



REVIEW PAPER

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Nanotechnology in medicine: A comprehensive review of emerging trends, innovations and therapeutic applications

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Key words: Nanomedicine, Drug delivery, Liposomes

<http://dx.doi.org/10.12692/ijb/26.5.174-201>

Article published on May 07, 2025

Abstract

Nanotechnology deals with the manipulation of materials at the nanometer scale and applied as a transformative approach in various fields including medicine. It offers an innovative solution for the prevention, diagnosis and treatment of various diseases. Nanoparticles play vital role in medicine due to their small size, stability and ability to interact effectively with ligands. Their size and shape, high carrier capacity and compatibility with hydrophilic and hydrophobic substances sort out the limitations of traditional treatments and enhance the tissue targeting. Nanoparticles not only improving treatment efficacy but also reducing adverse effects. Targeted drug delivery improves patient compliance and overall quality of life. Lipid based nanoparticles, polymeric nanoparticles, metal and metal oxide nanoparticles are not only utilized for drug delivery systems and diagnostic imaging, but also used for various therapeutic applications due to their antimicrobial, antioxidant, anti-inflammatory, antidiabetic, anticancer and cardioprotective effects. Green synthesis of plant-derived nanoparticles further enhances these benefits, providing an environment eco-friendly approach. Despite significant advancements, there remains a critical need for comprehensive evaluations of the latest progress in organic, inorganic and carbon-based nanoparticles and their applications across diverse therapeutic domains. This review addresses this gap by providing a detailed and updated analysis of the roles and applications of nanoparticles in treating critical diseases, emphasizing their transformative potential in influencing the future of medical therapies.

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Introduction

Nanotechnology offers significant advantages across scientific fields, particularly in medicine. In recent years, the development of nanoparticles for medical applications has led to an innovation and commercialization potential of nanotechnology. Nano-based drugs enable targeted delivery, minimizing side effects and enhancing stability, leading to prolonged therapeutic efficacy (Fig. 1). Their small size and high drug-loading capacity allow them to penetrate blood vessels without damaging the vascular endothelium, which protect drugs from enzymatic degradation as well as improving local drug concentrations and therapeutic efficacy (Singh *et al.*, 2019; Sun *et al.*, 2023).

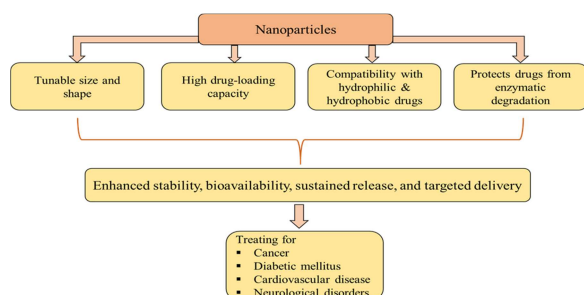


Fig. 1. Characteristic features of nanoparticle

In recent years, several researchers explored various FDA-approved nanoparticle-based products as chemotherapeutics and imaging agents which helped in treating several diseases (Malik *et al.*, 2023). Nanoparticles enable targeted drug delivery, reducing side effects and enhancing the efficacy of chemotherapeutic agents in cancer therapy. Nanoparticles facilitate precise drug delivery to inflamed tissues and improving treatment outcomes for cardiovascular diseases.

Nanoparticles that can cross the blood-brain barrier have advanced treatments for neurological disorders such as Alzheimer's and Parkinson's disease. Nanoparticle-based systems provide controlled release of insulin and other drugs, enhancing patient compliance and therapeutic outcomes in diabetes management (Cheng *et al.*, 2023; Singh *et al.*, 2019).

Lipid based nanoparticles, polymeric nanoparticles, metal and metal oxide nanoparticles are not only utilized

for drug delivery systems and diagnostic imaging, but also used for various therapeutic applications due to their antimicrobial, antioxidant, anti-inflammatory, antidiabetic, anticancer and cardioprotective activities. Green synthesis of nanoparticles further enhances these benefits by offering an eco-friendly approach (Bhardwaj *et al.*, 2020; Nikolova *et al.*, 2020). This review highlights the recent innovations in nanoparticle based therapies and provides a current perspective on their role in enhancing therapeutic outcomes in cancer, cardiovascular diseases, diabetes and central nervous system disorders.

Synthesis of nanoparticles

Nanoparticles are synthesized using physical, chemical and biological methods while, chemical and biological methods are known as the bottom-up approach, the physical approach is referred to as top-down approach (Fig. 2). The biological method of nanoparticles synthesis also known as green synthesis. Each of these approaches is further sub-categorized into various types based on the specific methods adopted (Fig. 3) (Joudeh *et al.*, 2022).

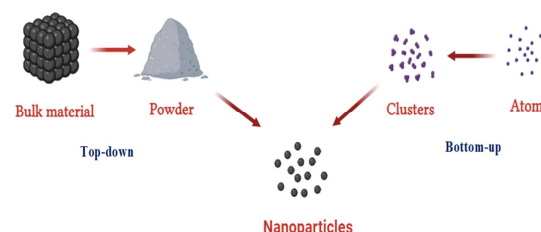


Fig. 2. Nanoparticles synthesis through top-down and bottom-up approaches

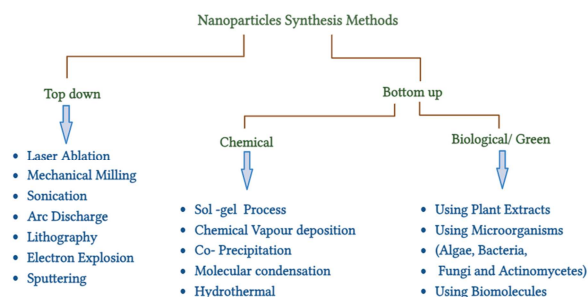


Fig. 3. Methods used for the synthesis of nanoparticles

Top-down approach

The top-down approach is also known as destructive method and involves breaking down of bulk materials into smaller fragments. These smaller fragments are further converted into nanoparticles. This method is considered as a simple and efficient approach to synthesize nanoparticles with desired properties and the major disadvantages of this method includes surface structure defectiveness and inability to control the size and shape of the nanoparticles (Joudeh *et al.*, 2022).

Bottom-up approach

It is an eco-friendly and cost-effective method that builds materials from the atomic or molecular level while reducing waste production. It is often preferred over the top-down approach for nanoparticle synthesis due to its ability to achieve greater homogeneity (Altammar, 2023).

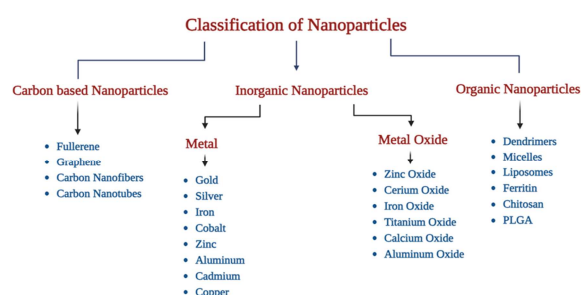


Fig. 4. Common classification of nanoparticles

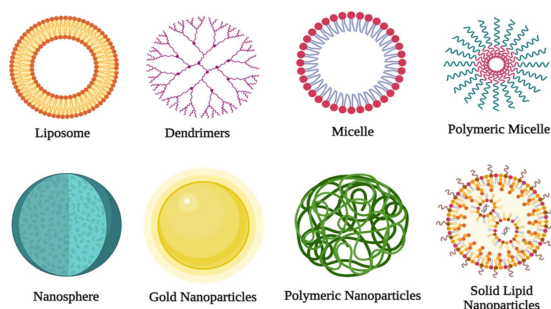


Fig. 5. Structural illustration of some important classes of nanoparticles

Nanoparticles classification

Based on their composition, nanoparticles are generally classified into three categories: organic, inorganic and carbon-based nanoparticles (Fig. 4).

Fig. 5. presents structural illustrations of some important types of nanoparticles.

Organic-based nanoparticles

Organic based nanoparticles are derived from organic compounds like proteins, carbohydrates, lipids and polymers. Examples include micelles, dendrimers, liposomes and ferritin. These nanoparticles are biodegradable and non-toxic and considering them more suitable for biological applications. Their formation relies on non-covalent intermolecular interactions, which make them more labile and easier to eliminate from the body (Joudeh *et al.*, 2022; Altammar, 2023).

Polymeric Nanoparticles

Polymeric nanoparticles are engineered nanostructures designed for controlled drug delivery and are broadly categorized into nanospheres and nanocapsules. Nanospheres are solid matrices in which drugs are embedded, while nanocapsules have a polymeric shell enclosing a drug containing core. These nanoparticles have several advantages such as high stability, structural flexibility and the ability to carry both hydrophilic and hydrophobic drugs. These properties could help in efficient drug and gene delivery that ensures protection of therapeutic agents from degradation, targeted delivery and reduced side effects (Zielińska *et al.*, 2020).

A range of chemotherapeutic drugs has been encapsulated in polymeric nanoparticles to enhance antitumor activity, minimize side effects and reduce the effective dose. Polymers used in parenteral administration must possess mechanical and physicochemical properties conducive to biocompatibility and biodegradability. The FDA approved synthetic polymers such as poly (D,L-glycolide) and poly (D,L-lactide) (PLA) are used for controlled drug release and in reducing systemic toxicity (Makadia and Siegel, 2011). Non-synthetic biodegradable polymers such as chitosan, gelatin, zein, alginate and albumin are also widely used due to their biocompatibility and safety in therapeutic delivery (Gagliardi *et al.*, 2021).

Dendrimers

Dendrimers are synthetic, star shaped macromolecules with a tree like structure composed of a central core, branched repeating units and functional surface groups. These functional groups can be modified to enhance chemical and physical properties, as well as bioavailability and biodegradability. Therapeutic drugs can either be attached to the surface or encapsulated within the dendrimer structure (Sim *et al.*, 2021). Dendrimers have significant applications in drug delivery. For example, conjugates of dendrimers with peptides or saccharides shows improved stability, solubility and enhanced antiviral and antibacterial effects. Dendrimer-DNA complexes (dendriplexes) explored as gene delivery vectors due to their potential in improving drug efficacy and targeting the gene of interest.(Wang *et al.*, 2022).

Liposomes

Liposomes are spherical and self-assembled vesicles consisting of an aqueous core surrounded by one or more phospholipid bilayers. This kind of structure allows them to encapsulate both hydrophilic and hydrophobic therapeutic agents. Hydrophilic drugs are retained within the aqueous core and hydrophobic drugs are integrated into the lipid bilayer which

facilitates the delivery of a wide range of pharmaceutical compounds with diverse solubility profiles (Nsairat *et al.*, 2022).

Liposomes are composed of natural or synthetic phospholipids, which contribute to their biocompatibility, biodegradability and low toxicity. The phospholipid types influences the liposome's stability, release characteristics and interaction with biological systems. The surface charge, size and lipid composition of liposomes can be precisely controlled to enhance their drug delivery properties. Liposomes can be engineered to improve their stability in circulation by modifying their surface charge. This modification prevents immune system recognition and target specific cells or tissues (Izadiyan *et al.*, 2025).

Liposomes are highly effective in drug delivery systems for anticancer drugs, vaccines and gene therapies. Their size and surface properties can be modified for controlled release and prolonged circulation, reducing side effects and enhancing therapeutic outcomes. Liposomes can also fuse with cell membranes, enabling targeted drug delivery, especially in cancer therapy (Table 1) (Joudeh *et al.*, 2022).

Table 1. Recent advances of liposomal delivery systems in cancer therapy

| Drug | Condition | Lipid platform | References |
|---------------|--|---------------------------|--------------------------------------|
| Doxorubicin | Breast cancer, ovarian cancer and Kaposi's sarcoma | Liposome | (Tejada-Berges <i>et al.</i> , 2002) |
| Patisiran | hereditary transthyretin-mediated amyloidosis | Liposome | (Yang <i>et al.</i> , 2019) |
| Dexamethasone | Multiple myeloma | PEG-coated liposomes | (Metselaar <i>et al.</i> , 2023) |
| Irinotecan | Pancreatic cancer | pH-sensitive liposomes | (Wang-Gillam <i>et al.</i> , 2016) |
| Doxorubicin | Liver tumors | Thermosensitive liposomes | (Lyon <i>et al.</i> , 2018) |
| Paclitaxel | Non-small cell lung cancer | Liposome | (Li <i>et al.</i> , 2024) |

Liposome-biological interactions - systemic circulation

Oral administration of liposomes always results in premature drug release due to digestive enzymes. However, incorporating liposomes with hydrogenated long-chain phospholipids improved liposome stability in gastrointestinal conditions. Intranasal administration is also effective due to high permeability and transdermal administration avoids gastrointestinal instability. Thus, selecting the proper route of administration and optimizing

liposome properties may enhance stability, bioavailability and therapeutic outcomes. Cancer treatment often employs intravenous injection for rapid drug distribution, although the capillary endothelium can limit tissue distribution. For abdominal tumors, direct intraperitoneal injection targets specific sites but faces clearance challenges. Liposomal drug delivery system can also be delivered intramuscularly with certain cancer vaccines (Chen *et al.*, 2024).

Types of liposomes

Liposomes have utilized to meet various clinical needs, with different designs tailored to enhance stability, targeting and drug release. The various types of liposomes with their advantages and limitations are presented in Table 2.

Combination therapy with liposomes

Combination therapy with liposomes enhances the efficacy of treatments like immunotherapy, radiation therapy, photodynamic therapy (PDT) and photothermal therapy (PTT). Liposomes can

co-deliver immune modulators or checkpoint inhibitors alongside chemotherapeutic agents, which increases the immune responses against tumors. They also improve the targeted delivery of photosensitizers for PDT or photothermal agents for PTT that ensures localized therapeutic effects with minimal side effects. Liposomes enhance radiosensitivity when combined with radiation therapy resulted in a synergistic approach for effective cancer treatment. Table 3 illustrates the combination therapy with liposomes and their applications.

Table 2. The various types of liposomes with their advantages and limitations

| Types | Key features | Applications | Advantages | Limitations | References |
|--------------------------------|--|--|---|--|---|
| Conventional Liposomes | Composed of natural phospholipids; encapsulate both hydrophilic and hydrophobic drugs. | Used in early drug delivery systems. | Biocompatible; simple composition. | Rapid clearance by the mononuclear phagocyte system (MPS) short half-life, limiting drug accumulation. | Nsairat <i>et al.</i> , 2022 |
| PEG-Coated Liposomes (Stealth) | PEG layer reduces immune recognition, prolongs circulation time. | Doxil®: Used for Kaposi's sarcoma, breast cancer, multiple myeloma. | Increased circulation time enhanced drug accumulation at target sites via the EPR effect. | PEGylation can induce side effects like palmar-plantar erythrodysesthesia (PPE). | Mohamed <i>et al.</i> , 2019; Labouta <i>et al.</i> , 2018 |
| pH-Sensitive Liposomes | Release drugs under acidic conditions (pH 5.0–6.5), common in tumors. | DepoCyt®: Treats lymphomatous meningitis. Onivyde®: Treats metastatic pancreatic cancer. | Tumor-specific drug release in acidic environments reduces healthy tissue exposure. | Stability issues in neutral pH potential premature release in normal tissue. | Abriaghdam <i>et al.</i> , 2019; Liu <i>et al.</i> , 2014 |
| Thermosensitive Liposomes | Release drugs at elevated temperatures (39–42°C), triggered by hyperthermia. | Used in hyperthermia-induced drug delivery systems. | Localized drug release with minimal systemic exposure. | Requires precise temperature control and reliable hyperthermia treatment may not reach all tumor areas. | Kneidl <i>et al.</i> , 2014 |
| Ultrasound-Sensitive Liposomes | Release drugs when exposed to focused ultrasound, inducing heating or cavitation. | Used in preclinical and clinical trials for non-invasive therapy. | High precision, localized release; minimal systemic effects. | Requires specialized ultrasound equipment; limited tissue penetration. | Schroeder <i>et al.</i> , 2009; Kim <i>et al.</i> , 2022 |
| Enzyme-Responsive Liposomes | Release drugs in response to specific enzymes overexpressed in tumors (e.g., MMP) | Targeted delivery for prostate and pancreatic cancers. | Minimizes off-target effects by exploiting tumor-specific enzymes. | Limited to cancers with overexpressed enzymes may not work in tumor lacking specific enzymes. | Fouladi <i>et al.</i> , 2017; Antoniou <i>et al.</i> , 2021 |
| Ligand-Targeted Liposomes | Functionalized with ligands (antibodies, peptides) to bind specific receptors on cancer cells. | Folate-receptor targeting for ovarian/lung cancers. HER2-targeted liposomes for breast cancer. | Highly specific drug delivery, reducing systemic exposure and side effects. | Complex synthesis potential immune responses to targeting ligands receptor overexpression required for efficacy. | Scrcombe <i>et al.</i> , 2015; Noble <i>et al.</i> , 2014 |

Table 3. Illustrated the combination therapy with liposomes and its applications

| Therapy | Mechanism | Challenges | Role of liposomes | Example | References |
|----------------------------|--|--|--|---|-----------------------------|
| Photodynamic therapy (PDT) | Utilizes a photosensitizer (PS) activated by light to generate ROS, damaging cancer cells. | Lipophilic PS, short plasma half-life, poor tissue permeability, low tumor specificity and tumor hypoxia. | Liposomes deliver PS to tumor sites, improving accumulation and therapeutic efficacy. | Foslip® for advanced head and neck cancer | Ghosh <i>et al.</i> , 2019 |
| Photothermal therapy (PTT) | Uses photothermal agents to increase tissue temperature, causing necrosis in cancer cells. | Lack of selectivity for tumor tissue, potential side effects from non-specific drug accumulation and light scattering. | Liposomes enable controlled drug release upon laser exposure, enhancing tumor targeting and minimizing side effects. | Liposomal DDS for PTT with glycoproteins | Forbes <i>et al.</i> , 2010 |
| Radiotherapy (RT) | Uses high-energy radiation to kill or damage cancer cells. | Inefficiency in tumor targeting and off-target radiation damage. | Liposomes carry radiosensitizing drugs to tumor sites, improving tumor response and reducing side effects. | Paclitaxel liposomes combined with RT in cervical cancer | Chen <i>et al.</i> , 2024 |
| Immunotherapy | Enhances immune system's ability to target and destroy cancer cells by modulating the tumor immune microenvironment. | Short half-life and poor retention of therapeutic agents in the tumor microenvironment (TME). | Liposomes can improve drug delivery to antigen-presenting cells and induce immunogenic cell death (ICD). | Doxil® (DOX-loaded liposomes) combined with immunotherapy | Gu <i>et al.</i> , 2020 |

Inorganic-based nanoparticles

Inorganic-based nanoparticles are composed of materials other than carbon or organic substances, including metals, semiconductors, metal oxides, ceramics and bimetallic alloys. Their diverse composition and unique physicochemical properties make them highly valuable in biomedical applications.

Metallic nanoparticles

Metallic nanoparticles such as gold and silver are widely explored in biomedical research due to their unique properties. Gold Nanoparticles (AuNPs) are known for their electronic and optical properties, chemical stability and ease of functionalization due to negatively charged surfaces.

AuNPs play a vital role in photothermal therapy, biosensors and bioimaging. Surface functionalization allows conjugation with ligands, antibodies or drugs, enabling both active and passive drug delivery systems. These nanoparticles

also show potential in real-time imaging and theranostics (Burlec *et al.*, 2023; Fan *et al.*, 2020). Silver Nanoparticles (AgNPs) are known for excellent antimicrobial properties, thermal and electrical conductivity and catalytic activity.

AgNPs are extensively used in antimicrobial agents, drug delivery systems, biosensors and thermal therapy. Their ability to disrupt microbial cell walls and induce oxidative stress signifies their therapeutic applications (Zhang *et al.*, 2016; Burlec *et al.*, 2023).

Metal oxide nanoparticles

Metal oxide nanoparticles consist of positive metallic ions and negative oxygen ions, enabling tunable properties through oxidation or structural modifications. Iron Oxide Nanoparticles (Fe₃O₄) exhibit superparamagnetic behavior, making them ideal for MRI contrast enhancement, hyperthermia treatment and targeted drug delivery. Their biocompatibility and ease of surface modification further enhance their biomedical utility (Ealia *et al.*,

2017). Titanium Dioxide (TiO₂) nanoparticles have excellent biocompatibility and chemical stability, widely used in drug delivery, bioimaging, photo ablation therapy and tissue engineering. Their optical properties enhance cellular adhesion, wound healing and photodynamic therapy (Jafari *et al.*, 2020). Zinc Oxide (ZnO) nanoparticles exhibit antimicrobial and anticancer properties by generating reactive oxygen species (ROS). They are used in bioimaging and drug delivery, though surface modifications are necessary for stability in biological environments (Jiang *et al.*, 2018). Cerium Oxide (CeO₂) nanoparticles (Nanoceria) are characterized by its redox properties and can switch between cerium (IV) and cerium (III) states. This enables potent antioxidant activity, making it valuable in treating neurodegenerative diseases, inflammation and cancer by modulating oxidative stress (Yadav *et al.*, 2022; Kim *et al.*, 2024).

Bimetallic or alloy nanoparticles

Bimetallic nanoparticles, such as Fe-Co, Fe-Ni and Cu-Ni alloy, exhibit synergistic chemical and magnetic properties, which improve their biomedical applications. Iron-Cobalt (Fe-Co) nanoparticles exhibit high Curie temperature, superparamagnetism and saturation magnetization, making them ideal for targeted drug delivery, MRI contrast enhancement and magnetic hyperthermia. Iron-Nickel (Fe-Ni) and Copper-Nickel (Cu-Ni) nanoparticles are having superparamagnetic nature which facilitates their use in hyperthermia treatments, site-specific drug delivery and advanced imaging techniques (Wahajuddin *et al.*, 2012; Jing *et al.*, 2009).

Semiconductor nanoparticles

Semiconductor nanoparticles are used in photocatalysis, biomedical imaging and optics. Their tunable bandgap enables fluorescence imaging, photoablation therapy and sensor development (Terna *et al.*, 2021; Han *et al.*, 2019a).

Ceramic nanomaterials

Ceramic nanoparticles, including oxides, carbides and phosphates, are synthesized through high-temperature processes and are widely applied in drug

delivery systems for tumors, glaucoma and bacterial infections (Thomas *et al.*, 2015).

Quantum dots (QDs)

Quantum dots are semiconductor nanocrystals, typically 2-10 nm in size. They have several optical properties such as size-dependent fluorescence, high quantum yield and photostability.

QDs resist photobleaching which make them suitable for long-term imaging. The presence of functional surface groups facilitates the conjugation of QDs with antibodies, peptides or small molecules, enabling targeted drug delivery and specific interactions with biomarkers or tumor cells (Matea *et al.*, 2017). In cancer research, QDs are promising for bioimaging, where they provide high-resolution visualization of tumor cells, fluorescence resonance energy transfer (FRET) for real-time molecular interaction studies and tumor tracking to monitor growth and metastasis. Additionally, QDs are utilized in theranostics, combining diagnostic imaging with therapeutic delivery to enhance precision in cancer treatment (Mohamed *et al.*, 2021).

Carbon-based nanoparticles

Carbon-based nanoparticles encompass various forms such as carbon nanotubes (CNTs), graphene, fullerenes, carbon nanofibers and carbon black. These nanoparticles possess exceptional optical, thermal and adsorptive properties, coupled with high strength, electron affinity and electrical conductivity. These traits make them highly versatile for applications such as drug delivery, bioimaging, tissue engineering and biosensing. Their biocompatibility and relatively low toxicity enhance their suitability for biomedical use (Astefanei *et al.*, 2015; Joudeh *et al.*, 2022).

Carbon nanotubes (CNTs)

Carbon nanotubes are formed by rolling graphene into hollow cylinders, which can vary in size, with diameters ranging from 0.7 nm (single-walled) to 100 nm (multi-walled) and lengths extending up to several millimeters (Rahamathulla *et al.*, 2021). CNTs

exhibit excellent cell penetration capabilities, high drug-loading capacity and superior mechanical and electrical properties. They offer enhanced drug bioavailability, prolonged half-life and reduced toxicity.

CNTs can adsorb or covalently bond with target cells, making them ideal carriers for anticancer drugs such as doxorubicin, camptothecin, carboplatin, cisplatin and paclitaxel (Zare *et al.*, 2021).

CNTs also have been used in gene therapy and imaging applications, further broadening their biomedical potential.

Graphene

Graphene, a single layer of carbon atoms arranged in a 2D honeycomb lattice, typically has a thickness of about 1 nm. Graphene has strong mechanical strength, electrical conductivity and surface area. These features make graphene suitable for drug delivery, bioimaging and biosensors. Functionalized graphene derivatives, such as graphene oxide (GO) and reduced graphene oxide (rGO), enhance solubility and biocompatibility, enabling applications in cancer therapy, tissue engineering and antimicrobial treatments (Han *et al.*, 2019b).

Fullerenes

Fullerenes, often termed "buckyballs," are spherical or ellipsoidal structures comprising 28-1500 carbon atoms, with diameters ranging from 8.2 nm (single-layered) to 4-36 nm (multi-layered).

Fullerenes has unique electronic and photophysical properties. They exhibit antioxidant activity due to their ability to quench free radicals and have been explored for drug delivery and photodynamic therapy. Their hydrophobic core also enables encapsulation of hydrophobic drugs, improving their solubility and stability (Kulkarni *et al.*, 2024).

Carbon nanofibers (CNFs)

Carbon nanofibers are elongated, fibrous structures derived from graphene, offering

excellent mechanical strength, high thermal conductivity and electrical properties. CNFs are utilized in tissue engineering, wound healing and biosensors, where their surface functionalization can enhance cell adhesion and growth (Yadav *et al.*, 2020).

Recent innovations in nanotechnology

Targeted drug delivery

Targeted drug delivery involves precise targeting of therapeutic agents directly to diseased cells or tissues. This approach reduces systemic side effects and maximizing therapeutic efficacy. A wide array of nanosystems is utilized for targeted drug delivery which includes lipid-based nanoparticles such as liposomes (Doxil® and Onivyde®), solid lipid nanoparticles (paclitaxel-loaded SLNs and curcumin-loaded SLNs), polymeric nanoparticles like nanocapsules (PLGA and PEGylated nanocapsules), nanospheres (chitosan and alginate nanospheres), metal-based systems such as metallic nanoparticles (gold and silver), metal oxides (iron oxide [Feridex®], titanium dioxide and zinc oxide). The advanced nano designs include antibody-conjugated nanoparticles and stimuli-responsive systems that release drugs in response to environmental triggers like pH or temperature. These nanoscale carriers enhance drug solubility, bioavailability, cellular uptake and controlled release which could help for improving therapeutic outcomes.

Targeted nanoparticles have proven valuable in diagnostic applications and treating cancer, cardiovascular diseases, neurological disorders and infectious diseases, advancing precision medicine and personalized therapies (Yetisgin *et al.*, 2020; Yusuf *et al.*, 2023).

Mechanism of targeted drug delivery

Active targeting

Active targeting is an advanced nanoparticle drug delivery strategy designed to enhance therapeutic effect by minimizing side effects and maximizing drug accumulation at disease sites.

Nanoparticles, such as polymeric nanoparticles, gold nanoparticles and lipid-based nanoparticles, are functionalized or loaded with specific ligands, including phytocompounds, anticancer drugs, CRISPR-Cas9 systems, siRNA, peptides, monoclonal antibodies, aptamers or small molecules.

These ligands selectively bind to overexpressed receptors on diseased cells, such as folate, transferrin, epidermal growth factor (EGFR) or HER2 receptors, commonly associated with cancer and other pathological conditions. Upon receptor-ligand binding, the functionalized nanoparticles are internalized into diseased cells via receptor-mediated endocytosis (Fig. 6) (Attia *et al.*, 2019). This targeted delivery system enables controlled and localized release of therapeutic agents, triggered by intracellular environmental factors such as pH changes, redox potential or enzymatic activity. Active targeting significantly improves drug bioavailability, reduces systemic toxicity and enhances therapeutic efficacy compared to traditional delivery methods (Dilliard *et al.*, 2023). This approach holds great promise for treating challenging diseases, including cancer, diabetes mellitus, cardiovascular and neurological disorders and inflammatory conditions, by providing efficient drug delivery at target sites.

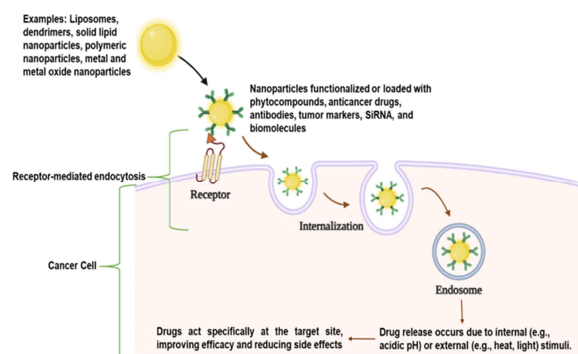


Fig. 6. Active targeting of nanoparticle

Passive targeting

Passive targeting is a nanoparticle drug delivery strategy that enhance drug accumulation in the diseased tissues such as tumors or inflamed areas. Passive targeting does not involve functionalizing nanoparticles with specific ligands. This strategy

exploits the enhanced permeability and retention (EPR) effect a phenomenon in which leaky blood vessels and poor lymphatic drainage in diseased tissues enable nanoparticles to accumulate preferentially in these regions. Nanoparticles designed for passive targeting are optimized in size, shape and surface properties to extend circulation time and avoid rapid clearance by the reticuloendothelial system (RES). Nanoparticles coated with polyethylene glycol (PEG) achieve stealth properties, enabling them to evade immune detection and prolong blood circulation. Passive targeting offers simplicity, reduced need for complex functionalization and effectiveness in diseases with well-defined EPR effects, such as solid tumors. However, it has limitations such as dependence on vascular characteristics and variability across patients and disease types (Subhan *et al.*, 2021).

Passive targeting remains a foundational approach in nanomedicine, particularly for delivering chemotherapeutic and imaging agents to tumors. Fig. 7 illustrated the passive targeting of nanoparticles.

Cancer treatment

The success of anticancer therapies often depends on the ability of therapeutic agents to effectively target cancer cells while minimizing side effects. Nanotechnology offers a powerful platform for delivering of drugs, phytoconstituents and nucleic acids, showing enhanced anticancer efficacy, better targeting and improved bioavailability. Nanoparticles can be tailored to extend circulation time, improve drug localization and efficacy, potentially reducing multidrug resistance and transforming cancer treatment outcomes (Senapati *et al.*, 2018; Yetisgin *et al.*, 2020).

A number of nanomedicine strategies have proven effective in clinical settings. One prominent example is the first FDA-approved nanomedicine for treating breast cancer, Poly (ethylene glycol) (PEG)-ylated liposomal doxorubicin (Doxil®), which was approved by the FDA in 1995.

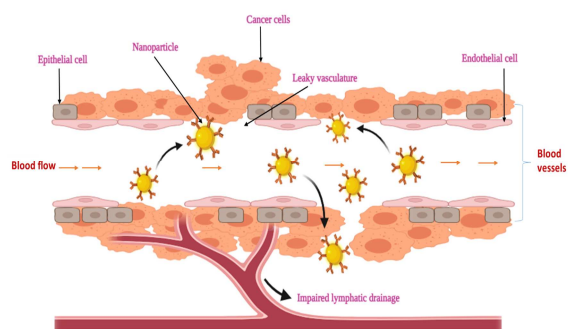


Fig. 7. Passive targeting of nanoparticles

Doxil® increases the drug's effective concentration in malignant effusions without raising the total dosage. Another example is the methoxy poly (ethylene glycol)-poly(lactic acid) mPEG-PLA micelles (Genexol-PM®), which are used in the treatment of metastatic breast cancer.

Eligard®, a leuprolide acetate formulation that uses Atrigel® technology, was authorized by the FDA in 2002 as a palliative treatment for prostate cancer. Leuprolide acetate (Lupron) is a synthetic GnRH analog that inhibits the production of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), resulting in hypogonadism and decreased levels of estradiol and testosterone. Atrigel®, composed of polylactic and polyglycolide polymers, solidifies upon injection and gradually releases the drug over a month. The success of these nanotechnologies in drug delivery can be attributed to improve *in vivo* distribution, circumvention of the reticuloendothelial system and enhancing pharmacokinetic profiles (Lombardo *et al.*, 2019; Farjadian *et al.*, 2019).

Polymeric nanoparticles drug delivery systems have attracted significant attention in oncology among the various types of nanoparticles. These delivery systems are particularly promising for their ability to deliver anticancer agents directly to tumor sites. While some of these nanotechnology-based treatments are still undergoing clinical trials, a few, such as HPMA (N-(2-hydroxypropyl) methacrylamide) copolymer-paclitaxel (PNU166945) and HPMA copolymer-doxorubicin galactosamine (PK2), showed better

effect to an improving therapeutic outcomes (Gavas *et al.*, 2021). Zhong *et al.* (2017) demonstrated that doxorubicin encapsulated in lipoic acid cross linked hyaluronic acid nanoparticles (LACHA-DOX) effectively targeted and inhibited human hematological cancers, including LP-1 human multiple myeloma and AML-2 human acute myeloid leukemia (AML), in xenografted nude mice. This approach highlighted the potential of LACHA-DOX nanoparticles for targeted cancer therapy. The LACHA-DOX formulation provided prolonged and concentrated drug activity at the tumor site while safeguarding nearby healthy tissues, thereby enhancing targeted cancer therapy. Lotfabadi *et al.* (2018) designed a unique formulation of cationic liposomes loaded with miRNA to target bone marrow cancer cells, which produced around 12% higher cytotoxicity than pure miRNA-101 in cancer cells while limiting harm in normal cells. This suggests a valuable strategy for gene therapy.

Yuan *et al.* (2017) showed that gemcitabine encapsulated in silver nanoparticles exhibited greater cytotoxicity and apoptosis in ovarian cancer cells compared to the free form of the drug. These nanoparticles also enhanced responsiveness to gemcitabine by increasing the production of pro-apoptotic genes and activating caspases 3 and 9. Hybrid delivery systems have shown greater potential than single-drug delivery methods. Zhang *et al.* (2016) developed iRGD peptide-decorated lipid-polymer hybrid nanoparticles for co-delivering doxorubicin (DOX) and sorafenib (SOR) to human liver cancer cells (HepG2). iRGD-integrin approach enhances the targeted recognition for drug delivery, resulting in enhanced cytotoxicity and improved antitumor effects in a liver cancer mouse model. Recent studies emphasize the potential of phytoconstituents combined with nanoparticles for anticancer therapy. Gomaa *et al.* (2024) demonstrated that Doxorubicin (DOX) and folic acid (FA)-loaded zinc oxide (ZnO) nanoparticles showed potent antiproliferative effects against Ehrlich ascites carcinoma (EAC) cells. The ZnO NP composites reduced tumor cell proliferation and improved apoptosis, while

decreasing inflammatory markers like IL-6 and TNF- α , thus protecting against liver and kidney damage in mice.

The green synthesis of nanoparticles has gained attention in cancer research due to its eco-friendly approach. Berehu *et al.* (2024) synthesized biogenic ZnO nanoparticles using *Tinosporacordifolia*, which demonstrated anticancer effects on colorectal cancer models. Nguyen *et al.* (2023) synthesized silver nanoparticles (AgNPs) using *Callisiafragrans* leaf extract, which showed activity against cancer cell lines, including MCF-7 and HepG2, suggesting their potential as anticancer agents. Ouyang *et al.* (2024) used *Psidiumguajava* leaf extract to synthesize Mg-doped ZnO nanoparticles, which acted as pH-sensitive carriers for 5-Fluorouracil, showing significant efficacy in gastric cancer treatment.

Bimetallic nanoparticles have also shown promising results in cancer therapy. They possess high tumor-targeting efficiency, rapid elimination and potent cancer cell destruction. Katifelis *et al.* (2019) reported that Ag/Au bimetallic nanoparticles inhibited tumor growth and metastasis in a mouse model by selectively inducing cancer cell apoptosis via the TRAIL-dependent pathway. Elsayed *et al.* (2022) demonstrated that ZnO-Ag bimetallic nanoparticles had significant anticancer effects against HCT-116 and HeLa cell lines, suggesting their potential for clinical applications in cancer therapy. Table 4 illustrates some of the important FDA or EMA-approved nanobased anticancer drugs (Rodríguez *et al.*, 2022; Farjadian *et al.*, 2018; Wicki *et al.*, 2015; NIH, National Cancer Institute, US, Update on 2023).

Table 4. FDA or EMA approved nanobased anticancer drugs

| Approval (year) | Product and company | Nanoparticle material used | Drug | Indication |
|--------------------------|--|---------------------------------|--------------------------------|---|
| EMA (2019) | Pazenir (Ratiopharm GmbH) | Protein-drug conjugates | Paclitaxel | Breast cancer and Lung cancer. |
| FDA (2017) EMA (2018) | Vyxeos (Celator/Jazz Pharma) | Liposome | Cytarabine/ Daunorubicin | Acute myeloid leukemia |
| FDA (2015) | Onivyde (Merrimack Pharma) | Liposome | Irinotecan | Pancreatic cancer and colorectal cancer |
| EMA (2013) | NanoTherm (Magforce) | Metallic nanoparticles | Fe ₂ O ₃ | Glioblastoma, prostate, and pancreatic cancer. |
| FDA (2012) | Marqibo (Talon Therapeutics/ Spectrum Pharmaceuticals) | Liposome | Vincristine | Acute lymphoblastic leukemia |
| FDA (2005) | Abraxane (American Biosciencem, Inc.) | Protein-drug conjugates | Paclitaxel | Breast and pancreatic cancer and lung cancer. |
| FDA (2002) | Eligard (Recordati Industria Chimica e Farmaceutica) | PLGA | Leuporelin acetate | Prostate cancer |
| EMA (1996) | Caelyx (Schering-Plough) | PEGylated liposomal doxorubicin | Doxorubicin | Metastatic breast, ovarian cancer and Kaposi's sarcoma. |
| FDA (1995) | Doxil (Ortho Biotech) | Liposome | Doxorubicin | Kaposi's sarcoma, ovarian cancer and multiple myeloma |

Diabetic treatment

Diabetes mellitus is a common metabolic syndrome that significantly affects patients' quality of life. Traditional drug delivery systems face challenges such as improper dosing, low potency and limited target specificity. It leads to potential side effects in non-target tissues. These challenges also extend to the use of natural products with nutraceutical value in managing diabetes mellitus.

Nanotechnology offers a promising solution through the loading of insulin and other antidiabetic agents into nanoparticles, providing a more convenient, non-invasive and safer approach through alternative routes of administration (Souto *et al.*, 2019).

Nanoparticle-based delivery systems have been developed to protect insulin from enzymatic degradation in the stomach and enhance its

absorption through the gastrointestinal tract (GIT). Ansari *et al.* (2016) formulated insulin-loaded solid lipid nanoparticles (SLNs), which showed that plasma glucose levels in rats were lower after oral administration of SLNs compared to oral insulin solution. The solid matrix of SLNs partially protected insulin from degradation in the GIT and enhanced its intestinal absorption, making SLNs a suitable carrier for oral insulin delivery.

Mohammad Jamshidi *et al.* (2018) demonstrated that insulin-loaded trimethyl chitosan nanoparticles reduced hyperglycemia, oxidative stress and inflammation in diabetic rats, suggesting enhanced bioavailability of insulin in its nanoparticle form. Rathore *et al.* (2020) investigated chitosan-engineered nanoparticles for ocular insulin delivery, focusing on the possibility of positively charged chitosan nanoparticles for protein injection via the eye.

Mineral-based nanoparticles, like zinc oxide nanoparticles (ZnO NPs), have also shown potential in diabetes treatment. Zn plays a role in insulin secretion and receptor activity, enhancing insulin signaling and glucose regulation (Debele *et al.*, 2022). ZnO NPs have demonstrated the ability to improve glucose tolerance, insulin levels and pancreatic function in diabetic models (Rehana *et al.*, 2017). El-Gharbawy *et al.* (2016) synthesized ZnO NPs using the sol-gel method and found that they, alone or with vildagliptin, significantly decreased the expression of microRNAs associated with type 2 DM, showing promising antidiabetic effects. Research on metal nanoparticles like gold (AuNPs) and silver nanoparticles (AgNPs) has also highlighted their antidiabetic activity. Barathmanikant *et al.* (2010) synthesized AuNPs to control hyperglycemia in streptozotocin-induced diabetic mice, showing inhibition of lipid peroxidation and reactive oxygen species (ROS) generation. Alkaladi *et al.* (2014) reported that AgNPs reduced blood glucose levels and increased insulin secretion in diabetic rats.

Nanoparticles functionalized with plant extracts also shown potent antidiabetic effects. For example, gold nanoparticles synthesized using *Hemidesmus indicus* root extract (Hire-Au NPs) demonstrated *in vitro* inhibition of α -amylase and α -glucosidase, as well as antioxidant properties. Hire-Au NPs have the potential to treat type 2 diabetes, as evidenced by *in vivo* experiments showing that they dramatically decreased blood sugar levels in streptozotocin-induced diabetic albino Wistar rats (Devaraj *et al.*, 2024).

Despite the potential of plant-derived molecules like curcumin, resveratrol and quercetin in alleviating diabetes, their clinical applications are limited due to low systemic availability, rapid metabolism and poor bioavailability (Dewanjee *et al.*, 2020; Alam *et al.*, 2022). Nanotechnology-based formulations can address these limitations by enhancing drug solubility, stability and absorption. Ahangarpour *et al.* (2018) demonstrated that solid lipid nanoparticles containing myricitrin improved various diabetic parameters in STZ-NA-induced type 2 diabetic rats, such as body weight, hyperglycemia and β -cell function. Panwar *et al.* (2018) reported that ferulic acid-chitosan nanoparticles showed improved therapeutic efficacy in reducing blood glucose levels and enhancing insulin levels compared to native ferulic acid.

Cardiovascular disease management

Cardiovascular diseases (CVDs) remain the leading global cause of death occurs due to sedentary lifestyles. The conditions such as stroke, hypertension and restricted blood circulation often result in long-term disability or death. The emergence of nanotechnologies has introduced transformative tools in CVD management, offering innovative therapeutic and diagnostic strategies. These advancements facilitate early diagnosis, enable targeted drug delivery and support minimally invasive interventions (WHO updates Cardiovascular Risk Charts, 2019; Smith *et al.*, 2023).

Inflammation plays a pivotal role in adverse ventricular remodeling after myocardial infarction (MI), which can impair the amount of blood pumped out of the heart with each beat and lead to heart failure (Chandarana *et al.*, 2018). Phytoconstituents, known for their anti-inflammatory, antioxidant and cardioprotective properties, have emerged as promising candidates for post-MI treatment. However, challenges related to their limited solubility and short half-lives in circulation hinder their clinical efficacy (Ullah *et al.*, 2024). Nanotechnology-based delivery systems, such as nanoparticles and lipid carriers, offer solutions to enhance the stability, solubility, bioavailability and therapeutic efficacy of these compounds, thereby reducing post-MI inflammation and promoting cardiac recovery.

Berberine, a cardioprotective isoquinoline alkaloid, has shown improved therapeutic outcomes when encapsulated in liposomes. Allijn *et al.* (2017) demonstrated that liposomal berberine showed potent efficacy then the free form in a mouse MI model, preserving cardiac function more effectively at 28 days post-MI. Liu *et al.* (2021) showed that Mesoporous Silica Nanoparticles (MSNs) loaded with quercetin (Q-MSNs) significantly enhanced its cardioprotective effects by activating the JAK2/STAT3 pathway in rats with myocardial ischemia-reperfusion injury (MIRI). This study revealed a reduction in infarction size and improved cardiac function compared to quercetin alone. Hwang *et al.* (2016) highlighted the efficacy of PEGylated liposomes loaded with angiogenic peptides in treating myocardial ischemia, showing that liposomes with a 100 nm diameter were more effective in myocardial uptake, improving cardiac perfusion and vascular density compared to larger size formulations (600nm).

Atherosclerosis, a significant contributor to CVDs, is characterized by plaque buildup in arteries.

Targeted nanoparticle therapies have emerged as a promising strategy for treating this condition.

Luo *et al.* (2024) developed ROS-sensitive nanoparticles using a low molecular weight heparin-lipoic acid (LMWH-LA) conjugate, which effectively reduced plaque inflammation and oxidative stress, providing a potential therapeutic avenue for atherosclerosis. Li *et al.* (2020) developed pH-responsive nanoparticles derived from cyclodextrin for the targeted delivery of an antisense oligonucleotide against microRNA-33 (anti-miR33) for atherosclerosis therapy. The nanoparticles, decorated with the cRGDfK peptide ligand for integrin targeting, enhanced the delivery of anti-miR33 to plaques and target cells. In apolipoprotein E-deficient mice, the treatment significantly attenuated atherosclerosis and reduced vulnerable plaques, promoting reverse cholesterol transport and regulating adaptive immunity, demonstrating the potential of targeted nanoparticle therapies for atherosclerosis treatment.

Thrombosis, a critical cardiovascular event that leads to myocardial infarction or stroke, presents challenges for traditional thrombolytic drugs due to their short half-lives and systemic side effects. Zhang *et al.* (2018) demonstrated that cRGD (cyclic Arg-Gly-Asp) functionalized liposomes encapsulating urokinase provided a targeted approach for dissolving blood clots.

These liposomes adhered to activated platelets and enabled controlled release of urokinase, reducing the required dosage by 75% while maintaining efficacy. Zamanlu *et al.* (2019) developed tPA (tissue plasminogen activator) loaded PEGylated PLGA nanoparticles for ischemic stroke, which enhanced thrombolytic activity and prolonged circulation time, offering a more effective and biocompatible alternative to traditional tPA therapy.

Pulmonary Arterial Hypertension (PAH) is a fatal condition caused by restricted blood flow in the pulmonary arteries, often leading to right heart failure. Conventional treatments targeting specific pathways such as prostacyclin and nitric oxide are associated with side effects that can hinder patient

adherence (Tettey *et al.*, 2021). Nanoparticle-based drug delivery systems offer a promising solution to improve drug delivery and reduce adverse effects. Akagi *et al.* (2016) demonstrated that prostacyclin Analogue, beraprost (BPS) nanoparticles administered intratracheally significantly lowered right ventricular pressure and improved survival rates in Pulmonary Arterial Hypertension rat models, without adverse effects. These advancements highlight the potential of nanotechnology-based therapies in managing complex cardiovascular conditions and improving patient outcomes.

Neurological disorders - Alzheimer's disease

Neurological diseases (NDs) have emerged as a major global health problem, with the World Health Organization (WHO) identifying them as a leading cause of death (Feigin *et al.*, 2020).

These diseases include frontotemporal dementia, Alzheimer's disease, Parkinson's disease, prion diseases, Huntington's disease, amyotrophic lateral sclerosis (ALS), brain tumors, spinal cord injuries and stroke. A significant challenge in treating these conditions is the inability of most medications to effectively cross the blood-brain barrier (BBB), which limits their pharmacological impact on the brain. There is an urgent need to develop strategies that enhance drug effectiveness while overcoming BBB restrictions. The use of nanomaterials offers a potential solution. In addition to providing stability, targeted administration and high drug-loading capacity, nano-based drugs can reduce toxicity and enhance therapeutic outcomes.

Various nanomaterials, including dendrimers, polymeric nanoparticles, carbon nanotubes, liposomes, quantum dots, metallic nanoparticles and micelles, have been explored for the treatment of neurological diseases. These nanoparticles are particularly useful for imaging and therapy due to their unique properties, including sensitivity, selectivity and their ability to cross the BBB (Waris *et al.*, 2022).

Alzheimer's disease (AD), a prevalent chronic neurodegenerative condition, is characterized by memory loss, synaptic dysfunction and behavioral changes. The key pathological features of AD include the accumulation of amyloid-beta ($A\beta$) plaques, hyperphosphorylation of tau protein, oxidative stress and immune inflammation. These factors contribute to neuronal damage and cognitive decline, making AD a challenging disorder to treat. The complex and not yet fully understood pathogenesis of AD makes early diagnosis and timely treatment, a significant challenge. However, nanoparticles (NPs) exhibiting unique physical, electrical, magnetic and optical properties, holds considerable promise for both the detection and treatment of AD (Song *et al.*, 2023). Targeting tau protein aggregation is a promising therapeutic approach for Alzheimer's disease.

Many inhibitors however have failed in clinical trials due to limited insights into their mechanisms and pharmacokinetics. Tannic acid is a polyphenol with a multibranched hairpin-like structure and has shown potential as an inhibitor of tau aggregation (Nagaraju *et al.*, 2022).

Hu *et al.* (2020) encapsulated tannic acid in a non-neurotoxic liposome composed of lecithin/ β -sitosterol and coated with Tween 80. The in vitro studies using transwell devices demonstrated that this formulation effectively crossed a BBB model which is made of mouse brain microvascular endothelial cells. It significantly reduced tau aggregation induced by tau peptide R3 fibrils in the human neuroblastoma cell line SK-N-SH. These findings suggest that tannic acid loaded liposomes could provide a valuable strategy for treating Alzheimer's disease, offering an innovative solution to the limitations of previous tau aggregation inhibitors.

Exosomes are extracellular nanovesicles that carry proteins, lipids and nucleic acids in body fluids and function as intercellular messengers, facilitating communication between cells.

Exosomes have great potential as bionanoparticles for drug delivery due to their unique characteristics. Their small size, ability to cross the blood-brain barrier (BBB) and low immunogenicity make them especially promising for brain-targeted therapeutics. However, the exact mechanism by which exosomes cross the BBB remains unclear (Di Bella *et al.*, 2022). A study by Wang *et al.* (2019) demonstrated that exosomes loaded with curcumin (Exo-cur) enhanced the solubility, bioavailability and BBB penetration of curcumin. This was achieved through active targeting, with interactions between lymphocyte function-associated antigen 1 (LFA-1) and endothelial intercellular adhesion molecule 1 (ICAM-1). In both *in vitro* and *in vivo* models of Alzheimer's disease (AD), Exo-cur effectively prevented neuronal death by inhibiting tau protein phosphorylation through activation of the AKT/GSK-3 β pathway. These results highlight the potential of Exo-cur as an efficient drug delivery system, improving neuronal function and alleviating AD symptoms. This approach offers a promising strategy for targeted therapies in neurodegenerative diseases.

Abozaid *et al.* (2022) found that resveratrol-selenium nanoparticles (RSV-SeNPs) significantly enhanced the therapeutic effects of resveratrol in an Alzheimer's disease (AD) rat model induced by aluminum chloride (AlCl₃). Selenium (Se) is an essential micronutrient for brain function.

RSV-SeNPs improved oxidative stress markers, mitochondrial function and cholinergic deficits and promoted amyloid β (A β) clearance. Additionally, it inhibited tau hyperphosphorylation by activating the PI3K/AKT pathway and deactivating GSK-3 β . RSV-SeNPs also reduced neuroinflammation by downregulating STAT3 and IL-1 β expression, while increasing SIRT1 levels and reducing microRNA-134, which enhanced neurite outgrowth. These findings suggest that RSV-SeNPs offer a potent antioxidant and anti-inflammatory treatment for improving neurocognitive function and modulating key signaling pathways in AD therapy.

Dos *et al.* (2020) found that in an Alzheimer's disease (AD) model induced by intracerebroventricular injection of okadaic acid (OA) in rats, long-term treatment with gold nanoparticles (AuNPs) at a dose of 2.5 mg/kg every 48 hours for 21 days effectively mitigated neuroinflammation, oxidative stress and cognitive impairment. In the cortex and hippocampus, AuNP therapy restored neurotrophic factors (BDNF and NGF- β) while preventing tau phosphorylation and spatial memory impairments. Additionally, AuNPs normalized mitochondrial function and reducing oxidative stress markers and improving antioxidant enzyme activities. AuNPs also modulated pro-inflammatory cytokines, indicating their anti-inflammatory effects. These findings suggest that AuNPs could serve as a promising therapeutic approach for preventing neurodegeneration and improving brain function in Alzheimer's disease when administered at the specified dose and duration.

Rivastigmine is a commonly used drug for treating Alzheimer's disease. However, its short half-life, low bioavailability and limited brain penetration after oral administration pose significant challenges. Nanoparticles-mediated drug delivery systems have gained increasing attention as a potential solution to enhance the drug's effectiveness (Birks *et al.*, 2015). ElMosbah *et al.* (2024) found that rivastigmine-loaded chitosan nanoparticles (RS-CSNPs) effectively mitigated Alzheimer-like disease symptoms in an aluminum chloride (AlCl₃)-induced rat model. RS-CSNP treatment improved neuronal viability, reduced tau protein expression, downregulated pro-apoptotic caspase-3 and pro-inflammatory NF- κ B genes and upregulated the antioxidant Nrf-2 gene. These findings suggest that RS-CSNPs alleviate Alzheimer's disease progression by blocking the inflammatory cascade and reducing oxidative stress.

Sanchez-López *et al.* (2018) studied Memantine-loaded PEG-coated PLGA nanoparticles (MEM-PEG-PLGA NPs) as a promising solution for enhancing Alzheimer's disease treatment.

These nanoparticles, with optimized production parameters, demonstrated small particle size, a negative surface charge and a controlled drug release profile, allowing for less frequent dosing.

The MEM-PEG-PLGA NPs were non-cytotoxic to brain cell lines and could penetrate the blood-brain barrier (BBB) both in vitro and in vivo. Compared to free memantine, these nanoparticles enhanced memory function and more successfully decreased inflammation and β -amyloid plaques in a transgenic mice model of Alzheimer's disease. These results suggest that MEM-PEG-PLGA NPs may be a more effective treatment option for Alzheimer's disease than traditional memantine therapy.

Zhao *et al.* (2019) demonstrated that a nanocomposite with a particle size of 14 ± 4 nm, composed of $A\beta$ -binding peptides (KLVFF, a segment of $A\beta_{16-20}$: Lys-Leu-Val-Phe-Phe), effectively removed toxic β -amyloid ($A\beta$) aggregates and mitigated $A\beta$ -induced neurotoxicity in a mouse model of Alzheimer's disease (AD). KLVFF functions as an effective ligand by selectively binding to full-length $A\beta$, preventing its aggregation into harmful oligomers and fibrils, which are key contributors to Alzheimer's pathogenesis. The nanocomposite significantly altered the morphology of $A\beta$ aggregates, promoting the formation of non-toxic $A\beta$ /nanocomposite co-assembled nanoclusters instead of harmful oligomers. This reduction in pathogenic $A\beta$ oligomers prevented apoptosis in hippocampal neurons, restored microglial phagocytic activity toward $A\beta$ and reduced neuronal damage. These findings suggest that small-sized nanocomposite technology holds great promise as a novel therapeutic strategy for addressing both $A\beta$ neurotoxicity and aggregation in AD.

Shan *et al.* (2024) proposed KLVFF@LIP-CeO₂ as a novel intranasal liposomal co-delivery system for the synergistic treatment of Alzheimer's disease. This approach combines ROS-responsive ceria (CeO₂) nanoparticles with the $A\beta$ -targeted KLVFF peptide. The ceria nanoparticle component enhances $A\beta$ removal through ROS-mediated interactions while

facilitating the targeted delivery of KLVFF peptides to the brain, improving its overall therapeutic effect. The use of liposomes as the delivery vehicle further enhances the ability of KLVFF and CeO₂ to cross the blood-brain barrier (BBB), offering a promising strategy for Alzheimer's disease treatment.

Tissue engineering

Tissue engineering seeks to regenerate, replace, or repair damaged tissues or organs by combining biomaterials, cells and growth factors. These components work together to form organized structures and controlled environments for cell culture and differentiation, ultimately facilitating the synthesis of new tissues (Lombello *et al.*, 2023). Scaffolds play a crucial role in this process by providing the necessary physical, chemical and mechanical support for cell growth. The key characteristics of scaffolds include a three-dimensional structure, interconnectivity and porosity, surfaces conducive to cell adhesion, controlled degradability and biocompatibility. Scaffolds can be made from various biomaterials, including natural, synthetic, hybrid and composite materials and can be designed using different technologies or chemically modified to improve their suitability for specific applications, such as bone regeneration, cartilage repair, skin healing and muscle restoration. This customization enhances the efficacy and functionality of implants (Pina *et al.*, 2019).

Naseri-Nosar *et al.* (2017) developed a 3D fibrillated scaffold using coaxial wet-electrospinning, where polylactic acid (PLA) was used as the core material and cellulose acetate as the shell material. The scaffold was coated with citalopram-loaded gelatin nanocarriers produced through nanoprecipitation. The resulting biodegradable and biocompatible scaffold supported Schwann cells, essential for repairing and regenerating injured peripheral nerves. An *in vivo* studies using a sciatic nerve lesion model showed that the citalopram-loaded scaffold significantly enhanced nerve regeneration at the damage site, indicating its potential in neural tissue engineering.

Metal nanoparticles, known for their unique antibacterial properties and versatility, have gained popularity in dental tissue engineering. Metals such as silver, gold, titanium dioxide and zinc oxide exhibit enhanced antibacterial effects when their properties are functionalized.

Additionally, the shape and size of nanoparticles influence their bactericidal action, with nanoparticles smaller than 10 nm and triangular-shaped nanoparticles showing increased antibacterial activity. Holden *et al.* (2016) synthesized Ag/Au alloy bimetallic nanoparticles using an electric current displacement technique to assess their antibacterial properties in periodontal disease. An *In vivo* experiment demonstrated that these biocompatible nanoparticles significantly reduced the lifespan of P83 plankton and exhibited potent antibacterial activity against *Porphyromonas gingivalis* W83, a major pathogen in periodontal disease.

Liu *et al.* (2013) developed a chitosan/hydroxyapatite (nHAp/CTS) biomimetic nanocomposite nanofiber scaffold to evaluate the effect of bone marrow mesenchymal stem cell (BMSC) production on nHAp/CTS for bone regeneration. Both *in vitro* and *in vivo* studies showed that the nHAp/CTS scaffold stimulated BMSC proliferation and activated the BMSC integrin-BMP/Smad signaling pathway. The combination of chitosan and hydroxyapatite enhanced osteogenic differentiation in osteoblasts, suggesting its potential for supporting bone regeneration. Xi *et al.* (2018) developed a hybrid polycaprolactone (PCL) – poly(citrate)- ϵ -poly lysine (PCE) nanofibrous matrix, combining PCE and PCL, to address multidrug-resistant (MDR) bacterial infections in wound healing. The PCL–PCE system effectively prevented MDR bacterial infections and significantly enhanced wound healing and skin regeneration in a mouse model. This hybrid nanofibrous matrix demonstrated promise as a multifunctional wound dressing, providing an effective solution for treating infected wounds and promoting skin regeneration, particularly in the context of MDR bacterial infections.

Gene therapy

Nanotechnology has transformed gene therapy by enabling precise and efficient delivery of genetic material to target cells. Nanocarriers such as liposomes, dendrimers, polymeric nanoparticles and viral-like nanoparticles are engineered to encapsulate DNA, RNA, mRNA, siRNA, or CRISPR-Cas9 components, protecting them from enzymatic degradation and immune clearance. These carriers can be functionalized with targeting ligands, such as peptides or antibodies, to enhance specificity and minimize off-target effects. Nanoparticles also improve cellular uptake, facilitate endosomal escape and enable controlled release of targeted genes, ensuring effective transfection with reduced cytotoxicity (Kaur *et al.*, 2024; Pan *et al.*, 2021).

The key areas of ongoing research in gene therapy include the development of nanoparticles for the treatments of genetic disorders like cystic fibrosis, silencing of oncogenes in cancer and delivering antiviral genes for infections like HIV and hepatitis (Riley *et al.*, 2017; Jiang *et al.*, 2023; Molle *et al.*, 2022). Fig. 8 represents the applications of nanoparticles in gene therapy.

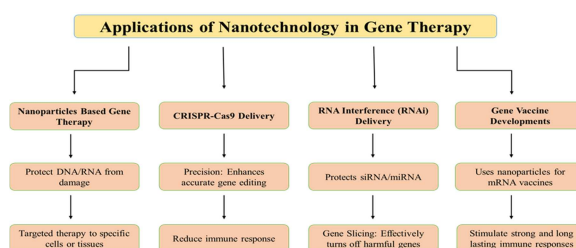


Fig. 8. Illustrates the some key applications of nanotechnology in gene therapy

Clinically developed liposome-based mRNA vaccines such as Pfizer-BioNTech's BNT162b2 (Comirnaty) and Moderna's mRNA-1273 (Spikevax) have revolutionized vaccine technology.

These vaccines utilize lipid nanoparticles (LNPs) to encapsulate and deliver mRNA encoding the SARS-CoV-2 spike protein that ensures protection from degradation and efficient cellular uptake. LNPs

enable targeted delivery enhances mRNA stability and promote strong immune responses. Both vaccines have shown significant effect in preventing COVID-19 and have served as a model for using nanotechnology in mRNA-based therapeutics (Wilson *et al.*, 2022).

Their success highlights the potential for lipid nanoparticles in advancing future vaccines and gene therapies. New hybrid and exosome-based systems are making gene therapy more effective by offering both safety and accuracy. This integration of nanotechnology has paved the way for safer, more effective and personalized therapeutic approaches.

Conclusion

Nanotechnology involves the manipulation of materials to create 1-100nm size and applied to various fields especially in the field of medicine to improve the diagnosis and treatment of several disorders. Nanosystems, engineered with specific physicochemical properties such as precise size, shape, surface charge and enhanced biological interactions have shown remarkable potential to improve therapeutic outcomes. These systems are distinguished by high cellular uptake, controlled pharmacokinetics and minimal toxicity, making them highly effective for treatment of cancer, diabetes, cardiovascular disorders and neurodegenerative conditions.

Engineered nanoparticles facilitate targeted drug delivery that facilitates drugs to reach diseased cells with greater precision and boosting treatment efficacy as well as reducing adverse effects.

This targeted approach not only enhances therapeutic results but also improves patient compliance and overall quality of life. This review highlights the recent innovations in nanoparticle-based therapies for cancer, cardiovascular diseases, and central nervous system disorders diabetes.

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