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 has 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 took 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).

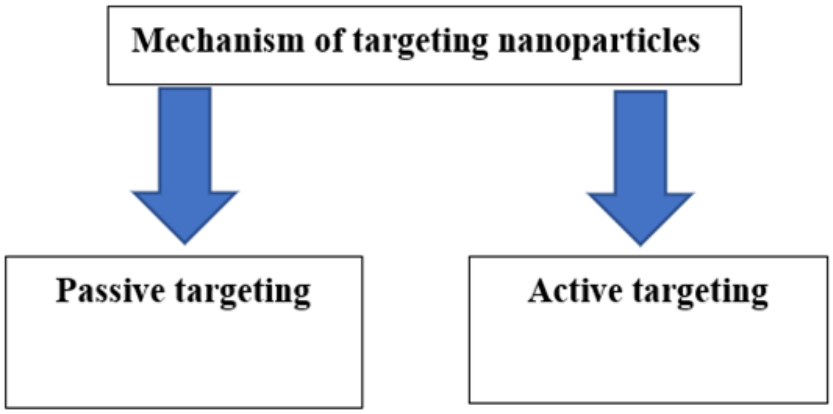

Fig. 1: The type of mechanisms of target nanoparticles

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. Furthurmore, certain enzymes such 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 (Garnett, 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).

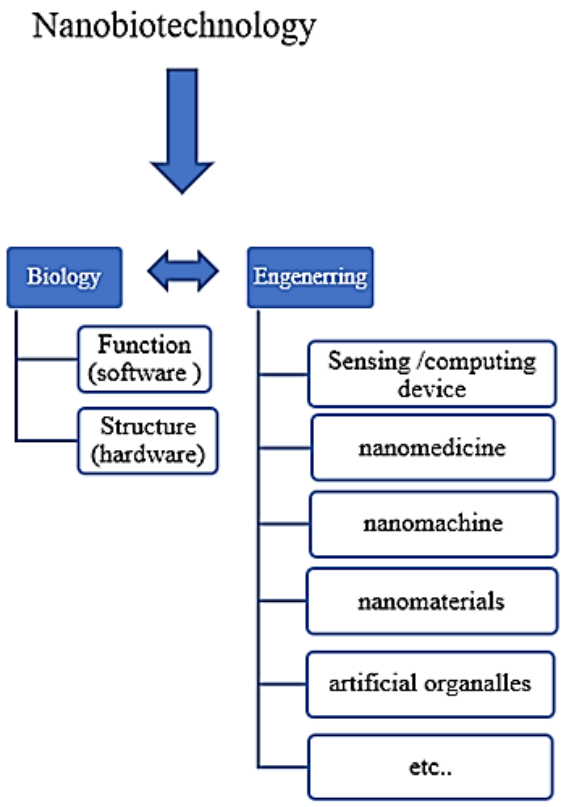

Fig. 2: Factors on which nanobiotecnology depends

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 Bioavalibility: 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 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

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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