionally, because they can mix various diagnostic and treatment features, nanoparticles show excellent potential for theranostics and are considered highly valuable for designing individualized nanomedicine therapies (Baetke et al., 2015).

Several studies involving quantum dots confirm the usefulness of QDs for finding tumor cells early, imaging multiplexed tissues, labeling cells inside a sample and detecting markers in cells during immune histochemistry. Biologically modified QDs replace commonly used organic fluorescent dyes for single source excitation, a relatively narrow emission band, a higher quantum yield, longer fluorescence time and greater stability when exposed to light. The reason many QDs are unsuitable in biomedicine and the biological field is because they are toxic and do not mix well with biological molecules. To solve these problems, researchers use InP QDs instead of cadmium-based ones and take steps to passivate the surface. The latest developments in QDs give cause to believe cancer cells can be detected at an early stage. They are designed this way because polymers wrap them and antibodies or biomolecules are attached, so they can be used to intentionally treat certain cancer cells. Therefore, because of their high fluorescent strengths and the way their light emission depends on size, quantum dots may be applied in the development of highly sensitive in vivo research and treatment tools (Devi et al., 2022).

4.1 Carbon Nanotubes (CNTs)

Nanotechnology in biomedicine has made considerable progress over the years because of how promising nanomaterials are. The special attributes of carbon nanotubes (CNTs) have made them a useful choice in cancer diagnosis and therapy. They are seen as a promising family of nanomaterials that can both spot cancerous cells and deliver medicines or small therapeutic molecules to them (Sabeti et al., 2024). During the past few years, CNTs have been tested in practically every cancer treatment approach, including methods for drug delivery, targeting the lymphatic system for chemotherapy, thermal treatments, photodynamic therapy and gene therapy (Murjani et al., 2022).

4.2 Nanowires

In the last ten years, silicon nanowire (SiNW) biosensors have been investigated as sensitive, label-free and electrical tools for finding biological molecules. Point-of-care (POC) devices for diseases could be realized using SiNW biosensors as these sensors have potential for being small and built into other devices (Namdari et al., 2016). The workflow of a nanobiosensor system begins with various sample sources, such as environmental, food, human, and cell culture samples. These samples are analyzed using different bioreceptors, including cells, bacteria, antibodies, DNA, and enzymes. The interaction between the samples and bioreceptors is detected through an electrical interface, incorporating electrodes, nanotubes, nanoparticles, and field-effect transistors. Signal transduction is performed using various transducer types, such as optical, acoustic, thermal, and electric. Finally, the processed signals are displayed and analyzed using a signal processor, enabling the detection and monitoring of specific biomarkers.

5. Benefits and Drawbacks of Nanotechnology in Diagnostics

Engineered nanomaterials help deliver drugs directly to afflicted areas, decreasing the harmful effects of many medications. Because of their very small size and high surface area, nanoparticles are now often used to deliver drugs. Because nanoparticles are so small, they deliver drugs more accurately within cells and throughout the body and their structure keeps the drug stable as it moves through the body. Essential benefits aside, using nanoparticles for drug delivery comes with many safety issues. Small guests are great, but there are a few issues they can bring. It is significant that new and lasting materials are being used to make the nanoparticles. A few nanoparticle types can induce inflammatory reactions and cause tissue scarring. Being small also means there is a large surface area capable of exposing more of what nano materials offer to cells. A further issue is how the nanoparticles are prepared and stabilized for drug delivery, since reducing agents and radiation can increase the level of toxicity in the cells (Anderson et al., 2016).

Conclusion

Ultimately, combining biosensors and nanotechnology is transforming diagnostics, allowing for quicker, more accurate and more sensitive detection of many diseases. Biosensors can be made smaller, work in real time and target specific biomolecules, so diagnostic devices are becoming wearable, implantable and available on lab chips. The use of nano-technology has made detection simpler for electrochemical, optical and magnetic biosensors. Consequently, the detection limits have improved and more testing methods are possible. Although there is great potential for change, issues such as stability, difficulties in making new substances, regulatory barriers and biocompatibility should be overcome for widespread use in medicine. AI-based changes to sensors and the development of green

nanomaterials may help get around these challenges. Rising interdisciplinary work is preparing nano biosensors to make a big difference in personalized medicine and world healthcare.

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Antimicrobial Activity of Silver Nanoparticles against *Pseudomonas aeruginosa* in Urinary Tract Infection

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Abstract

Urinary tract infection (UTIs) is a common health concern in both community and hospital settings, affecting men and women equally. *Pseudomonas aeruginosa* is an opportunistic bacterium that causes significant acute and chronic diseases in individuals with compromised immune systems. *P. aeruginosa* has considerable intrinsic antibiotic resistance, limiting the options for successful therapies. As a result, alternative antimicrobial agents such as including nanoparticles (AgNPs) are seen as promising candidates for infection management and prevention. AgNPs can deal with bacteria in various applications and are resistant to traditional antibiotics, including multiresistant strains such as *P. aeruginosa*. The dimensions of AgNPs are important in evaluating the medicinal value of nanopathy, as small particles provide more and more surface area for interaction with microorganisms, so they affect their important functions. Silver nanoparticles (AgNPs) follow microorganisms' cytoplasm and cell wall membrane, resulting in dissolution, cellular infiltration, cellular components, interaction with biomolecules, and production of reactive oxygen species and related free radicals. This chapter perfectly examines the role of antibacterial effectiveness of silver nanoparticles. Furthermore, elucidate the significance of silver nanomedicines in the treatment of urinary tract infections caused by *E. coli*.

Keywords: Urinary tract infection, *Pseudomonas aeruginosa*, Silver nanoparticles, Multidrug-resistant, Cytoplasmic membrane

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Introduction

Despite being common in both men and women, urinary tract infections (UTIs) are far more common in women because of their physiology. UTIs impact both the upper and lower urinary tracts. The infection is referred to as pyelonephritis (kidney infection) or cystitis (bladder infection), contingent upon the affected region (Neugent et al. 2020). Among the risk factors for UTIs include inadequate hygiene, sexual activity, and utilization of specific devices such as catheters, pregnancy, bladder or kidney disorders, compromised immune system, and menopause (Mansfield et al. 2022). Utilization of specific pharmaceuticals, including diuretics, and prolonged retention of urine (Pandey et al. 2022). The infection seems innocuous initially, the patient displays a range of symptoms as it advances, and in extreme instances, it may prove fatal (Suárez Fernández et al. 2021). The previously listed parameters are not exhaustive: the extent of damage, the frequency of recurrence, the manifested local symptoms, the presence of complicating disorders, and the likelihood of recurrence also differ. Kidney infections usually occur subsequent to bladder infections, potentially leading to systemic infections and, in severe instances, resulting in death. Pyelonephritis, an upper urinary tract infection, occurs subsequent to cystitis, which results from bacterial invasion of the lower urinary system, primarily involving the bladder (Wagenlehner et al. 2020), this may be attributable to a blood-borne infection (Chowdhury et al. 2024).

The urethra facilitates bacterial entry into the bladder, and both blood and lymph may also become contaminated (Figure 1). Certain strains develop Multi resistance to currently utilized antibiotics, especially carbapenems, due to adaptation and exposure to other medicines (Adekanmbi et al. 2022), they also adjust to the production of biofilms. Consequently, given the challenging nature of biofilm treatment, it is

imperative to devise novel therapeutic techniques that may effectively address both bacterial infections and biofilm formation. Therefore, using nanometric-scale materials to deliver biomolecules and antibiotics is a feasible strategy because it offers benefits like longer half-lives and systemic circulation durations, improved compound-pathogen interaction, increased absorption, and improved bioavailability, all of which lead to better therapeutic adherence and greater efficacy.

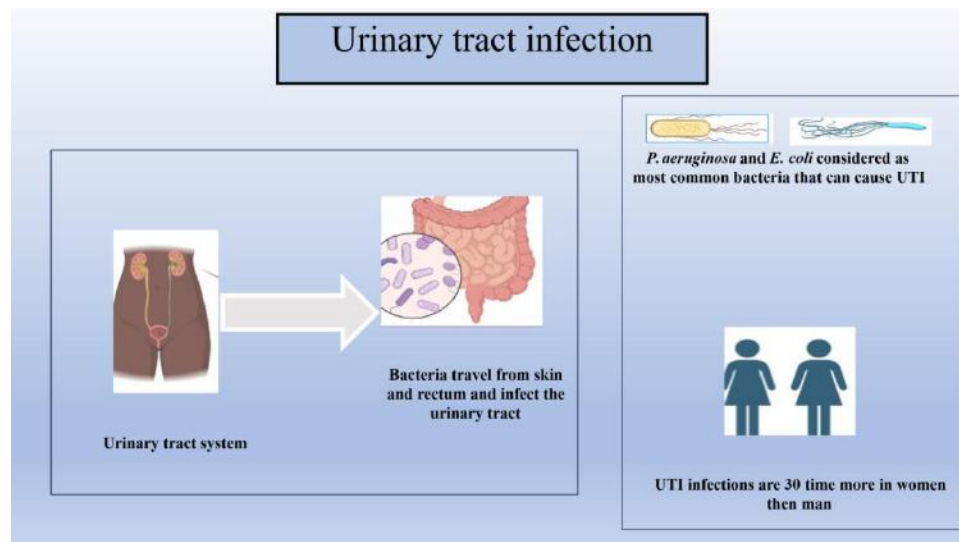


Figure 1: Urinary tract infection. Bacteria travel from skin or rectum and urethra.

UTI Epidemiology and Etiology

Urinary tract infections (UTIs) are projected to reach 93,300 cases year, constituting about 13% of all healthcare-associated illnesses. Catheter-associated urinary tract infections, the most prevalent nosocomial infection, are responsible for around one million hospital visits. With a mortality incidence of 2.3% (Wambui, 2021), the Centers for Disease Control and Prevention (CDC) notes that UTIs cause 13,000 annual deaths. Should urinary tract infections be linked to bacteremia, the rate might rise to 10%. While urinary tract infections account for 35% of recorded nosocomial infections (Chen et al., 2012). Both age and catheterization duration influences the incidence of urinary tract infections. Fifty percent of hospitalized patients with urinary tract infections are anticipated to return within 60 days (Kranz et al., 2020). Among bacterial diseases affecting newborns and children, urinary tract infections are the most common. Previous research indicates that 50% of women will at least once in their lifetime have a urinary tract infection (UTIs; 10% to 20% will contract annually, 1% to 2% will suffer from frequent bouts; 50% of women with asymptomatic bacteriuria will develop pyelonephritis (Fenta et al., 2020). Among the significant morbidities and long-lasting effects linked to pediatric urinary tract infections are chronic renal failure (Morgan et al. 2024). Increased incidence of urinary tract infections (UTIs) in patients with diabetes due to hyperglycemic urine promoting bacterial growth and colonization; these infections are prevalent during pregnancy, where cystitis can quickly progress to pyelonephritis (Kaur et al., 2022). Data from the Department of Health's Hospital Episode Statistics show that cystitis, or 0.096% of all hospital visits, accounted for 97% of hospital admissions in England over 2002–03 (Darwitz et al., 2024). The total amount of resources utilized or lost by people, businesses, and society as a whole as a consequence of an infection is the economic cost of a condition. It encompasses direct costs (such as diagnosis and treatment), indirect costs (including missed wages for patients, reduced productivity for the organization, and death costs), and intangible costs (such as expenditures associated with pain or suffering). Finding the precise economic burden could prove challenging. Five main groups define the general expenses of health care: physician appointments, hospital admissions, outpatient treatments, emergency room visits, and antibiotics linked with infections. Projected total spending for UTIs in 2000 was \$2.14 billion; by 2013, it had climbed to almost \$2.9 billion (Turner et al., 2015).

1. General Characteristics of *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is a ubiquitous bacteria found in both terrestrial and marine ecosystems. *P. aeruginosa* is regarded as a notable medicinal bacterium owing to its remarkable adaptability to diverse conditions and its potential to cause persistent infections in susceptible persons. *P. aeruginosa* is a gram-negative, bacillus-shaped bacterium, ranging from 0.5 to 3.0 μm in size, demonstrating aerobic metabolism and featuring a single flagellum for locomotion (Nassri et al. 2021). In aerobic conditions, this non-fermentative bacterium metabolizes glucose by glycolysis, employing oxygen as the final electron acceptor. Nitrogen can function as an electron acceptor in anaerobic environments. Additionally, ATP acquisition is facilitated by the function of several membrane ATPase that regenerate ADP and H^+ from prior activities (Grace et al. 2022). *P. aeruginosa* is the third most common pathogen linked to catheter-associated urinary tract infections acquired in healthcare settings *P. aeruginosa's* metabolic plasticity and environmental adaptation enable its presence in several habitats, including the human body, soil, water, healthcare facilities, sewers, and other aquatic environments such as swimming pools (Sanz-García et al. 2021).

2. Antibiotic Resistance

Antibiotics have shown therapeutic effectiveness in treating infectious diseases; nevertheless, researchers contend that this advancement

has resulted in resistance. The many forms of resistance presently observed are acquired for multiple causes. The capacity of bacteria to adapt via spontaneous or induced mutations is a major role in the development of antibiotic resistance. (Uddin et al. 2021). Bacteria acquire resistance genes by transmissible plasmids or horizontal gene transfer. Recent investigations have led to developing novel techniques for treating multidrug-resistant microorganisms. Enzyme LASB facilitates many pathophysiological processes in bacterial-host interactions, suggesting that these complex antibiotic-resistant *P. aeruginosa* can serve as a viable therapeutic approach to *P. aeruginosa*. These metal-based antibacterial complexes attack bacteria's membranes, DNA, and RNA to interfere with vital survival processes of bacteria. In addition to these contemporary counterparts, phase and bacteriosin have been examined as antibiotic options.

2.1 Intrinsic Antibiotic Resistance

Intrinsic antibiotic resistance is the congenital capacity of an antibiotic to be less effective because of structural or functional mechanisms that shield dangerous compounds and antimicrobial agents. *P. aeruginosa* has limited permeability, unlike certain other gram-negative bacteria. As a selective barrier to stop the passage are the asymmetric barriers of gram-negative membranes and asymmetrical antibiotics. *P. aeruginosa*, nutrients have to be let in. Porin is a water permeability channel designed from barrels, allowing this access (Qin et al, 2022). *P. aeruginosa* uses a congenital process whereby its outer membrane's permeability is lowered to prevent the hydrophilic drugs from entering. It is produced by replacing selective channels that support, especially in absorbing essential nutrients, non-specific porin proteins, which they aid (Saxena et al., 2023). Clinically identified carbapenem-resistant *P. aeruginosa* points to efflux pumps as one leading cause of natural antibiotic resistance. These efflux pumps can eject antibiotics from other structurally unrelated classes or specialize in particular substrates. Resistance-nodulation-division (RND), major facilitator, small multidrug resistance, ATP-binding cassette, and multidrug and toxic chemical extrusion define the five superfamilies of efflux pumps (Kavanaugh et al., 2024). Exporting the quinolone signaling molecule PQS reveals that by reducing its concentration, the MexEF-OprN and MexGHI-OpmD systems can modulate quorum sensing (QS), therefore reducing the synthesis of virulence factors supporting ongoing infections. After being extracted from the phospholipid bilayer in the cytoplasm or the inner membrane of the bacterial cell envelope by the inner membrane protein, the outer membrane protein in this complex transports the substrates into the extracellular media.

These proteins interact with a periplasmic protein. Carried on by the AmpC gene, another natural resistance component in *P. aeruginosa* is the hydrolytic enzyme β -lactamases. Based on their amino acid sequences A, B, C, and D four types can be separated among β -lactamases. Class B β -lactamases hydrolyse β -lactams with divalent zinc ions. Classes A, C, and D hydrolyse β -lactams (Barceló et al., 2022) by an active site serine. Through outer membrane porins, a β -lactam antibiotic enters the periplasmic space and attaches itself to certain penicillin-binding proteins (PBPs). The increasing pools of 1.6-anhydromuropeptides (Klebba et al., 2021) make AmpD unable to control the elevated amounts of these fragments. When they attach to AmpR, anhydro-MurNAc peptides conformational switch UDP-MurNAc-pentapeptides, changing the protein structure. AmpR turns into a transcriptional activator, so periplasmic zone AmpC expression rises. AmpC functions as a β -lactamase, engaging with the antibiotic to facilitate its degradation. *P. aeruginosa* may produce extended-spectrum β -lactamases (ESBLs) by the acquisition of ESBL genes, rendering it highly resistant to most β -lactam antibiotics, including penicillins and cephalosporins. Antimicrobial peptides (AMPs) may facilitate the development of innovative antibiofilm antibiotics (Nasser et al., 2020). Research on the antibacterial effectiveness of numerous antimicrobial peptides is in progress (Assoni et al., 2020). Although its chiral orientation does not compromise its metabolic activity, HBD2 (human beta-defensin 2) dramatically reduces *P. aeruginosa* biofilm development at nanomolar concentrations. The reduction in biofilm development underscores the role of HBD2 in innate host defense during the first encounter between the host and the virus. Jelleine-1 (Grassi et al., 2020) is another AMP used to examine its antibacterial and toxicological properties. Jelleine-1 has, under investigation, shown minimal antibacterial effect against gram-negative and gram-positive bacteria. Amino acids were tried to be replaced in order to increase the challenge's efficacy. Trp and Arg added increased the jelleine-1 sequence's antibacterial activity. While more research is needed, this AMP may be able to treat bacterial infections categorized as gram-negative. Recent studies show *P. aeruginosa* can change its membrane to react to phosphate stress, increasing its resistance to drugs, including polymyxin B (Jones et al., 2021).

2.2 Acquired Resistance

Some drugs can acquire intrinsic resistance independent of past antibiotic use. Plasmids, for instance, lack genes for bacteria to thrive in normal conditions. However, they have genes that help bacteria thrive in hostile environments, including virulence, antibiotic resistance, and heavy metal tolerance. It has been shown that *P. aeruginosa* acquires plasmid-encoded carbapenemases (single metallo- β -lactamases), which can hydrolyse the majority of β -lactams, including carbapenems, whilst many other bacteria obtain resistance genes. Horizontal gene transfer is made possible via transformational, transductional, and conjugational processes. Bacteria acquire several resistance genes from their counterparts, including resistance to aminoglycosides, fluoroquinolones, and β -lactam resistance genes (Glen & Lamont, 2021). Usually, bacteria utilize this mechanism to disrupt the efficacy of antibiotics by disrupting pharmacological targets. One resistance strategy is quinolone target site modification; quinolones stop DNA gyrase and topoisomerase IV (Anyanwu et al., 2020), thereby preventing bacterial DNA replication. *P. aeruginosa* develops resistance to carbapenems via an acquired resistance mechanism in which changes in the outer membrane porin channel unique to OprD either decrease or completely eradicate resistance (depending on a mutation in the oprD gene or one of its regulatory proteins, such MexT) (Silva et al., 2020).

2.3 Adaptive Resistance

In contrast to other types of resistance, adaptive resistance is dependent on shifting conditions that activate cellular regulatory systems; once the triggers are removed, vulnerability often resurfaces. Biofilm-forming bacteria are known to be more immune system resistant than

other bacteria and more resistant to antimicrobial treatments. For instance, the *P. aeruginosa* biofilm matrix a key component of Edna can acidize the cellular environment, alter the permeability of the membrane, and produce structural alterations in lipid A of LPS. These modifications could cause different responses for various polymyxins or antibiotics like colistin (Lewenza et al, 2020).

3. Silver nanoparticles (AgNPs) and their antimicrobial properties

Silver is considered an effective treatment against microorganisms as it disrupts both cell membranes and metabolic processes. Silver-based nanosystems have been investigated both alone and in conjunction with other materials for the treatment of urinary tract infections. AgNPs are acknowledged as a prospective application inside nanosystems owing to their significant physicochemical features vital for fighting pathogens, including stability, colloidal form, and favorable chemical interactions. AgNPs are small reduced particles of silver with significant potential for biological applications. With sizes varying from 1 to 100 nm, they may have spherical, flat, triangular, tetrahedral, prismatic, cubic, octahedral, or irregular geometries. Consequently, there is a growing interest and expansion in research focused on the creation or modification of substances exhibiting antibacterial and antibiofilm properties, especially against strains of *P. aeruginosa* (Mikhailova, 2020).

3.1 Synthesis of AgNPs

AgNPs have several qualities and can be produced with several methods. The most often used techniques comprise chemical synthesis using inorganic reducing agents and organic solvents. Talance reagent, elemental hydrogen, sodium citrate, ascorbate, sodium borohydride. Converts metal ions into subsequently meticulously collected atoms by reducing them. Chemicals stored on the surfaces of the AgNPs generated by this synthesis can be hazardous and toxic, some especially so. This will make AgNPs useless and raise their toxicity to human cells to an unacceptable level. AgNPs may be physically synthesized using evaporation-concentration methods and laser ablation. AgNPs may be synthesized via laser ablation, which involves introducing silver into a liquid media that absorbs laser pulse radiation. The liquid media, the laser-beating period, and the wavelength at which the laser kills the metal target influence the attributes and efficacy of nanoplates (Rabbi et al., 2024). Additionally, electrochemical synthesis is growing in popularity, where a stable substance and silver plate electrodes are used in an electrical device with electrolytic cells (Wirtanen et al, 2021) produces a low intermediate metal salt in the cathode. Biosynthesis, which enhances stability and eliminates the need for harmful reagents and organic solvents, is the most inexpensive and ecologically benign means of producing AgNPs (Jayaprakash & Kannappan, 2022). Within nanotechnology, biosynthesis is a pertinent method and a less detrimental approach. Exogenous stabilizers help them to be created both enzymatically and non-enzymatically, at room temperature and under pressure. The reducing and stabilizing agents applied in this synthesis come from proteins, sugars, plants, algae, bacteria, yeasts, and fungi. Plants are believed to be faster than other techniques, dependable, non-toxic, and ecologically benign (Alharbi et al., 2022).

4. Antimicrobial mechanism of action of AgNPs

The prevalence of bacterial infections caused by multidrug-resistant organisms has increased dramatically over the last 20 years, primarily as a result of the careless use of antibiotics in both clinical and agricultural contexts. Therefore, there is a need to develop new treatments that target MDR strains, and AgNPs have gained more recognition in this regard. AgNPs' antibacterial activity stems from their large surface area, which promotes more interaction with microbes and kills them even at low concentrations (Tripathi and Goshisht et al., 2022). AgNPs' antimicrobial effectiveness is attributed to four distinct mechanisms: (1) adhesion to the membrane surface and cell wall; (2) AgNPs infiltration into the cell, which damages intracellular structures (mitochondria, vacuoles, and ribosomes); (3) AgNPs-induced cellular toxicity and oxidative stress due to the generation of free radicals and reactive oxygen species (ROS); and (4) modulation of the signal transduction pathway.

4.1 Adhesion of AgNPs onto the Surface of Cell Wall and Membrane

When bacterial cells are exposed to silver nanoparticles (AgNPs), the particles initially adhere to the microbial cell wall and membrane. This adhesion is primarily facilitated by the positive surface charge of AgNPs (Pokhrel et al., 2022). Due to their negatively charged membranes, microbial cells are electrostatically attracted to the positively charged nanoparticles, which enhances their attachment. This interaction leads to observable morphological alterations, such as membrane detachment from the cell wall and shrinkage of the cytoplasm, ultimately resulting in rupture of the cell wall. In addition to electrostatic interactions, AgNPs engage with sulfur-containing proteins embedded in the cell wall, causing irreversible structural damage and degradation of the wall. These disruptions compromise membrane permeability and disturb the organization of the lipid bilayer. Altered cell morphology disrupts transport mechanisms by increasing membrane permeability. The proper translocation of precursor proteins to the membrane depends on energy supplied by ATP and proton motive force (Almatroudi, 2024). The peptidoglycan in Gram-positive bacteria is about 30 nm thick and negatively charged, while in Gram-negative bacteria, it is much thinner, around 3–4 nm. The greater thickness and dense structure of the Gram-positive cell wall act as a barrier, retaining silver ions and limiting their intracellular effects (Vaiwala, et al., 2022). For instance, *Staphylococcus aureus*, a Gram-positive bacterium, exhibits greater resistance to AgNPs due to its thick peptidoglycan-rich wall, which hinders silver ion penetration.

In contrast, the outer membrane of Gram-negative bacteria contains lipopolysaccharide (LPS), which provides structural reinforcement but also contributes to increased susceptibility to AgNPs. The negatively charged LPS enhances AgNP binding to the cell surface, facilitating nanoparticle accumulation (Yahya et al., 2023). Barani et al. (2021) observed that this interaction leads to more efficient deposition of AgNPs on Gram-negative bacterial surfaces. Therefore, the relationship between AgNP concentration and treatment efficacy may vary significantly depending on the microbial class, negating a uniform dose-response correlation.

4.2 Penetration of AgNPs into Cells and Destabilization of Intracellular Structures and Biomolecules

When AgNPs engage with microbial cell membranes, they induce several forms of cellular malfunction. AgNPs are initially linked to the

cell membrane, altering its permeability, structure, and transport capacity. Conversely, once AgNPs pass the cell membrane, they can infiltrate the cells and disrupt vital biological processes (Tripathi & Goshisht, 2022). AgNPs can interact with biomolecules like proteins, lipids, and DNA as they enter microbial cells, interacting with biological structures and biomolecules that damage bacteria. (Wypij, et al., 2021). Interactions between Ag⁺ ions and their functional groups can deactivate proteins (Yang et al., 2024). The proteins help to generate transmembrane ATP and regulate the ion flow across the cell membrane (Girma, 2023). Breaking the hydrogen bonds between the anti-parallel DNA strands causes the Ag (+) ion to intercalate between purine and pyrimidine base pairs, weakening the double helical structure (Jiménez-Pérez et al., 2024). AgNPs induce the DNA molecule to move from a relaxed to a compacted form, reducing its replicating capacity, claims by (Vadakkan et al. 2024).

4.3 AgNPs Induced Cellular Toxicity and Oxidative Stress

Heavy metal ions like Ag⁺ have a negative impact on microbial systems, as seen by increased oxidative stress. As a result, cells often benefit from a larger concentration of Ag⁺ ions when it comes to reducing oxidative stress (Khan et al., 2019). Silver nanoparticles (AgNPs) show great antimicrobial potential antibacterial, antifungal, and antiviral. AgNPs' production of ROS and free radicals, which increase cellular oxidative stress helps to explain their efficacy against bacteria, mostly (Mammari et al., 2022). Upon adhering to the cell membrane, Ag⁺ ions are supposed to disturb microbial signaling pathways and hamper mitochondrial respiration (Morozova, 2021). These ions disrupt respiratory chain enzymes, breaking the electron transport chain and disconnecting oxidative phosphorylation from ATP generation (Garcés et al., 2021). The concentration of free radicals that is too high destroys mitochondrial membranes, starting necrosis and later cell death. Additionally, oxidative stress causes hyperoxidation of lipids, proteins, and nucleic acids (Dyall et al., 2022). By transforming reduced glutathione (GSH) into its oxidized form, glutathione disulfide (GSSG), therefore upsetting the redox homeostasis of the cell, AgNPs also induce oxidative imbalance and death (Jiang et al., 2021). Further compromising the function of antioxidant enzymes like catalase, superoxide dismutase, glutathione peroxidase, and NADPH-dependent flavoenzymes is this imbalance (Ucar et al., 2024).

4.4 Modulation of Signal Transduction Pathways

Phosphorylating many protein substrates is known to be bacterial (Sultan et al., 2021). A signal transduction system for cellular activity and microbial proliferation in microorganisms involves the phosphorylation and dephosphorylation cycle. This method helps one understand the transduction path under the influence of the AgNP bacterial signal. Essential for metabolism, bacterial cell cycles, DNA replication, and recombination are the phosphorylated proteins generated. Furthermore, the synthesis and transport of exopolysaccharides and capsular polysaccharides are connected to the tyrosine phosphorylation of proteins in several Gram-positive and Gram-negative bacteria. AgNPs influence cellular communication and slow microbial growth by dephosphorylating tyrosine residues on important bacterial peptide substrates (Zohra et al., 2021).

5. Antibacterial activity of AgNPs against *Pseudomonas aeruginosa*

Silver has been employed for therapeutic purposes since ancient times, long before the advent of modern antibiotics. It was notably applied in treating burn injuries and open wounds due to its antimicrobial capabilities (Shrestha et al., 2024). Both Gram-positive and Gram-negative bacteria are sensitive to the antibacterial action of silver nanoparticles (AgNPs), however research indicates that Gram-negative bacteria are often more vulnerable. This increased sensitivity is explained by the distinct structure of Gram-negative bacteria, which consists of a relatively thin peptidoglycan layer and an outer membrane rich in lipopolysaccharides. AgNPs are capable of penetrating and exerting antimicrobial effects on both bacterial types (Zhou et al., 2024). Ghosh et al. (2022) state that bacterial poisoning depends on the makeup of the cell wall. With structural and physical differences, due to the protective mechanisms that allow them to come in contact with high concentrations of AgNP, toxicity for more complex species, including human cells, may vary (Tortella et al., 2020). Additionally, AgNPs consists of a positive charge compared to the negative charge of the bacterial cell membrane, which causes them to accumulate inside the membrane, causing structural changes and more permeability (Muddassir et al., 2022). The activity of AgNPs is directly affected by their dimensions, such as bacteria in small AgNPs, especially *P. aeruginosa* (Agreles et al., 2020).

6. Conclusions and Future Perspectives

The widespread misuse of antibiotics globally has contributed to the development of pathogenic microorganisms that are resistant to multiple drugs. Hospital-acquired infections represent a major public health concern because they are often difficult to treat. In this context, nanotechnology has emerged as a promising approach in combating bacteria that have developed multidrug resistance. Among the various nanomaterials, metal-based nanoparticles show potential for treating infections caused by these resistant strains. Interestingly, silver nanoparticles (AgNPs) have been used to good efficacy against pathogens including Enterobacteriaceae, multidrug-resistant *S. aureus*, and *A. baumannii* and *P. aeruginosa*. AgNPs work via a multi-level interaction mechanism. The discharge of intracellular contents brought on by the change in plasma membrane permeability causes cell death. They inhibit the synthesis of ribosomal subunits, stop DNA replication, and deactivate proteins and enzymes. AgNP toxicity depends on a number of factors, including dose, size, shape, and the presence of coating or capping agents. Compared to nanoparticles with larger diameters, those with dimensions between 5 and 30 nm are more effective against bacteria. Future studies must include the examination of possible bacterial mechanisms of resistance to nanoparticles.

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Nanotechnology Advancement for Therapeutic Discovery for Neurodegenerative Disorders

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Abstract

Progressive dopaminergic neuronal loss and peripheral neuronal degeneration are central to neurodegeneration. This is mechanistically linked to misfolded proteins and tauopathies. These harmful processes, often involving blood-brain barrier (BBB) disruption, underlie neurodegeneration in disorders such as dementia, Parkinson's disease, Alzheimer's disease, and traumatic brain injury. Such conditions pose significant challenges for diagnosis and treatment. Recent advancements in nanotechnology have facilitated the development of nanoparticles capable of crossing the BBB, enhancing drug delivery efficiency, and minimizing invasiveness. However, current animal models are inadequate in fully replicating human disease pathology, and nanomaterial synthesis remains complex. Advancements in nanomedicine are expected to address these challenges; it is poised to revolutionize neurodegeneration therapy.

Keywords: Nanoparticles, Bio imaging, Stem cell, Tauopathy, Genome editing, Drug delivery

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Introduction

Primary pathological aspects that contributing to neurodegeneration and cognitive decline include higher concentrations of α -syn in neuronal cells, fibrillary accumulation of amyloid β , and a hyperphosphorylated tau protein (Wu et al., 2024). These processes trigger progressive neural cells degradation, NDs are an extensive range of diseases that can result in motor, cognitive, and other neurological disorders. Kormas & Moutzouri (2023) identify ALS, HD, PD, and AD as examples of such prevalent diseases (Kormas & Moutzouri, 2023). Significant pathological and cellular mechanisms are commonly shared by various factors and demonstrating the possibility of collaboration and development of interconnected treatment strategies (Leng & Edison, 2021). These disorders influence millions of residents globally. Chronological age is a significant risk factor. However, genetic susceptibility and external variables such as lifestyle and environmental factors have an essential effect on the emergence and development of disease (Figure 1) (Liu et al., 2022).

Nanoscience examines the molecular and atomic structures of materials with characteristics at the nanoscale. By integrating this data into useful purposes, nanotechnology provides it accessible to generate cutting-edge technologies and procedures in an abundance of industries. Nanostructured materials, nanomaterials, nanoparticles, and nanocomposites are fundamental concepts (Lagashetty & Bhavikatti, 2019). Researchers from various scientific fields, including physics, predict that the application of nanoscale technologies and manufacturing approaches-ranging from robotics and nanomachines to nanomedicine and diagnostic tools, which will enable remarkable biomedical advancement (Erkoc & Ulucan-Karnak, 2021; Modi et al., 2021; Avula & Grodzinski, 2022; Talukdar et al., 2022).

The application of nano-biotechnology is rapidly advancing in the medical field to address a broad spectrum of medical problems, including disease detection, treatment, drug development, personalized medical approaches, cancer therapies, diagnostic methods, pharmaceutical developments, and novel techniques (Vaishampayan et al., 2023). Jennifer Doudna and Emmanuelle Charpentier were awarded the Nobel Prize in Chemistry for pioneering the CRISPR/Cas9 genome editing system (Ledford & Callaway, 2020).

Nano-based medicines and nano vaccines are gaining regulatory approval at an increasing rate, like traditional vaccines. In addition to advanced drug delivery systems such as polymeric nanoparticles and liposomes, various nanotechnology-based diagnostic devices, including nano-sensors and PCR assays are progressing. Commercialization of antibacterial drugs and nanomedicines, such as gene protocols and Doxil, is proceeding for both medical and scientific uses (Dessale et al., 2022). Recently, several kinds of nanoparticle developed including paramagnetic nanoparticles, nanocrystals, quantum dots, nanoshells, and nanosomes are utilized in medical purposes (Wang et al., 2021).

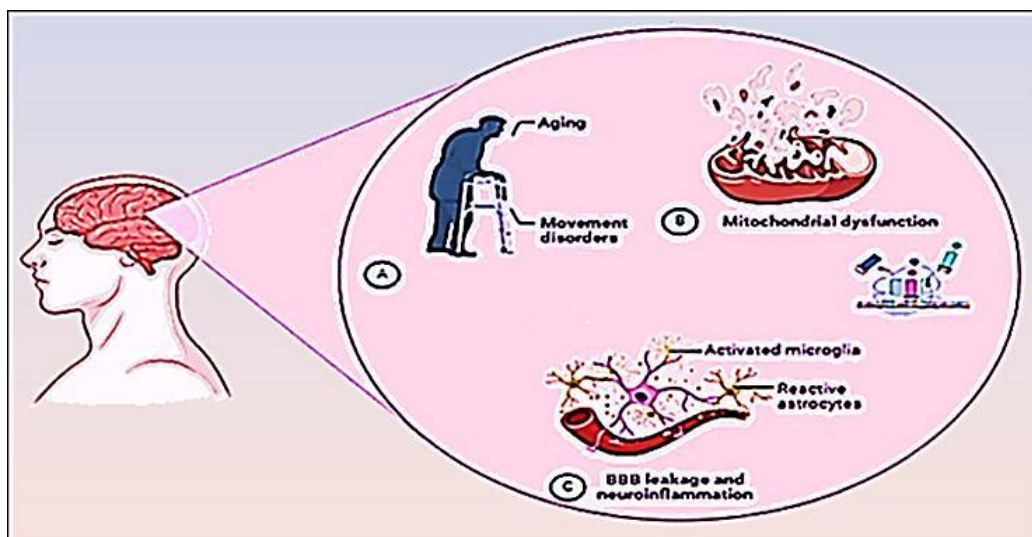


Fig. 1: Several risk factors involved in the progression of neurodegeneration

Structure, dimensions, charge, shape, and other physicochemical properties of nanocarriers significantly influence their safety and therapeutic efficacy. These factors affect toxicity, tissue penetration, and interactions with biological components. Because nanocarriers are more reactive than bulk materials, comprehensive risk assessments are necessary, accounting for their physicochemical properties across diverse biological systems (Domingues et al., 2022; Awashra & Mlynarz, 2023).

Nanoparticles with nanoscale dimensions are effective in drug delivery due to surface modification, biocompatibility, PEGylation processes, and controlled drug release. Ahlawat et al. (2018) demonstrated their ability to prolong circulation, inhibit phagocytosis and cross the BBB (Ahlawat et al., 2018). Essential oils and green nanotechnologies (biopolymers) are advancing treatments for neurodegenerative disorders. Their novel usage involves drug delivery, brain regeneration, and biosensors (Cui et al., 2022; Monika et al., 2024).

Nanoparticles face challenges including low transfection efficiency, batch variability, limited drug loading, and accumulation. Polycationic carriers may trigger immune activation and lysosomal rupture, leading to oxidative stress, proteostasis disruption, mitochondrial dysfunction, and apoptosis (Wolfram et al., 2015).

1. Nano sized Drug Delivery Systems in Neurodegeneration

Compared to conventional medications, the use of nano-sized drug delivery systems offers superior electrical, mechanical, optical, and magnetic properties, making them highly advantageous for managing neurological disorders. Liposomes' low toxicity, low immunogenicity, high biocompatibility, and ability to cross the blood-brain barrier (BBB) make them highly valuable for neurological therapies. Intranasal delivery of nanoparticles containing mucoadhesive polymers extends their residence time in the nasal cavity, enhancing therapeutic efficacy. Polyphenols exert their antioxidant effects by activating cytoprotective proteins and NRF2-mediated pathways (Vieira & Gamarra, 2016; Yang et al., 2018).

Solid lipid nanoparticles are biodegradable lipid structures providing benefits such as enhanced absorption for poorly soluble drugs, decreased cytotoxicity, adequate biocompatibility, and resistance to drug degradation. Nanogels, characterized by their nanosized network structure and surface modifications, provide excellent retention rates and controlled drug release, helping to prevent drug degradation. Dendrimers, due to their highly branched and functionalized structure, serve as biocompatible carriers that enhance BBB permeability. Nano-emulsions, known for their ability to prevent premature drug release and interact effectively with serum proteins, improve drug solubility, bioavailability, stability, and CNS targeting (Naeimi et al., 2018; Scuto et al., 2021; Scuto et al., 2022).

Several applications require specifically designed engineering techniques. Currently, four key pathways for nanoparticles (NPs) to cross the BBB are being investigated. The first is passive diffusion, involving small hydrophobic molecules that can cross the BBB and enter the brain. The second is active transport via ABC transporters, which move molecules through endothelial cells by using ATP. Carrier-mediated transcytosis, the third transport mechanism, relies on endogenous cellular carriers to transport drugs. NPs can penetrate the blood-brain barrier (BBB) via four distinct mechanisms: ABC transporter activity, ligand-facilitated receptor-mediated endocytosis, carrier-mediated transcytosis, and passive diffusion of lipophilic molecules. Liposomal and polymeric nanocarriers are strategically used for organ-specific drug distribution, especially to hepatic and cardiac tissues, while inorganic NPs are critical to advanced ultrasound imaging through precise anatomical resolution with reduced cytotoxicity (Table 1) (Brown et al., 2020; Del Amo et al., 2021; Lomis et al., 2021; Sun et al., 2022).

2. Use of Nanoparticles Based Imaging Strategies in Neurological Disorders

Silver, gold, iron oxide, silica, and other inorganic nanoparticles (NPs) can penetrate the blood-brain barrier, reduce oxidative stress, and deliver diagnostic imaging agents (Rzagalinski et al., 2017; Dash et al., 2020; Kesharwani & Jain, 2022).

Nanowires and exosomes serve as advanced nanosystems for targeted drug delivery and controlled release kinetics. Quantum dots (QDs) are nanoscale semiconductors that exhibit size-dependent fluorescence, surpassing conventional imaging tools in sensitivity and multiplexing capacity (Figure 2). Their favorable bio interface properties and optical stability make them indispensable for biomedical applications such as molecular imaging, biosensing, and drug delivery (Villalva et al., 2021; Phafat & Bhattacharya, 2023).

Table 1: Categorization of nanoparticles based on their physicochemical properties, defined specifications, and application scopes with a focus on neuroprotection

Category	Sub-Category	Application	Reference
Carbon Nanoparticles	Graphene oxides, nanotubes, Fullerenes, carbon dots, Nanodiamonds	Carbon Facilitate drug delivery, Bioimaging, Blood glucose detection, Electric stimulation, Tissue reconstruction, Interaction with amyloid fiber, Antioxidants, Energy storage, Nanomedicine	(Park et al., 2019; Azimi et al., 2020; Ke et al., 2020; Xiang et al., 2023)
Organic Nanoparticles	Lipids, Nanocapsules, dendrimers, Protein based NPs, Micelles	Enhance drug efficacy, Control drug release, Drug toxicity reduction, Therapeutic agent, Self-healing system, Gene therapy, Biosensor	(Chen et al., 2020; Fonseca-Gomes et al., 2020; Kong et al., 2020)
Inorganic Nanoparticles	Metals, Metal oxides, Quantum dots, Bimetallic, Silica, Magnetic	Energy semi-conductor, Biosensor, Drug delivery, Magnetic applications, Chemical resistance, Environmental remediation, Solar cells	(Ke et al., 2020; Saghatchi et al., 2020; Mishra et al., 2021)
Exosomes	Based on cellular origin, Based on DNA cargo types, Based on functional Biomarker, modifications, Artificial or mimetic exosomes, Based on disease-Specific applications	Pathogenesis of diseases, Immune regulation, Drug delivery, Target cell-specificity	(Aheget et al., 2020; Zhang et al., 2020; Kugeratski et al., 2021; Cummings et al., 2023)

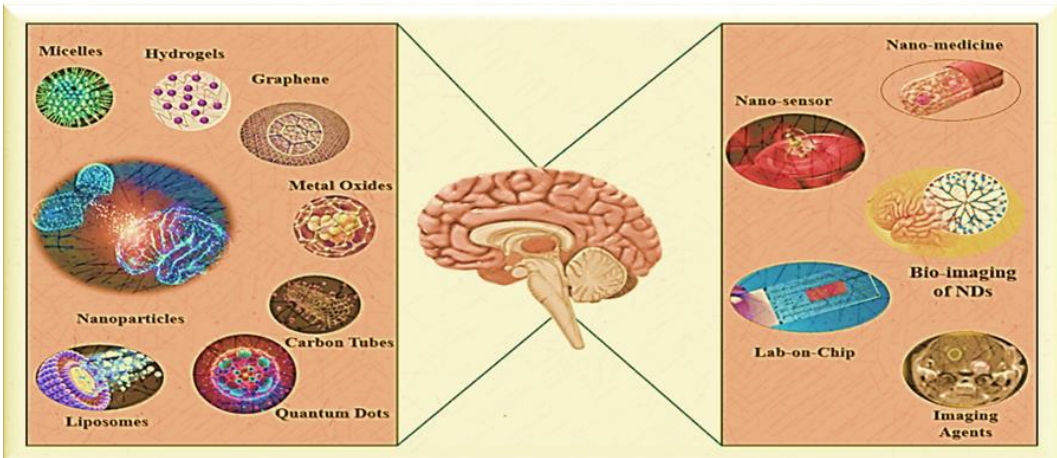


Fig. 2: Use of nanoparticle-based imaging applications in neurological disorders

3. Nanoparticle-Based Cell Targeting for Neurodegeneration and Reduction of Neuroinflammation

Greater expertise in neuroinflammation and CNS physiology is driving force behind the surface changes of NPs with ligands that boost cellular specificity and BBB penetration. These modifications, featuring CNS-targeted interventions, may improve the efficacy and safety of therapies for neurological diseases. (Chung et al., 2020; Hoyos-Ceballos et al., 2020; Juthani et al., 2020; Saha et al., 2020; You & Sabel, 2021; Landolina et al., 2022).

By eradicating cytotoxic agents, microglia provide a crucial role in protecting neurons. Chronic activation can lead to neurotoxicity by releasing inflammatory cytokines. Utilizing biocompatible, biodegradable materials with low immunological reactivity, taking advantage of microglial phagocytosis, and functionalizing NPs with receptor-specific ligands or peptides for targeted delivery are strategies needed for targeting microglia in neurological diseases. Additionally, incorporating co-delivered modulators that alter microglial activation and stop protein aggregation can improve the therapeutic stability and bioavailability of nanoparticles (Zhao et al., 2020).

4. Use of Nanotechnology in Protein Aggregation and Misfolding Cause Neurodegeneration

Nanotechnology has been employed in biomedical research to improve medication delivery, cerebral targeting, bioimaging, and stimuli-responsive chemotherapy for brain cancers. These advances are largely driven by the development of nanodrugs and nanocarriers. Molecular interventions in nanoparticle form demonstrate improved interaction with biological substrates and greater control over biochemical processes. The efficacy of anti-amyloidogenic small molecules can increase by up to 100,000-fold when formulated as colloidal nanoparticles. This advantage has been observed across a broad range of molecular therapeutics (Caballero & Gamez, 2021).

Tau dysfunction is central to Alzheimer's disease (AD) and more than 20 tauopathies, neurodegenerative disorders characterized by abnormal tau aggregation (Kovacs, 2018). These aggregates impair neuronal function, contributing to conditions such as AD and frontotemporal dementia (FTD). Despite growing interest in tau as a therapeutic target, no FDA-approved drugs exist, though clinical trials are ongoing (Cummings et al., 2023). Key therapeutic strategies aim to reduce tau hyperphosphorylation, enhance degradation, prevent aggregation, and improve cerebral blood flow (Cummings et al., 2023). NPs provide innovative approaches by enhancing drug delivery efficiency and interfering with tau aggregation mechanisms. Through advanced biochemical and mass spectrometry analysis, the discovery and development of next-generation therapeutics have identified to the identification of several significant phosphorylation sites associated with the advancement of disease (Figure 3) (Cummings et al., 2023).

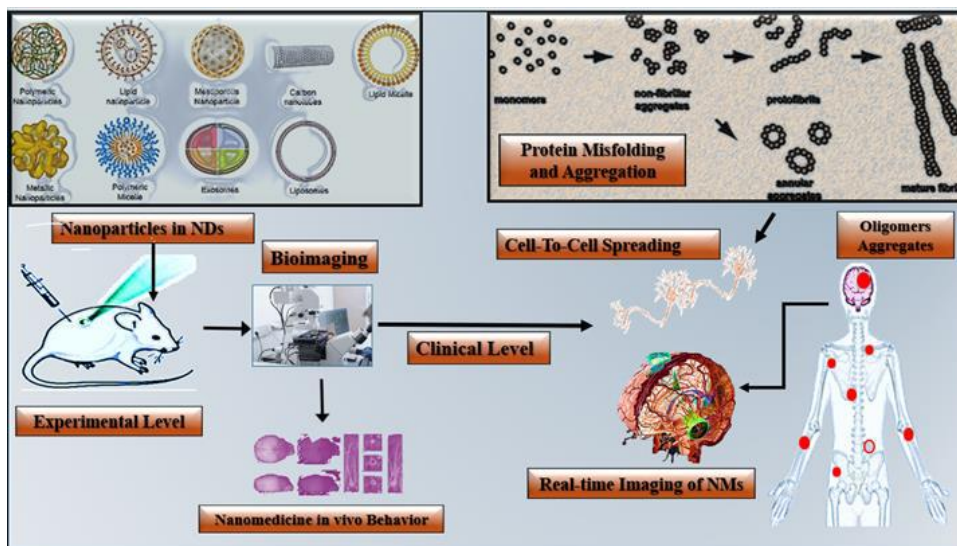


Fig. 3: Protein aggregation and role of nanoparticles at experimental and clinical levels

5. Nanocarriers for DNA, miRNA, and siRNA Delivery in Neurodegenerative Disease Models

The genes being targeted are effectively silenced by siRNA gene editing, which reduces the formation of phosphorylated Tau (p-Tau). However, due to both immune response and enzymatic degradation, nucleic acid therapies often exhibit low bioavailability. Although, nanocarriers inhibit these therapies prevent inactivation while in circulation. As a result, significant advancements have been made in the development of nanocarrier-based delivery systems for nucleic acid treatments in recent years (Aimo et al., 2022).

i. Gene Editing Technologies for Neuroprotection

Gene replacement, editing, and regulatory therapies for ophthalmology are advancing rapidly due to the neurodegeneration for gene therapy. Its small size reduces therapeutic dosages, while its accessibility facilitates precise delivery and real-time imaging. Moreover, genome editing minimizes systemic side effects. CRISPR-CasRx has shown potential for reducing choroidal neovascularization (CNV) and preventing vision loss in an AMD mouse model by specifically targeting the *Vegfa* gene. CRISPR-CasRx shows significant possibilities for the temporary silencing of damaging genes relevant to eye disease because of its superior specificity and efficacy. (Ong et al., 2019; Ziccardi et al., 2019).

Genome editing and therapeutic strategies employ zinc finger artificial transcription factors (ZFTFs), artificial transcription factors (ATFs), and antisense oligonucleotides (ASOs) for targeted gene regulation, as well as transcription activator-like effector nucleases (TALENs) for precise genome modifications. These genome editing tools enable critical processes such as gene disruption, modification, and regulation, positioning them as potential treatments for genetic disorders. Their broad applicability to target virtually any DNA-associated protein has made them a central focus of research and therapeutic exploration (Figure 4) (Fry et al., 2021).

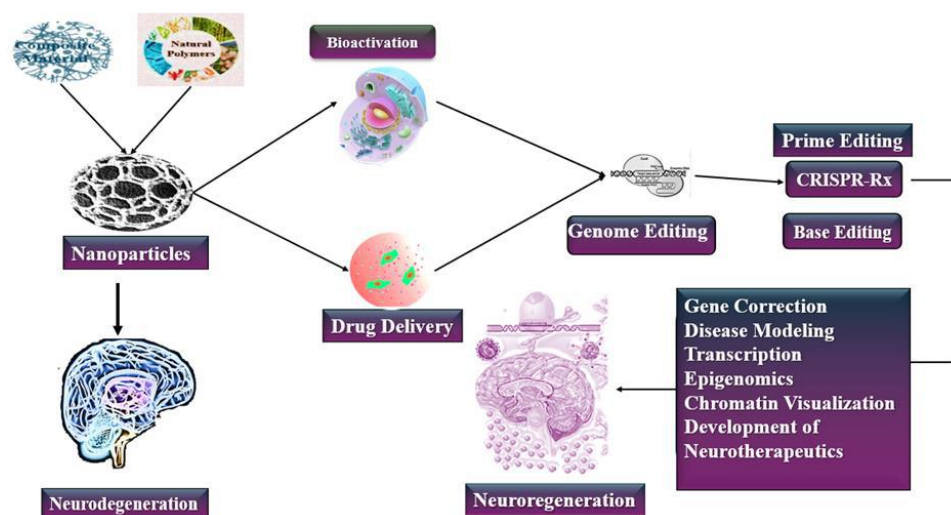


Fig. 4: Genome editing and its approaches in neurodegeneration

ii. Prime Editing Approach

Prime editing is a highly adaptable and precise genetic modification method, enabling the insertion of deletions, insertions, and all 12 nucleotide substitutions, along with their combinations. Although its application in neurodegeneration is promising, it remains in the early stages. This method facilitates the correction of mutations in genes such as CEG, SNCA, and LRRK2. It utilizes a Cas9 nickase (dCas9) combined with reverse transcriptase (RT) and is guided by a primary editing guide RNA (pegRNA). PE2, a Cas9 nickase-RT fusion, is more efficient than

PE1, its predecessor, specifically when using shorter primer binding sites. By introducing an additional guide RNA to target the non-edited DNA strand, PE3 and PE3b, advanced variants of the primary editing system, enhanced overall editing efficiency (Song et al., 2021; Jang et al., 2022).

iii. Site-specific Modifications in Neurodegeneration

Base editing is an advanced gene-editing approach that uses engineered base-editing enzymes fused to CRISPR-Cas9 proteins to directly convert one base in DNA or RNA to another without inducing double-stranded breaks (DSBs). This technique enables precise point mutations or corrections at specific genomic loci. Base editing enables CRISPR-Cas9-fused enzymes to target nucleotide substitutions and achieve precise point mutations in nucleic acids, reducing DSB-associated genomic instability and off-target changes common in homology-directed repair and non-homologous end joining (Suh et al., 2021).

6. Nanoscale Biomaterials for the Repair and Regeneration of Neural Tissue

To promote brain regeneration, researchers are advancing nanotechnology-based strategies to target both intracellular and extracellular pathological environments and to counteract injury-induced inhibitory mechanisms. This study underscores the significance of age-specific therapeutic strategies for an infant's brain. Despite advancements in regenerative medicine, spinal cord injury remains a significant challenge. Studies focus on the development of nanomaterials and their potential in SCI therapy. Furthermore, nanomaterials are highlighted for their ability to enhance emerging therapeutic strategies such as immunotherapy, CRISPR/Cas9, and optogenetic techniques (Cabeza et al., 2019).

Biomaterials are engineered to ensure integration with tissues and reduce adverse effects after implantation. Their broad application in the medical and diagnostic fields is primarily due to their low immunogenicity, remarkable biocompatibility, and regenerative potential. Chemical and modified surface scaffolding can control key cellular processes such as adhesion, proliferation, migration, and differentiation, supporting tissue healing both in vitro and in vivo. Synthetic biomaterials can be precisely designed for custom modifications in properties like stiffness, porosity, and biodegradability to suit specific needs. However, their biocompatibility can be influenced by the lack of recognition sites, necessitating chemical modifications to improve cell attachment and replicate the binding characteristics of native tissues (Ali & Bhuiyan, 2021; Li et al., 2021; Reddy et al., 2021; Xiang et al., 2023). Graphene-based nanomaterials (GBNs), PEG, chitosan, metal antibacterial agents, and CRL peptides are key components to the regeneration of SCI (Yari-Ilkhchi et al., 2024).

7. Stem Cell Therapy Using Nanomaterials in Neurodegenerative Diseases

The differentiation of stem cells is influenced by key physical properties of NPs, including the size, surface chemistry, morphology, and charge. Signaling pathways which facilitate differentiation can be stimulated mechanically by NPs. Neuronal differentiation has been observed to be improved via carbon-based NPs, including graphene, carbon nanotubes (CNTs), and C60 derivatives. It was previously and in the next illustration in figure 5 demonstrated that a water-soluble C60 derivative modified with alanine residues (Ala-C60) promotes neural stem cell (NSC) differentiation and proliferation while exhibiting resistance to oxidative stress. Moreover, in animal models, CNTs and NSCs together have demonstrated promise in regaining cognitive function and minimizing neurodegeneration. Due to their distinct optical, electrical, and magnetic characteristics especially when impacted by external electromagnetic fields metal NPs also aid in the regulation of stem cell fate (Lee et al., 2020; Hao et al., 2021; Hung et al., 2022; Ren et al., 2022).

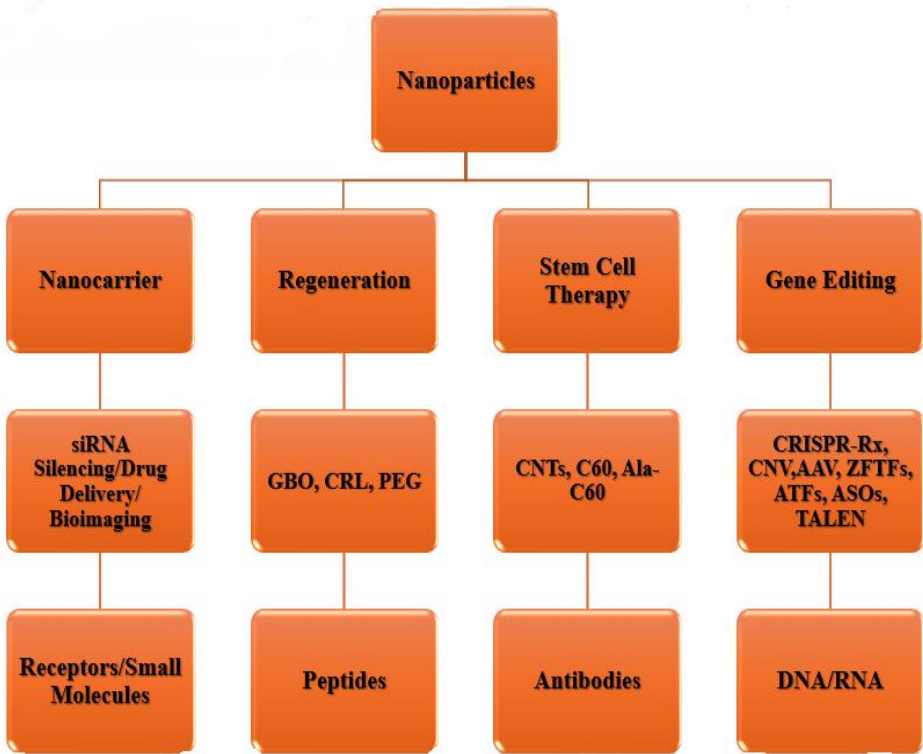


Fig. 5: Illustration of nanoparticle’s mechanism in regeneration, stem cell therapy and bioimaging

8. Problems and Safety Issues with Nanotechnology in Neurodegenerative Medicine

Comprehensive nanotoxicology investigations have become significant as analysis on nanoparticle (NP) toxicity and its negative impacts on the environment and population remain in their early stages. Toxicity evaluation is important during the manufacturing of nano-therapies to deal with potential issues interlinked with their commercial and therapeutic applications (Abdul Basith Khan et al., 2020; Attarilar et al., 2020).

If nano-biomaterials break apart in the body's tissues, they could result in adverse effects because they are cytotoxic and have other detrimental effects. Clinical research highlights the composition of NPs has significantly influences cellular effects, including asbestosis. Carbon nanotubes (CNTs) have been linked with effects such as endosomal escape, chromosomal translocations, and plasma membrane permeability. Determining the cytotoxic processes become challenging by variability in surface chemistry, charge, and structure. CNTs based on graphene often include metal contaminants, are poorly soluble and biodegradability, and interact with other biomolecules, potentially disrupting genomic and proteomic processes in tissues and organs (Figure 6) (Augustine et al., 2020; Spurgeon et al., 2020).

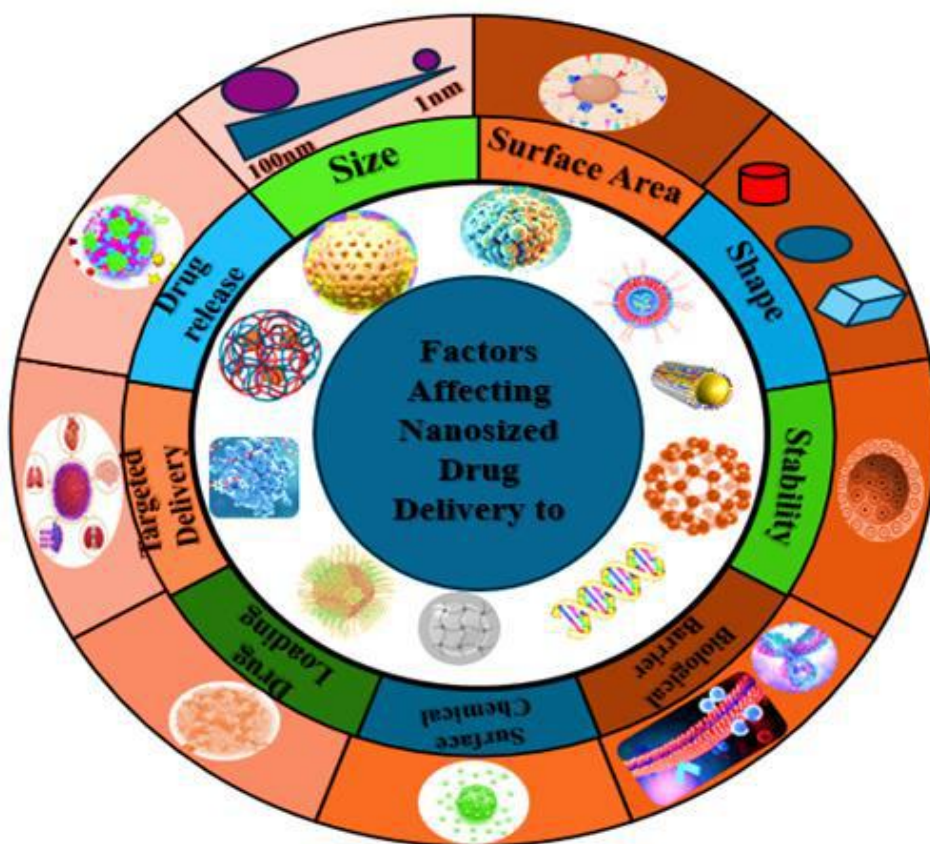


Fig. 6: Factors affecting nano-medicine drug delivery system to BBB

NPs can penetrate the sensory cells of the olfactory epithelium and migrate via the olfactory nerve to the olfactory bulb and cross the blood-brain barrier. Metallic NPs accumulate in the CNS and initiate a range of neurotoxic effects through oxidative stress, mitochondrial damage and DNA damage, inflammatory signaling, and cell death. The underlying mechanisms include ROS generation, apoptosis, cytokine release, microglial activation, and autophagy. The resulting dysfunction of both microglia and astrocytes exacerbates neurodegenerative outcomes in Alzheimer's and Parkinson's disease. MNPs@SiO₂ activate excitotoxicity via D-serine-mediated microglial signaling, AgNPs promote oxidative imbalance in the presence of Trolox, and AuNPs exhibit concentration-dependent cytotoxicity in neurons. CBNPs modulate inflammatory and apoptotic balance, while ZrO₂NPs are neurotoxic to the embryonic brain (Su et al., 2021).

9. Future Directions in Nanotechnology for Neurodegenerative Disorders

Nanotechnology offers bio-responsive biomaterials that have the potential to enhance the medical management of neurological disorders. These materials can adapt to patient-targeted needs and disease progression by monitoring CNS-specific signals and modulating drug delivery accordingly. Advanced imaging techniques combined with nanoparticles enable adaptive and precise therapeutic approaches by offering real-time feedback on treatment efficacy. Nano-biosensors further facilitate prompt detection and intervention by improving biomarker specificity and sensitivity. Additionally, nanotechnology aims to develop synthetic NPs that mimic the vital functions of natural tissues, reduce systemic toxicity, and optimize drug delivery methods.

Conclusion

The potential of therapies based on nanotechnology for neurological disorders is highlighted by developments in CNS-targeted medication

delivery. Although these nanoscale devices provide efficient brain-targeting techniques, they face challenges including a lack of models for assessing efficacy, material-specific limitations, immune activation, therapeutic agent degradation, and rapid clearance. Long-term efficacy and enhanced nanoparticle stability are necessary since gene therapies and nanoparticle treatments carry risks of off-target effects. Improved formulations, such as antibody-based NPs, can increase biomarker specificity. Interdisciplinary collaboration is crucial to overcoming these obstacles and developing nanotechnology for the treatment of neuronal diseases.

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