Chapter 11

Nanoparticles in Targeted Drug Delivery and Therapeutics

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ABSTRACT

Numerous scientific domains can benefit greatly from nanotechnology. Nanoparticles are fundamental building components of nanotechnology. Recent developments in nanotechnology have demonstrated enormous potential of nanoparticles in medicinal applications. Because of their high carrier capacity, capacity to establish ligand-stabilized connections, and ease of obligatory molecules that are both hydrophilic and hydrophobic, nanoparticles are an advantageous platform for targeted and monitored administration disease-related micro and macromolecules treatment. The problems by conventional therapy are solved when therapeutic chemicals are mixed with nanoparticles (protein, nanogels, carbon nanotubes, quantum dots, nano-medicines); however, some issues as toxicity and side effects are still up for debate and should be carefully considered before being used in biological systems. Therefore, it's critical to comprehend unique characteristics of medicinal nanoparticles as well as methods of distribution. Here, we give an explanation of the special qualities that nanoparticles in biological systems possess. In this discussion, we will focus on the kind of therapeutically utilized nanoparticles, their specificity for therapeutic purposes, and their current delivery approaches for various illnesses like infectious, cancer, and cardiovascular, autoimmune, neurological, pulmonary, and ophthalmic disorders. Acquiring knowledge about properties of nanoparticles and how they interact with the biological environment can help us develop new approaches for analysis, treatment, and prevention of many ailments, especially those that are incurable.

KEYWORDS
Nanoparticles, Targeted delivery, Therapeutic NP, Disease, Treatment

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INTRODUCTION

The features of nanoparticles (1–100 nm) make them appropriate for use in medicine. These substances are sufficiently tiny to get into the appropriate tissues within the body, bind selectively to the target cell, and circulate with ease. The main aim of producing nanoparticles as provision system is to transmit active therapeutic compounds during treatment by controlling the particle size, surface characteristics, and effective release without causing side effects. The ability to construct multifunctional nano systems for simultaneous diagnosis and treatment is made possible by availability of nanoparticles known as thermo nucleic nanoparticles exhibiting both therapeutic and diagnostic properties concurrently (Anani et al.,2021; Kandasamy and Maity, 2021; Lu, 2022). Theranostic nanoparticles are perfect for biomedical applications because of number of attributes, including sufficient drug delivery, fast clearance, no negative effects on other organs, precise and rapid distribution, and comprehensive morphological and biochemical properties of targeted spot (Jokerst and Gambhir, 2011).

Drug efficacy and side effect reduction can be achieved through nanoparticle engineering with unique surface characteristics that allow them to aim for diseased cells, avoiding those that are healthy (Huang et al., 2010). Furthermore, nanoparticles can be engineered to release their contents in an appropriate manner, enabling long-term, continuous

medication delivery (Bajpai et al., 2018). The utilization of nanoparticles (NPs) in the pharmaceutical sector has experienced a significant surge in past few years. This can be attributed to their smaller size, which facilitates their easy penetration of cellular plasma membranes through cellular endocytic mechanisms (Zhang et al., 2015; Torrano et al., 2016). Numerous nanomaterials and nano-carriers have had their anticancer capabilities investigated in recent years. Old nano-medicine based cancer treatments are still in use to cause unwanted immunotherapeutic and photochemical effects (e.g., responses to inflammation, both acute and chronic) despite the previously mentioned properties, benefits, medical uses and NPs' improvements in cancer diagnosis and therapy that is, if NPs are not effectively functionalized for medicinal purposes (Braakhuis et al., 2014; Jeong et al., 2022). Preclinical and clinical research continues to recommend a comprehensive examination of NPs prior to their regular therapeutic usage (Desai, 2012; N.-Y. Lee et al., 2019; Ramos et al., 2022).

Recent advances in biomedical science have successfully improved the design of therapeutic medicines for the treatment of disease. The transport of therapeutic chemicals towards target location stands in the way of effectiveness of treating numerous diseases. Common therapeutic drugs have drawbacks including inadequate bio-distribution, unfavorable side effects, minimal efficacy, and non-selectivity (Kadam et al., 2012). Thus, the design of multifunctional, well-controlled delivery systems is main focus of current research efforts.

Delivering a variety of compounds to specific parts of the body through the association of therapeutic medicines with nanoparticles that have distinctive biologic and physicochemical characteristics engineering their paths for appropriate directing is auspicious strategy (Jahan et al., 2017). Delivering a variety of compounds to specific parts of the body through the association of therapeutic medicines with nanoparticles that have distinctive physicochemical and biologic characteristics and engineering their paths for appropriate targeting is a promising strategy. By improving the therapeutic agents' efficacy and/or tolerance in biological systems, raising their concentration at the target area also raises their therapeutic index. Combining water-insoluble medicinal compounds with nanoparticles can enhance their bioavailability and shield them from physiological obstacles. Conversely, when therapeutic nanoparticles are associated with contrast agents, it becomes possible to monitor their delivery location and track their journey in in vivo systems. The preceding advantages make it possible to use targeted therapeutic nanoparticles in a variety of medical specialties. In this paper, we outlined the physicochemical characteristics of nanoparticles that make them essential tools in nanomedicine and reviewed the past ten years of research on therapeutic nanoparticles and their targeted delivery uses in a range of illnesses, including cancer and neurological diseases (Yetisgin et al., 2020).

Nanoparticles as Nano-medicines

Numerous domains within nano-medicine, including medication and imaging, diagnostics, and gene delivery have included nanotechnology (Thakur et al., 2015; Martinho et al., 2011). The term "drug delivery" (DD) describes the procedures, formulations, technologies, and methods used to move pharmacological substances through body in order to provide intended therapeutic effect (Mohammad et al., 2017). It includes methods of delivering medication to both humans and animals in order to achieve therapeutic efficacy. The focus of recent advancements in drug delivery systems (DDSs) has mostly been on smart DDSs, which aim to administer drugs at the right time, dosage, and place for optimal safety and efficacy (Thakur et al., 2015).

The use of personalized medication designs and dosage adjustments in precision medicine has significantly altered the context of cancer treatment. It is possible to precisely alter a medication's absorption properties, how it behaves in target and nontarget tissues, and how it is administered in therapeutic combinations that work well together (Manzari et al., 2021). Among the intriguing uses of NPs in precision medicine include suppression or immuno-activation, intracellular targeting, genome engineering (Mitchell et al., 2021). Targeted-delivery nano-medicines can be made with varied variety of nanoparticles (NPs), due to their conjugated polymers, polymeric micelles, distinctive structural characteristics, polymeric, liposomes, and dendrimers. Particularly in the context of cancer treatment, numerous issues pertaining to drug-targeting techniques for irrefutable application have been found, studied, and determined. Integrating knowledge with technical advancements and multidisciplinary research could pave the path for the introduction of safer nano-medicine (Tewabe et al., 2021).

Types of Therapeutic Nanoparticles

Metallic Nanoparticles (NPs)

Therapeutic agents can be disseminated in a polymer carrier matrix, encased in a polymer shell, covalently bonded or adsorbed to the particle surface, or contained within a structure in solid colloidal particles with sizes ranging from 10 to 1000 nm are known as metallic nanoparticles for drug delivery (Brigger et al., 2002; Kroll et al., 2009; Sahoo and Labhasetwar, 2003). By avoiding multidrug resistance, site specificity, effectively delivering therapeutic agents and enhancing, metallic nanoparticles aim to raise the therapeutic index of pharmaceuticals (Brannon-Peppas and Blanchette, 2004; Byrne et al., 2008).

Metallic nanoparticles can carry large doses of drugs, outcomes in great concentrations of anticancer medications at the targeted location. This avoids harmfulness and other painful side effects that arise from high drug concentrations in other parts of the body, and is the main reason why metallic nanoparticles are useful as cancer therapy probes (A. H. Lu et al., 2007). Cancer therapy might be carried out both within cells and within sub cells with use of metallic nanoparticles, which would significantly boost therapeutic efficacy and decrease adverse effects (M. Z. Ahmad et al., 2010).

Bimetallic Nanoparticles

Numerous uses for bimetallic nanoparticles have been reported in the medical field, including bio-imaging, cancer therapy, antibacterial, antioxidant, and anti-diabetic medication delivery. Because of their strong magnetic characteristics, gold based Au–Fe and nickel based Ni–Co bimetallic nanoparticles suitable for use as contrast agents in CT and MRI imaging tests for diagnosis and prognosis (Amendola et al., 2014) and a tumor-targeting theranostic agent (Y. Lu et al., 2022). Cu–Fe has also been applied to improved chemodynamic treatment (Koo et al., 2022), Ag-Cu, Au-Pt, Pd-Pt, and Au-Co have all been utilized for anticancer activities and cancer therapies (Garfinkel et al., 2022; H. Yang et al., 2022; Koyyati et al., 2022; Oladipo et al., 2020; Seifi et al., 2020). Additionally, Au-Bi has been utilized to suppress tumor cells (He et al., 2021). Human health concerns have been raised by heavy metal ion contamination of water sources and dye emission from numerous industries worldwide. It is well recognized that dyes released by companies are harmful to human organs like the liver and kidney (Ge et al., 2018). But water bodies must be cleaned up and made free of many kinds of pollution. For this, bimetallic nanoparticles have been employed (Idris and Roy, 2023). Nano-chips, nano-sensors, nano-coating, and nano semiconductors, have all been created using bimetallic nanoparticles. For instance, bimetallic nanoparticles of Pd–Au, Au–Cu, Pd–Ru, Fe–Mn, Co–Ni, Ag–Cu, Au–Pt, Au–Ag, Cu–Sn, and Ag–Cu have been utilized to create biosensors and detectors that are able to detect dimethoate (Ansari et al., 2018), evaluate milk samples for Salmonella typhimurium (Sohrabi et al., 2022), and hydrazine (Amiripour et al., 2018) as well as anti-inflammatory drug 4-aminoantipyrine (Saeed et al., 2022), anti-cancer drug (Sravani et al., 2022), favipiravir (Mehmandoust et al., 2021), luteolin (Tang et al., 2022), diclofenac (Eteya et al., 2019), coal mine gases sensor (W. Zhang et al., 2022), and glucose in serum (Huan et al., 2022).

Green Nanoparticles

Emerging uses for green synthesized metal and metal oxide nanoparticles in biomedical field include immunotherapy, regenerative medicine, dentistry, wound healing, tissue treatment, and bio sensing platforms (Pandit et al., 2022). Significantly more beneficial impacts of silver nanoparticles include their anticancer characteristics, broad spectrum antibacterial response, non-toxicity, and other therapeutic uses (Cadinoiu et al., 2022; Safaya and Rotliwala, 2022; Y. Yang et al., 2022). Natural form Au nanoparticles produced using green synthesis. Complementing photosensitizers with gold-based nanoparticles can enable photodynamic antimicrobial chemotherapy (Hossain et al., 2022; Shivaramakrishnanet al., 2017). Furthermore, a different study found that elemental mercury was removed from soil and air by using green synthesized selenium nanoparticles, which also work to remove heavy metals (zinc, copper, and nickel) from soil (Ramezani et al., 2021; X. Wang et al., 2018; Zohra et al., 2021). Medicine using selenium nanoparticles is a significant bio therapeutic agent that has no negative effects (Hosnedlova et al., 2018).

Polymeric Nanoparticles

Lipid-based compounds like liposomes and polymeric-based particles like polymeric micelles, dendrimers, and polymer/drug composites make up the majority of drug-delivery nanoparticles (Jokerst and Gambhir, 2011; Lin et al., 2019). Due to the discovery of the special qualities of polymer nanoparticles, polymeric nanoparticles have gained favour over other nanoparticles in recent years. They are a good choice for creating theranostic nanosystems. The benefits of these nanoparticles include medication release control, biodegradability, biocompatibility, and flexibility for hydrophobic and hydrophilic payloads (Ferrari et al., 2018).

Uniform spherical shapes, polymer nanospheres range in size from 10 to 200 nm (Hosseini et al., 2023). Nanospheres are utilized as substitute carriers for the administration of imaging and anti-cancer medicines (Elkharraz et al., 2006; Grayson et al., 2005; Liu et al., 2009; Ranganath and Wang, 2008). It has been written that drug-loaded nanospheres can be modified with ligands for specific therapy. Nanospheres of wheat germ agglutinin (WGA), for instance, have been utilized to identify N-acetylglucosamine and sialic acid shown in prostate cancer cells (Xie et al., 2007). Typically, polymeric micelles have a size of less than 100 nm. Many studies have focused on polymeric micelles because of their ideal properties, which include tissue penetration, biocompatibility, nano-size, high stability, low toxicity, in physiological conditions, high drug concentration in the target site, high loading capacity, free control property, and the potential for ultimate functionalization of the group target ligand composition (Arshad et al., 2020; Rana and Sharma, 2019; Yadavet al., 2019; Y. Zhang et al., 2014). Novel type of polymeric materials known as dendrimers are huge molecules having a structure like a tree with branches or arms that are symmetrical in the center, interior portion, and external shell. These structures are composed of Units of symmetric branching that remain arranged around central linear polymer core or tiny molecule. Having just emerged as a class of nanoscale macromolecules utilized as carriers, their unique advantage in precision structural engineering makes their emerging applications in cancer treatment and bio imaging particularly noteworthy (Fréchet, 2003; Larson and Ghandehari, 2012; Pearson et al., 2012).

Micelles

Water-insoluble medicinal compounds are mostly delivered systemically by polymeric micelles. They form as aggregates in solution and have a size of less than 100 nm. Their excellent stability in physiological systems is ensured by their hydrophilic surface, which also helps to protect them against nonspecific uptake by reticulo-endothelial system. As a result, dynamic structure of polymeric micelles offers a significant therapeutic agent delivery

mechanism that enables a range of loading capacities, controlled ligand conjugation, and a decreased rate of dissolution (Z. Ahmad et al., 2014).

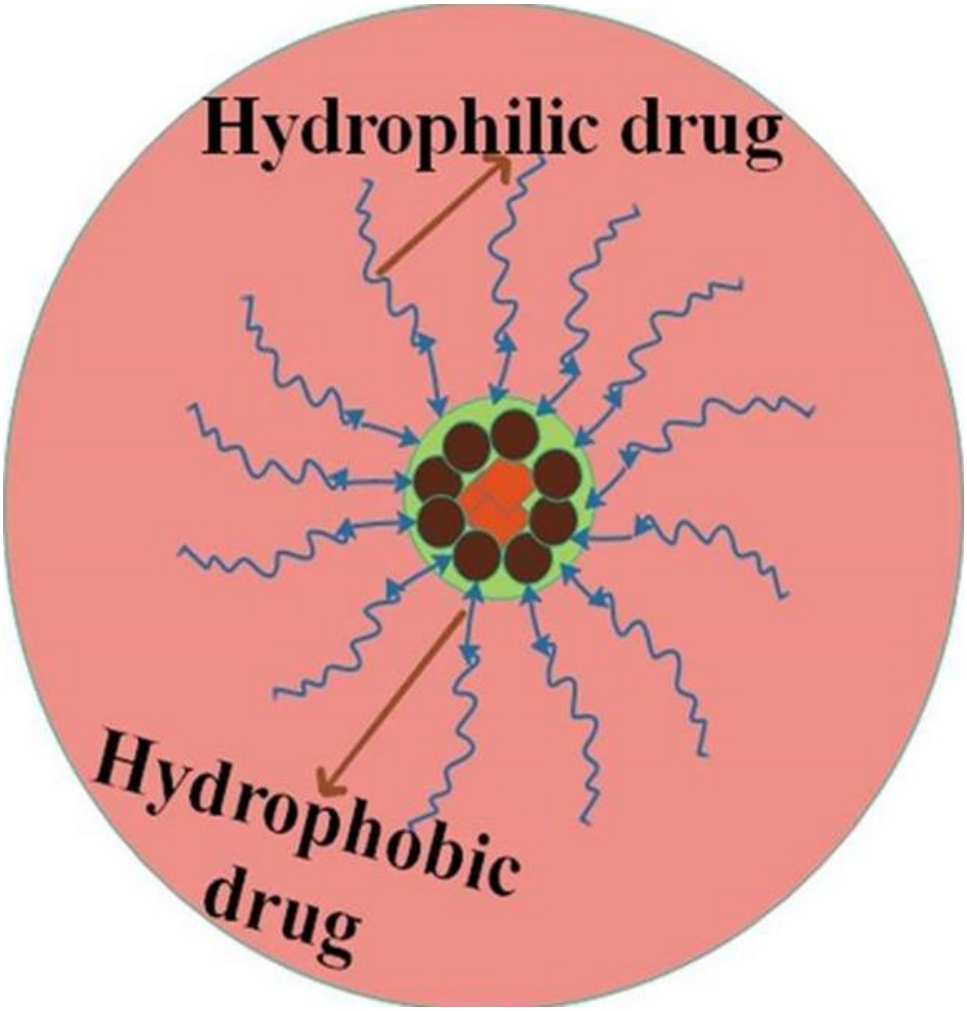

Fig. 1: Diagrammatic depiction of polymeric micelles structure

Nanosheets

The scientific world has been very interested in two-dimensional (2D) nanosheets ever since graphene was discovered in 2004 (Novoselov et al., 2004). Due to their special qualities, 2D nano-sheets can be helpful in several biological research areas, such as the transfer of nucleic acids for gene therapy (Choi et al., 2018). The first known carbon-based 2D nanomaterial is grapheme (Ge et al., 2018). To our knowledge, this work is the first that describes GO-based nano-carriers used for photo thermal and gene therapy was made by (Feng et al., 2013). Yin et al. introduced multifunctional GO nano-sheets that have the capacity to target cancer in addition to performing gene and photo thermal therapy concurrently (Yin et al., 2017).

Discovered in 2014, Black phosphorus (BP) is a recently discovered kind of 2D nano-sheet that has been thoroughly explored in the last few years (L. Li et al., 2014). Because of its biocompatibility, it has been thought to offer significant deal of potential for biological applications (Qian et al., 2017). Chemo/gene/photothermal therapy mediated by BP nano-sheets demonstrated a novel approach to overcome medication resistance in cancer (Kim et al., 2020).

Carbon Nanotubes

One way to characterize carbon nanostructures (CNSs) is as a very practical class of nanostructure. As a subset of smart nano-carriers made completely of carbon, carbon nanotubes (K. P. Loh et al., 2018). In addition to offering a wide range of potential advantages, such as the encapsulation of both hydrophobic and hydrophilic molecules, which improves drug stability and enables site-specific administration, nanostructures can be applied to the targeted delivery of pharmaceuticals (Niezabitowska et al., 2018). One important area of CNT use is functionalization in applications in biology through a variety of techniques. These techniques are crucial because they not only make the CNTs stable and biocompatible in the biological environment, but also allow them to combine or conjugate with different biomolecules, therapeutic agents, and diagnostic devices to produce accurate, cost-effective, and therapeutic systems (Kumar et al., 2014; Rogers-Nieman and Dinu, 2014). Using nanotubes as a drug delivery system, cancer is treated (Inoue et al., 2009). CNTs are frequently employed as nanocarriers for anti-tumor drugs, such as camptothecin, doxorubicin, methotrexate, and cisplatin. In particular, cisplatin has been utilized as a treatment for a number of conditions related to cancer (Saleemi et al., 2020).

These CNTs' primary function is to preserve the structural integrity of the pharmaceuticals, as encapsulation or "endohedral modification" frequently reduces the rate at which pharmacological substances degrade in order to maximize drug release under carefully monitored conditions (Perry et al., 2011). Because hydrophobic and capillary forces are what drive the encapsulation of pharmaceuticals, this technique works best with medications that have a lower surface tension. For instance, gold nanoparticles are used in the fabrication of oxidized carbon nano-bottles to inhibit the uncontrolled release of the medicine that is enclosed (cisplatin) (J. Li et al., 2012), as shown in Fig. 2.

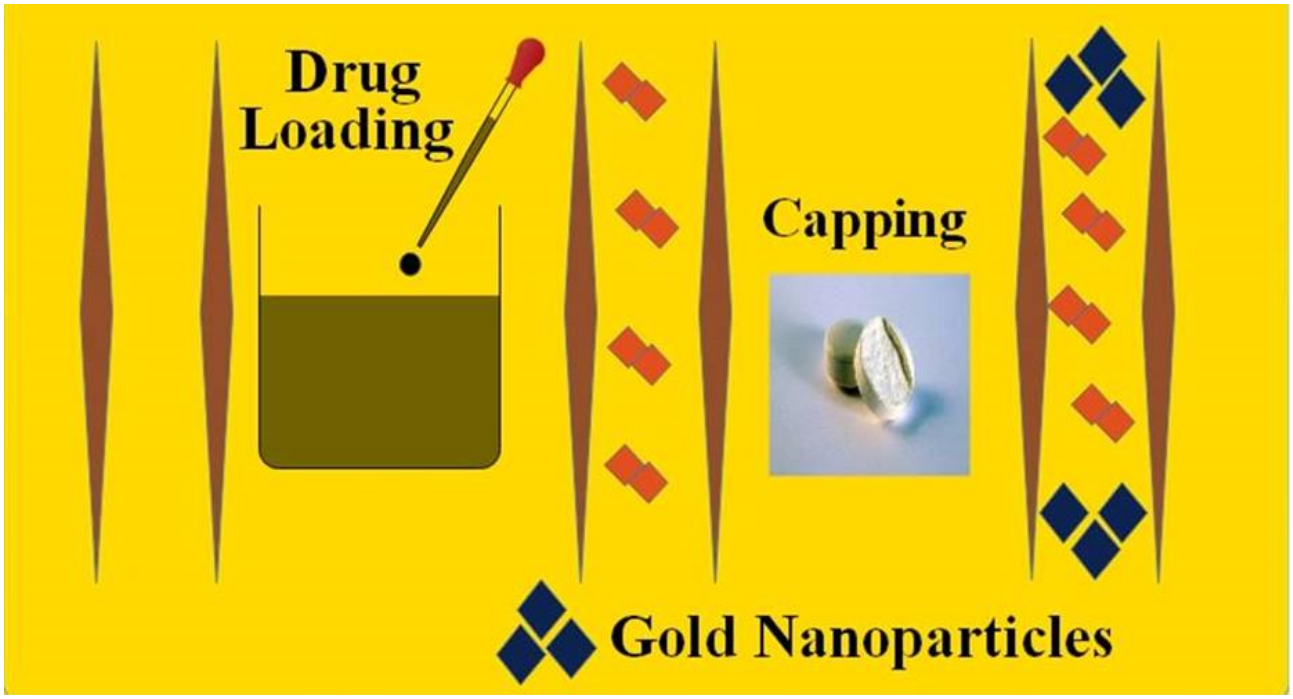

Fig. 2: Carbon nanobottle synthesis, in which the ends of the encased carbon nanotubes are made of gold nanoparticles.

Nanogels

Hydrogels with a sub micrometer particle size ranging from 20 to 250 nm and a three-dimensional (3D) tunable porous structure are known as nanogels, and they are a type of systemic drug delivery carrier. They are characterized by their particle size range of 1 to 350 μm, which sets them apart from hydrogels that develop in situ and facilitate local delivery (Jiang et al., 2014). Unlike ordinary nanoparticles (NPs), nanogels possess customizable particle size, shape, and sensitivity to various external stimuli such as temperature, pH, redox conditions, ionic strength, and others, which enables them to have excellent controlled drug release properties (Sahiner et al., 2006). One of the main obstacles to effective drug delivery to cancer cells and better clinical results in cancer therapy is drug resistance. Hyaluronate (HA) nanogels carrying doxorubicin and cisplatin have been developed to reverse drug resistance, according to (Ma et al., 2021). The purpose of the nanogel's design was to keep the cancer cells' medication concentrations at their ideal levels. The assessment of the nanogels demonstrated their potential for reversing drug resistance (Attama et al., 2022).

Quantum Dots

Due to their special qualities, Quantum dots (QDs), which are semiconductor nano-crystals, are a preferred nano-carrier for chemotherapeutic drugs above other kinds (Field et al., 2018). Because of its size and characteristics, QDs are widely used in therapeutic applications. Additionally, due to QDs' exceptional physical, optical, and exciting electrical properties, they are used in a variety of other applications, including tissue engineering, bio imaging, cancer treatment, photo thermal therapy, bio sensing, preventing bioterrorism, and most notably drug delivery (Duan et al., 2019). Numerous anticancer medications today exhibit undesirable traits in clinical trials, including inadequate targeting, toxicity, and lack of selectivity. It is anticipated that recent advancements in QDs, therapy-based multifunctional nanoparticle medicines, and their drug delivery to the target organ would have an impact on cancer detection and treatment (Badılı et al., 2020).

QDs are useful agents for medication delivery tailored to the microenvironment. For this reason, graphene QDs were assessed by (Wei et al., 2018). GQDs can be used to achieve classic cell visualization using tailored high quality PL colors and images but their lack of cell selectivity makes it difficult to extract cellular-level information from molecules. Targeted imaging was suggested by researchers as a possible substitute for cell identification and detection. This can be accomplished by adding specific groups and polymers to the surface of GQDs to increase their internalization efficiency. According to published research, the most popular cell targeting substances are arginine–glycine–aspartic acid (RGD), folic acid (FA), proteins, and even hyaluronic acid (HA) (D. Zhang et al., 2018; J.-E. Lee et al., 2013; S. Li et al., 2017; Zheng et al., 2013). Through endocytosis, FA demonstrates a strong affinity for folate receptor (FR) found upon the exterior of

different human cancerous cells (Biswas et al., 2021), as shown in Fig. 3. These nanoparticles have additional benefits in that they can be employed to the manufacture of sensitive sensors. For industrial and clinical research, the sensitive, selective, dependable, quick, and affordable drug analysis approach is essential (Badılı et al., 2020).

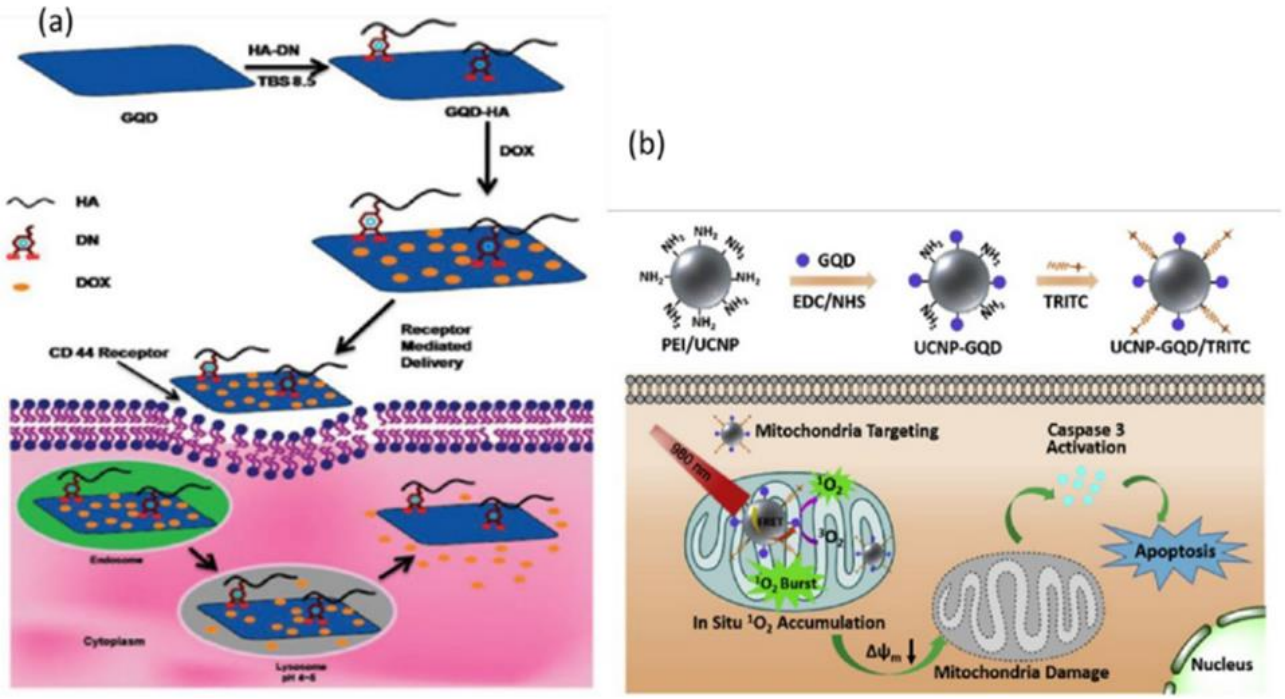

Fig. 3: a): Hyaluronic acid (HA) is used to target deliver GQDs, and the medicine is then released from the surface of the GQD into an environment of tumor cells. Copyright 2021 American Chemical Society. b): Diagram demonstrating the synthesis of UCNP-GQD/TRITC with mitochondria-targeting effectiveness. Tumor cell death can be triggered very effectively by an in situ $^1O_2$ burst in mitochondria upon laser irradiation. Copyright 2021 American Chemical Society.

Protein NP

Nanotechnology has shown enormous impending in the arena of medicine (Kamaly et al., 2012; Shi et al., 2011). The use of nanoparticle technology in protein delivery can: 1, shield proteins in the biological environment against early deterioration or denaturation; 2, increase the shelf life of proteins having poor pharmacokinetic properties in the circulatory system; 3, regulate an adaptable, steady release that keeps the drug's application inside medicinal range; and 4, target damaged cells, tissues, and intracellular spaces to increase the safety and effectiveness of biologic therapies. The investigation of nanoparticle technologies for protein delivery has been made possible by the notable success of small-molecule nanoparticle formulations of daunorubicin (DaunoXome), doxorubicin (Doxil and Myocet), amphotericin B (Ambisome), and paclitaxel (Abraxane) (Peer D et al., 2007).

Nanoparticles Characteristics for Therapeutics

New and improved nanomaterials for biomedical applications have been created attributable to advances in nanotechnology (Dessale et al., 2022). Because of their distinct qualities, NPs are used in variety of presentations (Machado et al., 2014). The capabilities of multifunctional nanoparticles (NPs) include transportation of hydrophobic compounds, active and passive targeting of disease cells, prolongation of drug circulation, enhancement of drug entry and accumulation at tumor sites, mitigation of drug resistance, augmentation of medication safety and tolerability, and advancement of other technological fields (Q. Yang et al., 2014; Zeineldin and Syoufjy, 2017).

Size

Another significant element influencing circulation and bio distribution of medicinal nanoparticles is size. Particles bigger than 200 nm may be removed by phagocytic cells in reticulo-endothelial system (RES), but smaller particles can be readily removed by physiological processes (percolation over kidney). As a result, therapeutic nanoparticles smaller than 100 nm circulate in the bloodstream over an extended duration. Numerous investigations revealed that because therapeutic nanoparticles in 20–200 nm size range are not recognized by RES and cannot be filtrated by kidney, exhibit a greater accumulation rate in tumors (Bhatia and Bhatia, 2016; Ernsting et al., 2013; W. Wu et al., 2018). In addition, compared to normal tissues, quantity and volume of blood vessels are greater in tumor sites. Therefore, increased permeability and retention (EPR) effect occurs when nanoparticles of the right size are able to enter the tumor area relatively quickly and remain there for a longer period of time (Nakamura et al., 2016; Fang et al., 2011).

Surface Charge

The expulsion and targeted delivery of therapeutic nanoparticles are significantly influenced by their surface charge. When associated to neutral or negatively charged nanoparticles, positively charged nanoparticles elicit stronger immunological response. Furthermore, it has been demonstrated that nanoparticles with an exterior potential of between -10 and +10 mV are less prone to non-specific interactions and phagocytosis (Bhatia and Bhatia, 2016; Ernsting et al., 2013). The substance of the nanoparticles, however, may determine the optimal range. The surface charge of nanoparticles and their sensitivity to pH are also strongly connected. These nanoparticles can be made to identify and localize themselves in particular cell partitions. To release their payload, acidic nanoparticles can be directed towards endosomes or lysosomes, which have a pH of less than 6.0 (Casey et al., 2010; W. Wu et al., 2018; C. Wang et al., 2017).

Surface Modifications

PEG is an ideal polymer for therapeutic nanoparticles because of its inherent physicochemical characteristics, which lessen phagocytic absorption and limit aggregation in non-target regions (Walkey et al., 2012). Therapeutic nanoparticle PEGylation should take into account factors that affect surface hydrophilicity and phagocytosis, such as PEG chain length, shape, and density. Target-specific delivery of PEGylated nanoparticles can be enhanced by conjugating targeting ligands to their surface; however, this also has an impact on the nanoparticles' bio-distribution (Yetisgin et al., 2020), as shown in Fig. 4.

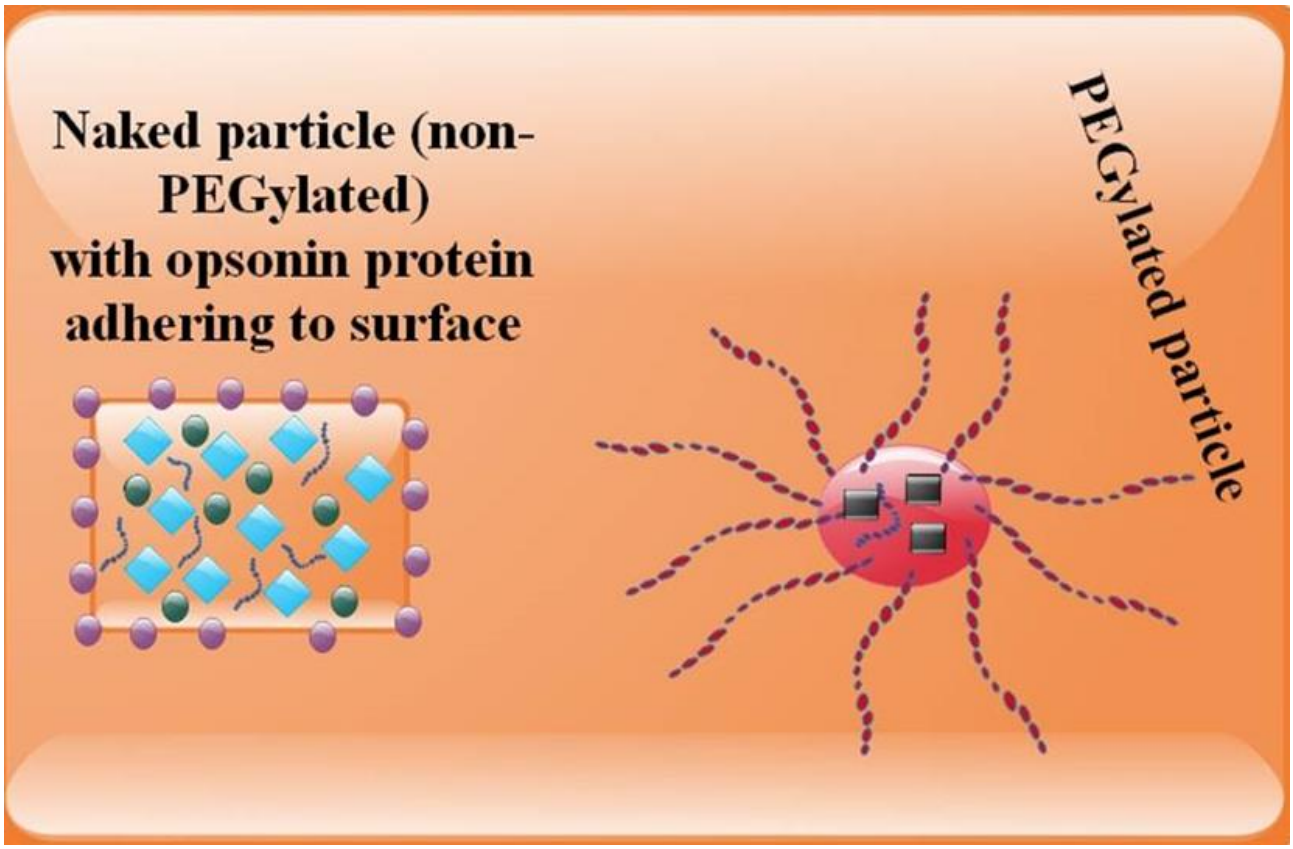

Fig. 4: PEG offers stealth. PEGylation of particles can be used to mask surface characteristics and balance the net charge, which will lessen the likelihood that opsonin proteins will bind to them and that macrophages will eventually clear them. This tactic can increase how long particles circulate within the body.

Nanoparticles Application in Therapeutics

Distinct advantages of nanotechnology for imaging, diagnostics, and medication administration, additionally its potential for developing synthetic vaccines, tiny medical devices, and therapeutic properties of certain nano-materials themselves, have made it increasingly popular for use in cancer treatment. Many therapeutic nanoparticle (NP) stages, including liposomes, polymeric micelles, and albumin NPs, have been accepted for use in the treatment of cancer (Shi et al., 2017). NPs are used in medical applications due to their unique properties, which include their quantum nature, higher surface-to-mass ratio than other particles, and ability to absorb and transport other molecules like proteins and drugs. The composition of NPs can vary greatly as they can start with dextran, chitosan, phospholipids, biological lipids, lactic acid, or other substances like metals, carbon, silica, or other polymers (Guo et al., 2013; Jani et al., 2020; Mukherjee and Bhattacharyya, 2020; Nikolova, 2020; Saxena et al., 2020).

Cancer

A major cause of death and burden on world health is cancer. By 2018, it was predicted that there would be 9.6 million cancer-related deaths and 18.1 million new cancer cases (Bray et al., 2018). Uncontrolled cell growth, which begins at one focal site and spreads to other parts of the body until it kills, is hallmark of disease known as cancer. Nanotechnology has yielded some promising results in detection and treatment of cancer, including the administration of medication (Hu et al., 2016), targeted therapy, molecular imaging, biomarker mapping, drug carriage, gene therapy, and detection and diagnostics (Tran et al., 2017).

One essential feature of nano-carriers for drug delivery is their ability to preferentially target cancer cells, which increases therapeutic efficiency while shielding healthy cells from damage. The two main categories of targeting mechanisms are passive targeting and active targeting (Yao et al., 2020). The purpose of passive targeting is to take advantage of distinctions between normal and tumor tissue. When medications are successfully transported to target site, they can function therapeutically. This is known as passive targeting. The neovascularization caused by high cancer cell proliferation and increased perm selectivity of tumor vasculature relative to normal vessels are caused by big vascular wall pores (Carmeliet and Jain, 2000). Active targeting uses direct interactions between ligands and receptors to target cancer cells in particular. To differentiate between targeted and healthy cells, ligands on surface of NPs are specifically designed to target molecules that are expressed on surface of tumor cells (Kamaly et al., 2012; Shi et al., 2011). Receptor-mediated endocytosis is triggered by interaction between ligands on NPs and receptors on surface of cancer cells. This process enables internalized NPs to effectively release therapeutic medicines (Farokhzad and Langer, 2009).

Infectious Diseases

Transmissible illnesses brought on by infectious pathogens, including bacteria, viruses, fungi, and parasites, are referred to as infectious diseases. One of main concerns for global public health is infectious diseases, which cause millions of deaths annually, the majority of which take place in developing nations (Markwalter et al., 2018). The primary treatment strategy for infectious diseases involves the utilization of antimicrobial medications (Hillaireau and Couvreur, 2009; Sendi and Proctor, 2009). Liposomes that increase antimicrobial activity of medications and polymer-based and non-polymeric nanoparticles are examples of nano-delivery applications for the treatment of infectious disorders (Zazo et al., 2016). A broad-spectrum antibiotic called ciprofloxacin is recommended to treat lung infections. With LipoquinTM, ciprofloxacin liposome formulation, systemic effects of the high-dose antibiotics are avoided because it is intended for inhalation and has a 24-hour sustained release (Yetisgin et al., 2020).Similar to this, amphotericin B's related toxicity is intended to be decreased by the anti-fungal liposomal transporter Ambisome® (Walsh et al., 1999).

Liposomal amphotericin B is appropriate for much disseminated histoplasmosis or immuno-compromised patients with HIV infection because of its minimal systemic toxicity (Cornely et al., 2007). Medical gadgets are also adorned with antimicrobial nano-drugs to prevent the production of biofilms (L. Wang et al., 2017), for example, Ag-NPs in central venous catheters CVCs (K. Wu et al., 2015). Additionally, some nanoparticles like Verigene®, Silverline®, Acticoat™, or Endorem™ SPIONs are employed as medical devices or in diagnosis (Beal et al., 2013; Bozzuto and Molinari, 2015; Weissig et al., 2014).

Pulmonary Disease

Asthma, pulmonary tuberculosis, chronic obstructive pulmonary disease (COPD), cystic fibrosis, and idiopathic pulmonary fibrosis (IPF) are examples of pulmonary lung illnesses (Sugawara and Nikaido, 2014). Delivery systems based on nanoparticles enable increased bioavailability, reduction in dosage, regulated release, and frequency of treatment. Natural polymeric nanoparticles including chitosan, gelatin, and alginate, as well as synthetic polymers like PLGA, poloxamer, and PEG, are frequently utilized in creation of nanomedicine inhalation formulations (Lim et al., 2016; Yhee et al., 2016). Furthermore, pulmonary inhalation of polyamidoamine (PAMAM) dendrimers combined with anti-asthma beclometasone dipropionate (BDP) proved to be an effective method (Nasr et al., 2014).

Regenerative Therapy

Regenerative therapy is centered on creation and utilization of biocompatible materials that can augment tissue regeneration and repair through their inherent biological mechanisms. Using stem cells in therapy is one way to encourage the body's own repair or regeneration process (Yetisgin et al., 2020). Interest in creating and administering therapeutic nanoparticles directly to support bone regeneration has grown over time (Gera et al., 2017). One of treatment techniques based on nanoparticles and stimulation of osteoblasts for bone formation is the delivery of several growth factors (Kong et al., 2014; Ortega-Oller et al., 2015; Park et al., 2016; S. Zhang et al., 2010). Furthermore, another therapeutic approach in bone tissue is the nano-delivery of synthetic chemicals, which may inhibit osteoclasts, cells that break down bone. Because they encourage osteoclast apoptosis, bisphosphonate medications are frequently used to treat osteoporosis. Bisphosphonate medications have been delivered via variety of metallic nanoparticles, either polymeric or non-polymeric (Giger et al., 2013; X. J. Loh et al., 2016). In bone tissue, another method for using therapeutic nanoparticles is to lessen inflammation, especially in cases of extensive wounds (Warabi et al., 2001; Gonçalves et al., 2015).

Targeted Drug Delivery Application of NP

Targeted delivery is efficient administration of medicinal substance with focus on target location of accumulation. After spending ideal amount of time in physiological system, drug-loaded system should evade immune system, target specific cell or tissue, and release loaded medicine (Colombo et al., 2012). At present, much research is being done on targeted nanoparticle delivery as a cancer treatment. In clinical trials or now being evaluated in clinics, more than 20 per cent of therapeutic nanoparticles were created with anti-cancer purposes in consideration. Moreover, related studies have focused on using nanoparticles to treat a range of other conditions, such as viral, neurodegenerative, and autoimmune diseases (Baranwal et al., 2023).

Limitations and Disadvantages

The application of nanoparticles shows promise in treatment of wide range of illnesses, including glaucoma and cancer. Regrettably, there are certain drawbacks and restrictions associated with nano-medical techniques that rely on nanoparticle technologies. When employing nanoparticles in living things, there are number of factors to carefully consider, including their toxicity, ability to elude phagocytic system, avoid physiological barrier, and incite an immunological response (Ferrari, M. 2005). The propensity of smaller nanoparticles to aggregate presents another challenge. For example, micelles, dendrimers, and QDs of smaller sizes are more likely to aggregate, which leads to inadequate bio distribution (Angra et al., 2011; D. Li and Kaner, 2006; Rizvi and Saleh, 2018; Sadauskas et al., 2009).

When pharmaceuticals that are currently utilized in medical applications are mixed with therapeutic nanoparticles, medications gain new functions and improve treatment effectiveness. However, Manzoor et al. (2012) discovered that the heterogeneities of vascular permeability may limit medication concentration and penetration into tumor regions utilizing nanoparticle-based drug delivery methods. To get around the issue, they proposed a controlled delivery method utilizing drug-loaded liposomes that release the medication *in vitro* when exposed to ambient heat (Manzoor et al., 2012).

Future Perspectives

Nanoparticle-based treatments is at the core of nano-medicine, which is the medical field of the future. But before affluence, there is still a long way to go. Above all, it is crucial to look into the nanoparticles' long-term safety and toxicity. In the meanwhile, research on disease causes and novel medications will pave the way for the inclusion of safer and more effective nanoparticle-based treatments in patient regimens (Yetisgin et al., 2020).

Conclusions

The creation of therapeutic drugs based on nanoparticles has been subject of much research during past ten years, and nano-delivery systems are crucial for precisely targeting intended location in treatment of numerous illnesses. Nowadays, polymers or lipids make up majority of nanoparticles utilized in the targeted delivery method, despite of the fact that polymeric nanoparticles show promise for treating diseases. In addition, expense of producing nanomedicine and doing it on a greater scale is a significant issue that requires attention. Thus, by comprehending properties of nanoparticles and their connections with biological environment such as their targeting of receptors or mechanisms of action in the pathophysiology of disease, we will be able to get around obstacles and develop novel approaches for the diagnosis, treatment, and prevention of wide range of diseases, especially incurable ones. Nano-medicines, future of medicine, will be built on therapeutics based on nanoparticles. Nanoparticle-based treatments will become safer and more effective in patient regimens as a result of new pharmaceuticals and discoveries about causes of diseases.

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