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THE MAIN DIRECTIONS OF NANOTECHNOLOGY APPLICATIONS IN MEDICINE

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Abstract. Nanotechnology has transformed medicine through advances in tissue engineering, diagnostics and therapy. In bone and cartilage repair, biomolecule-coated implants and hydrogels release growth factors to promote regeneration. Cardiovascular care benefits from nanomaterials mimicking vessel structures, reducing inflammation and clotting, while techniques like electrospinning improve stents and vascular grafts. In oncology, nanocarriers such as liposomes, dendrimers and micelles enable targeted drug delivery, minimizing side effects. Nanotechnology also shows promise in neurodegenerative diseases like Alzheimer's and Parkinson's by enhancing diagnostics and delivering therapies against amyloid-β plaques, tau tangles and α-synuclein aggregates. Overall, nanotechnology improves precision and efficacy across diverse medical applications, from tissue repair to treatment of complex disorders. Although current research highlights the great potential of nanotechnology, significant gaps still remain in areas such as safety, biocompatibility, long-term effects and integration into clinical practice. Systematic resolution of these challenges will not only define the future directions of nanomedicine but also accelerate its translation into real clinical applications.

Keywords: *Nanomaterials, tissue regeneration, cancer therapy, alzheimer's and parkinson's treatment.*

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1. Introduction

Nanotechnology-based biomaterials represent a rapidly growing discipline that bridges materials science and biology, significantly influencing modern medicine. Known as "nanotechnology-derived biomaterials", these substances consist of structures or components at the nanoscale (1-100 nm or 10^{-9} to 10^{-7} meters in diameter), which possess unique and enhanced characteristics due to their minute size. These properties have led to widespread use in various biomedical and biological applications, such as medical imaging, targeted drug delivery and the creation of artificial implants (Khalilov, 2023). Nanotechnology now plays a pivotal role in cancer research, with nanoscale molecular diagnostic tools - like biomarker development - enabling fast and accurate cancer detection. Additionally, nanoscale drug delivery platforms offer targeted delivery to tumor tissues, significantly reducing side effects. Thanks to their ability to target tumors both actively and passively, nanomaterials have become essential in cancer therapy. Present cancer treatments and diagnostic methods prioritize early identification, inhibition of cancer cell growth and the prevention of metastasis (Jin *et al*., 2020). The scope of nanotechnology in biomedical fields continues to grow, showing strong potential for future advancements, particularly in the treatment of neurodegenerative disorders (Li

et al., 2021). Although many nanomaterials currently demonstrate promising results in animal models and cell lines, significant challenges remain in translating these findings into human clinical trials. The doses, metabolic rates and immune responses observed in preclinical studies often do not accurately reflect human physiology. As a result, many nanodrugs validated in animals fail to show the same efficacy in humans or present additional toxic effects. Therefore, more reliable models that closely mimic human physiology are needed to enable successful clinical trials.

2. Applications of Nanomaterials and Smart Hydrogels

The natural interaction between bone cells and surfaces with high nanoscale roughness is well-established. Enhancing implant surfaces by coating them with biomolecules - using methods such as antigen-antibody binding, DNA hybridization or ligand-receptor interactions - greatly improves their biocompatibility and performance. Spiral rosette nanotubes, which are bio-inspired organic structures capable of self-assembling at the nanoscale, are believed to engage with bone cells in a manner similar to titanium surfaces coated with HRN. These physical modifications can serve as internal triggers to release drugs from smart hydrogels. In addition to internal stimuli, external triggers can be employed to engineer responsive hydrogels specifically for bone and cartilage tissue regeneration. These intelligent hydrogels enable the localized delivery of growth factors or therapeutic cells, enhancing the repair of damaged tissues while also offering necessary biological and mechanical support. Nanoclays have emerged as a valuable group of inorganic nanomaterials in the field of bone and cartilage engineering. Commonly researched types include laponite, montmorillonite and halloysite. When exposed to biological fluids, nanoclays release bioactive ions through the exfoliation of their layered silicate structures, aiding in bone regeneration. Remarkably, laponite nanoplatelets have been shown to stimulate osteogenic differentiation in stem cells even without added growth factors, underscoring their potential as intrinsic bioactive agents (Khalilov, 2023; Nasibova *et al*., 2015).

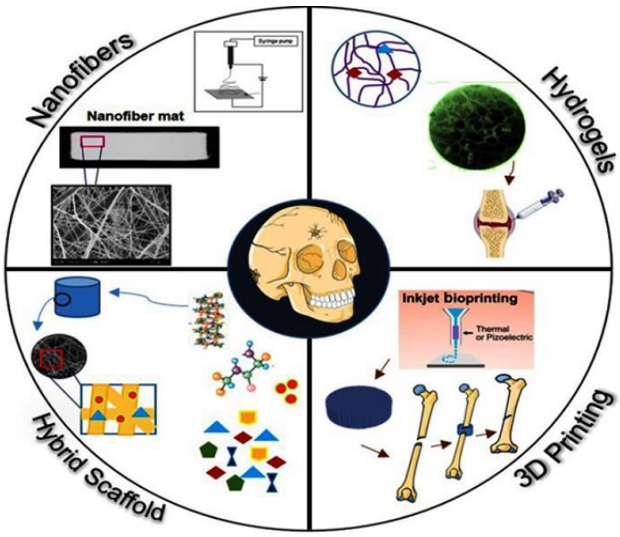

Figure 1. Technologies used in scaffold fabrication
Source: Qasim et al. (2019)

2.1. Nanomaterials in Vascular Tissue Engineering

The extracellular matrix (ECM), primarily made up of nanoscale collagen and elastin fibers, exhibits a hierarchical nanostructure characteristic of natural vascular tissues. Significant progress has been made in utilizing nanomaterials to mimic these intricate structures for vascular tissue engineering. Specifically, nanomaterials have been engineered to promote the function of vascular cells - such as endothelial and smooth muscle cells - while also reducing the risks of thrombosis and inflammation on stent surfaces (Khalilov, 2023).

A variety of nanostructured grafts and 3D nano-scaffolds have been created for cardiovascular applications using techniques like electrospinning and self-assembly. Nano-textured surfaces have shown particular promise in the development of vascular stents. For example, Punshon et al. (2008) introduced an innovative nanocomposite vascular graft by incorporating polyhedral oligomeric silsesquioxane into urethane chains. Laboratory studies revealed that endothelial cell layers formed on these nanocomposites within 14 days and remained viable and intact for up to 35 days (Khalilov, 2023; Kannan *et al*., 2006; Punshon *et al*., 2008).

In vivo studies have also yielded encouraging outcomes. Biodegradable nanofibers loaded with tacrolimus, when implanted in rats, promoted endothelialization and decreased intimal thickening, suggesting that nanostructures may play a key role in preventing venous anastomosis complications (Khalilov, 2023).

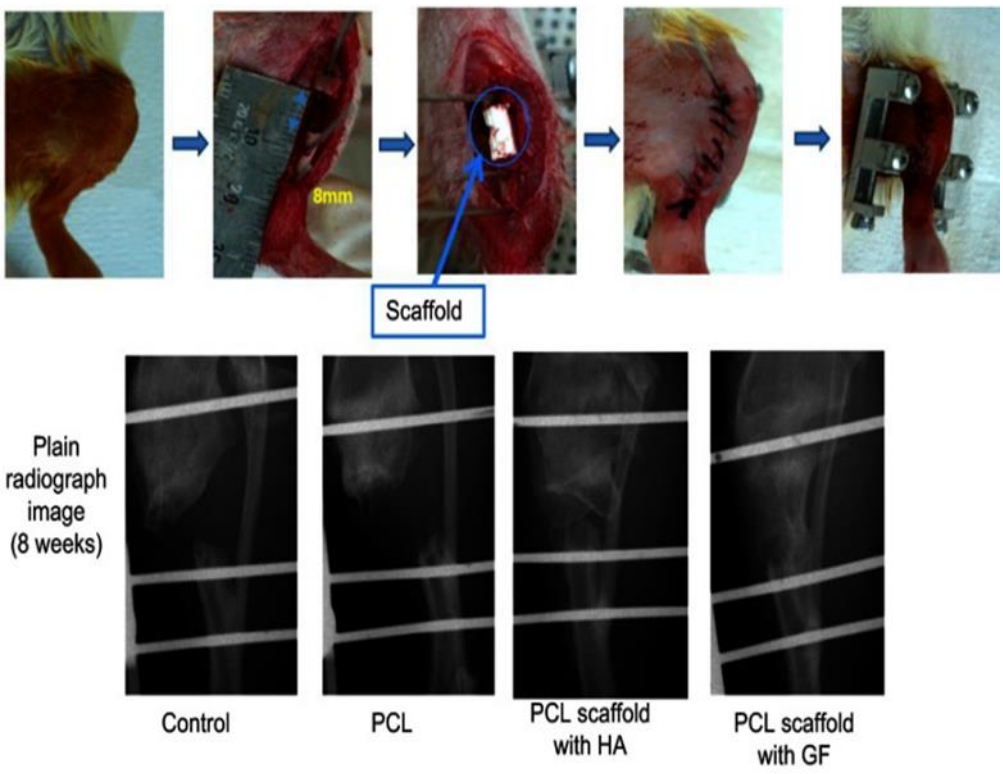

Figure 2. Eight-week X-ray analysis of PCL scaffold implanted in a rat model
Source: Qasim et al. (2019)

3. Nanoparticles in Cancer Imaging

In recent decades, nanoparticles have gained significant attention for their applications in cancer diagnosis and monitoring, with various types now commonly used in molecular imaging. Nanoparticles such as semiconductors, quantum dots and iron oxide nanocrystals possess unique optical, magnetic and structural properties that distinguish them from traditional molecules. Specifically in lung cancer, the detection of metastases has been enhanced through the use of immune superparamagnetic iron oxide nanoparticles (SPIONs), which are utilized in MRI to selectively target cancer cell lines. Studies have demonstrated that SPIONs exhibit high specificity and cause minimal side effects, making them promising agents for aerosol-based imaging of lung cancer. Additionally, magnetic particle imaging has shown effectiveness by delivering high-resolution and sensitive tomographic images of cancerous tissues. In animal models, magnetic nanoparticles (MNPs) targeting the Epidermal Growth Factor Receptor (EGFR) - a protein often overexpressed in non-small cell lung cancer (NSCLC) - have been successfully employed. Moreover, in vitro research has introduced novel nanosystems for positron emission tomography (PET) imaging. These involve self-assembling amphiphilic dendritic molecules that form uniform supramolecular nanoparticles enriched with PET signal units on their surfaces. Utilizing the multivalent nature of dendritic structures and the enhanced permeability and retention (EPR) effect, these nanosystems efficiently accumulate in tumors, enabling highly sensitive imaging with minimal toxicity across different cancer types (Jin *et al*., 2020; Khalilov *et al*., 2024; Nasibova *et al*., 2021).

3.1. Advanced Imaging with Quantum Dots and Gold Nanoparticles

The shallow tissue penetration capability of visible spectrum imaging limits its effectiveness in medical diagnostics. To overcome this challenge, quantum dots that fluoresce in the near-infrared (NIR) range (700-1000 nm) have been developed, proving particularly useful for imaging cancers such as colorectal, liver, pancreatic cancer and lymphoma (Jin *et al*., 2020). Furthermore, the introduction of a second near-infrared window (NIR-II, 900-1700 nm) has enhanced cancer imaging by offering deeper tissue penetration and improved spatial and temporal resolution. Innovations such as sulfur-containing, silver-rich Ag_2Te quantum dots (QDs) have also enabled the production of high-resolution images across an even broader infrared spectrum (Zhang *et al*., 2020).

Gold nanoparticles (AuNPs) have demonstrated effectiveness in both passive and active tumor targeting. In passive targeting, AuNPs leverage the enhanced permeability and retention (EPR) effect to accumulate in tumor tissues, thereby improving imaging clarity (Khalilov & Nasibova, 2022). Active targeting involves modifying AuNPs with tumor-specific agents, such as monoclonal antibodies against EGFR, to directly bind to cancer cells. In a study by Rand et al. (2011) combining AuNPs with liver cancer cells led to significantly enhanced X-ray images, with cancer clusters in the AuNP-treated group appearing far more distinct than in untreated samples. This method holds considerable promise for early cancer detection, potentially enabling the identification of tumors just a few millimeters in size (Jin *et al*., 2020; Rand *et al*., 2011; Nasibova, 2022).

Gold nanoparticles have been tested for cancer treatment in mouse models. This is clearly illustrated in Figure 3 below. In Figure 3a, on the left is a schematic showing an enzymatically activated radiographic contrast agent, in which activity-based probes are attached to gold nanoparticles (NPs). On the right, micro-CT images reveal the distribution and uptake of both targeted and untargeted probes using 10-nanometer NPs.

In Figure 3b, the left side presents a schematic of glucose-modified gold nanoparticles, where the glucose group is bonded at the C2 position. On the right, images illustrate the distinction between cancerous and inflamed tissue:

1. A photograph of a mouse injected with turpentine oil, with green arrowheads highlighting the site of inflammation caused by the subcutaneous injection and red arrowheads marking the location of A431 tumors.

2. Surface-rendered PET/CT scans using fluorine-18 fluorodeoxyglucose show the same mouse after administration of glucose-functionalized gold nanoparticles. “ID” refers to the injected dose (Liu & Grodzinski, 2021).

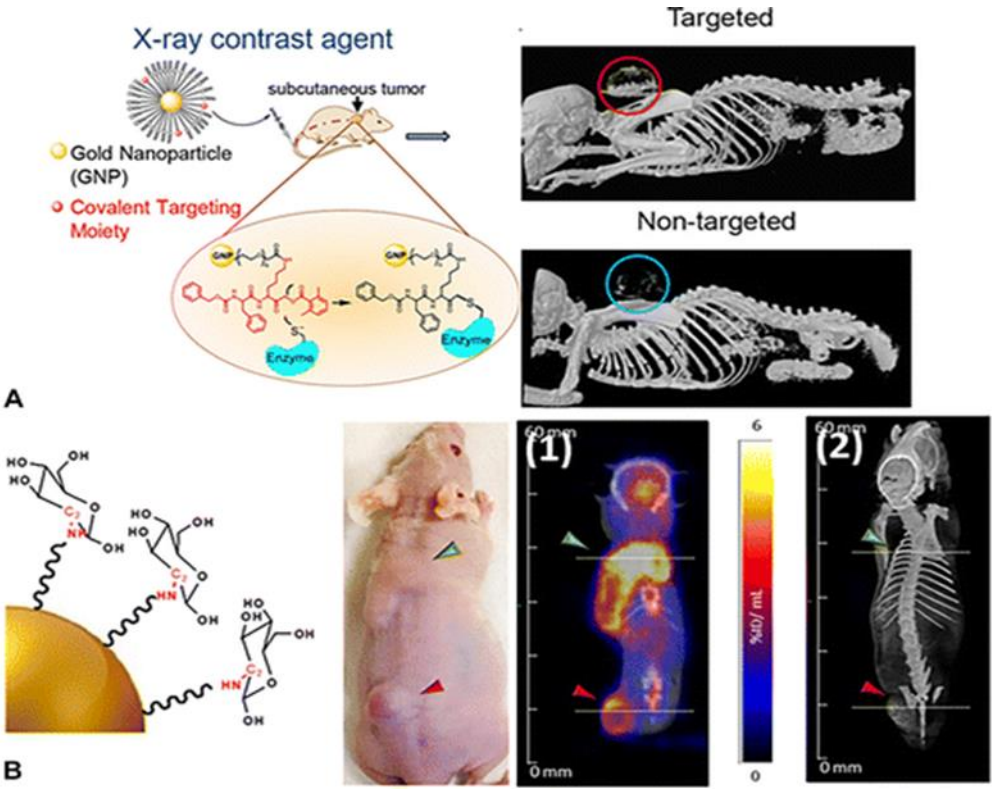

Figure 3. Gold Nanoparticles for Cancer Imaging in Mice
Source: Liu and Grodzinski (2021)

3.2. Nanotechnology in Cancer Biomarker Detection

Cancer biomarkers are biological indicators whose levels reflect the presence or progression of tumors. These markers help investigate cellular processes and track changes in cancer cells, thereby enhancing our understanding of tumor biology (Jin *et al*., 2020).

Geho et al. (2006) and Luchini et al. (2010) developed a nanoparticle-based technique to capture and concentrate low molecular weight proteins from biological fluids, greatly improving the efficiency of biomarker screening.

Another strategy utilizes nanotechnology to fabricate lab-on-chip microfluidic devices for immuno-screening and tumor cell analysis. A notable example is a lab-on-chip platform designed for multiplexed protein detection, which employs cadmium selenide (CdSe) quantum dots coated with a zinc sulfide (ZnS) shell. These quantum dots are conjugated to antibodies targeting carcinoembryonic antigen, cancer antigen 125 and Her-2/Neu (Jokerst *et al*., 2009). Furthermore, studies have demonstrated that nanoscale

surfaces can distinguish tumor cells based on their growth behavior on surfaces with different sizes (Hung *et al*., 2010).

3.3. Nano-Carriers in Cancer Therapy

Nanocarriers such as quantum dots, dendritic macromolecules, carbon nanotubes, micelles and liposomes have been extensively utilized in cancer therapy (Jin *et al*., 2020).

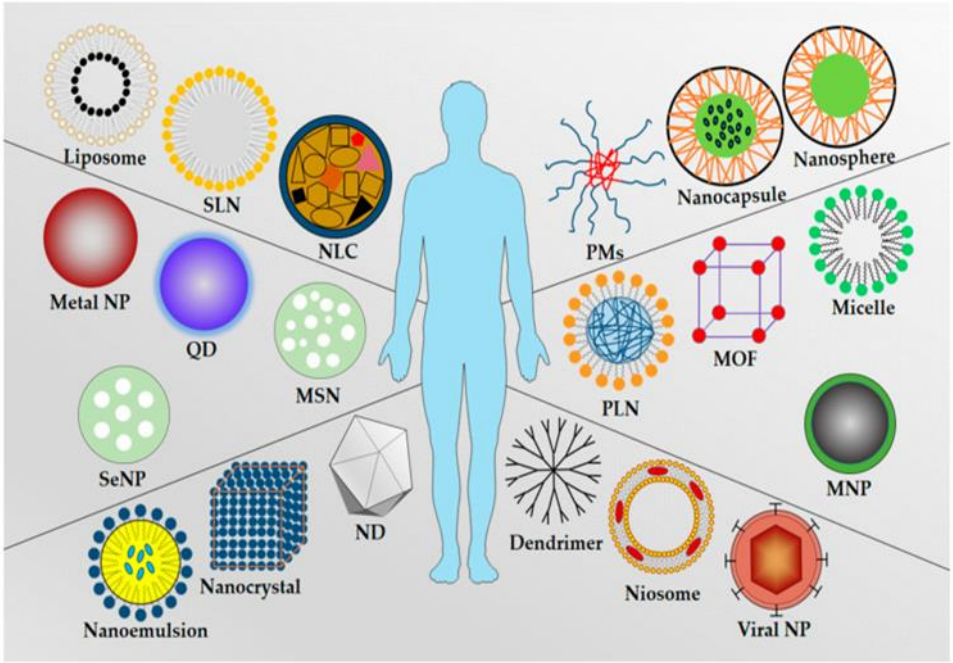

Figure 4. Nanocarriers used in nanobiotechnology
Source: Wei et al. (2020)

Liposomes: By exploiting the Enhanced Permeability and Retention (EPR) effect (Nasibova *et al*., 2016; Khalilov & Nasibova, 2010), vesicles approximately 4000 kDa or 500 nm in size can pass through vascular gaps to enter tumors. Once inside, they can merge with tumor cells, be taken up through endocytosis and deliver their drug payload within the cells. Research indicates that the size of liposomes plays a crucial role in determining their circulation half-life. Liposomes smaller than 100 nanometers show better tumor penetration and longer persistence in the body, while larger liposomes are quickly detected and removed by the mononuclear phagocyte system. For instance, liposomal formulations of adriamycin have shown notable clinical success in the treatment of metastatic ovarian cancer (Jin *et al*., 2020).

Carbon nanotubes: With a high surface area and proper functionalization, it can efficiently deliver drugs and genetic materials into cells and is also utilized in thermal therapy. These nanotubes have the ability to absorb near-infrared (NIR) light and convert it into heat via the thermal effect, enabling them to selectively target and eliminate tumor cells (Jin *et al*., 2020).

Polymeric micelles: Polymeric nanoparticles (PNPs) are frequently utilized as carriers for hydrophobic drugs in cancer nanomedicine. Their biocompatible and tunable surfaces facilitate controlled drug release while minimizing toxicity. Nonetheless, challenges persist in delivering drugs accurately while minimizing side effects and resistance. For example, nanomaterials conjugated with adriamycin have demonstrated

effectiveness against multiple cancers but caused serious side effects such as cardiotoxicity, restricting their clinical application. These problems have been mitigated by Doxil, a liposomal formulation of doxorubicin, which considerably lowers the risk of cardiotoxicity (Jin *et al*., 2020).

Dendrimers: These structures release drugs by covalently attaching antitumor agents to their outer functional groups. Studies have demonstrated that cancer cells exhibiting high levels of folate receptors can efficiently bind to dendritic molecules decorated with folate groups. Additionally, dendrimers can interact with DNA, as seen with DNA-polyamides and DNA-poly(amidoamine) (DNA-PAMAM), which enhances their effectiveness in targeting cancer cells that overexpress folate receptors (Jin *et al*., 2020).

Quantum dots (QDs): Its fluorescence enables real-time tracking of targeted drug delivery and in certain cases, application in photothermal therapy. Quantum dots (QDs) have the ability to accumulate in specific tissues, facilitating targeted drug delivery and reducing the side effects of chemotherapy. Due to their stability and strong, long-lasting luminescence, they are also widely used as biomarkers. For instance, some research has linked QDs with prostate-specific antigen for cancer labeling, while others use QDs to improve immunohistochemistry techniques (Jin *et al*., 2020). Chen et al. (2009) successfully employed QD-based probes to detect breast cancer, showing that quantum dot immunohistochemistry (IHC) can identify even low levels of HER2 expression and enable multichannel detection, surpassing the performance of traditional methods (Sung *et al*., 2019).

4. Alzheimer and Parkinson disease

Alzheimer's Disease is mainly characterized by the abnormal accumulation of amyloid-β (Aβ) plaques and tau neurofibrillary tangles, which cause brain damage and disrupt vital cognitive functions. Parkinson's Disease (PD) involves the buildup of misfolded α-synuclein (α-syn) protein inside Lewy bodies (LB) within dopaminergic neurons, resulting in notable motor impairments (Li *et al*., 2021; Nasibova *et al*., 2023). However, recent research indicates that additional factors - such as chronic oxidative stress, hormonal imbalances, mitochondrial dysfunction, inflammation, calcium imbalance, errors in cell division, genetic susceptibility and blood-brain barrier (BBB) dysfunction - also play a crucial role in disease progression (Cano *et al*., 2021; Nasibova *et al*., 2015).

4.1. Nanoparticles for Alzheimer's disease diagnosis

The Aβ peptide, found in senile plaques, was the first clinical biomarker identified for Alzheimer's Disease (AD) due to its buildup in the gray matter of affected brains. This finding paved the way for the creation of nanodevices aimed at detecting Aβ for diagnostic purposes (Derakhshankhah *et al*., 2020). Among these, superparamagnetic iron oxide nanoparticles (SPIONs) combined with magnetic resonance imaging (MRI) were the earliest technologies utilized for AD diagnosis. SPIONs, which are surface-modified with antibodies to selectively target AD biomarkers, have demonstrated effective targeting in vitro, in vivo and ex vivo AD models. For instance, SPIONs coated with ganglioside carbohydrates (sialic acid), Aβ1-42 antibodies or curcumin act as MRI contrast agents to identify Aβ plaques (Kouyoumdjian *et al*., 2013; Viola *et al*., 2015; Kavetskyy *et al*., 2019).

Additionally, a hybrid nanodevice composed of graphene oxide functionalized with antibodies against both tau and Aβ, attached to magnetic core-plasmonic coating nanomaterials, was developed and successfully used to detect Aβ and tau proteins in an in vitro AD model (Derakhshankhah *et al*., 2020; Kavetskyy *et al*., 2022).

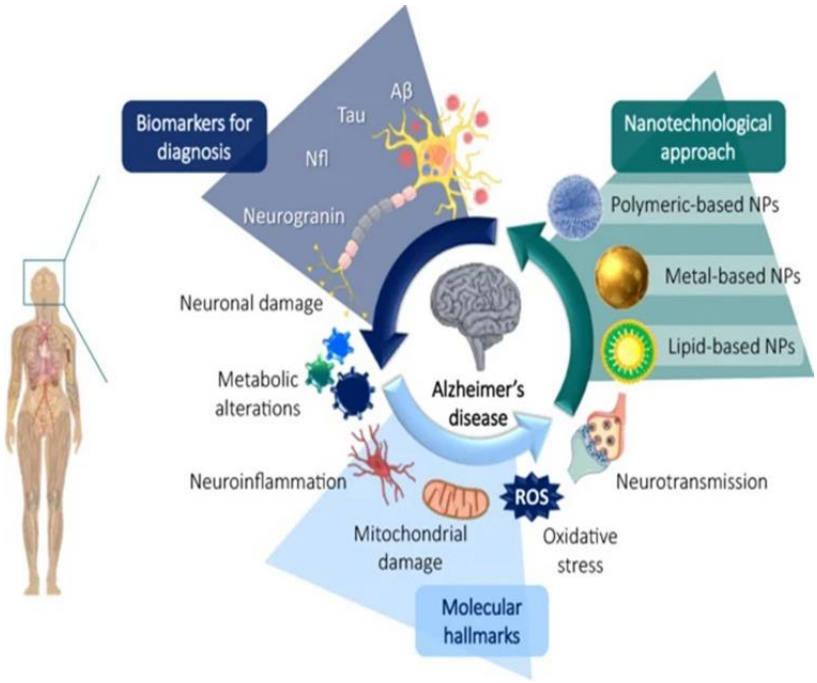

Figure 5. Nanomaterial-based strategies for treating and managing Alzheimer's disease
Source: Karthika et al. (2024)

4.2. Advances in Nanoparticle Therapies for Alzheimer's Disease

Lipid-based nanoparticles: Recent preclinical studies have shown encouraging outcomes using advanced lipid nanoparticles (LNPs) in animal models of Alzheimer's Disease (AD). Almuhayawi et al. (2020) created LNPs encapsulating pomegranate extract and evaluated their effects in a rat model of AD induced by aluminum chloride (Cano *et al*., 2021). The extract, which is rich in antioxidants such as alkaloids and tannins, significantly reduced neurofibrillary tangles (NFTs) and amyloid-β (Aβ) buildup, improved cognitive performance and boosted antioxidant levels in treated rats compared to the control group (Amrahov *et al*., 2023). The study also presented a hybrid nanocarrier featuring a lipid core with a PLC coating to improve solubility, which led to better spatial memory and lowered neuroinflammation in the hippocampus and cortex. Moreover, erythropoietin (EPO), which supports neuronal survival and neurogenesis in both Parkinson's and Alzheimer's diseases, has limited ability to cross the blood-brain barrier (BBB) due to its hydrophilic nature, rapid clearance and large size. Encapsulating EPO in solid lipid nanoparticles (SLNs) improved its effectiveness in reducing oxidative stress and Aβ deposits in an Aβ42-induced rat AD model. Rats treated with EPO-loaded LNPs exhibited enhanced spatial memory compared to those given free EPO (Cano *et al*., 2021).

Polymeric-based nanoparticles: Dhas et al. (2020) developed core/shell nanoparticles (NPs) composed of a cationic biopolymer and loaded with lutein (LT), a dietary carotenoid commonly found in green vegetables, eggs and corn. Their study showed that these nanocarriers possess ideal physicochemical characteristics for in vivo applications. The nanoparticles achieved high entrapment efficiency, provided sustained

release of LT, preserved its stability, were compatible with brain cell models and successfully crossed an in vitro blood-brain barrier (BBB). Furthermore, intranasal administration in rats resulted in brain accumulation of the LT-loaded NPs, demonstrated low toxicity and exhibited strong reactive oxygen species (ROS)-scavenging activity (Dhas & Mehta, 2020).

Metal-based nanoparticles: Magnetic nanoparticles (MNPs) are typically made from metals like gold, silver, iron, zinc and copper, each imparting unique properties to the nanocarrier. Their potential as therapeutic agents for Alzheimer's disease (AD) has garnered significant attention (Cano *et al*., 2021). For instance, Liu et al. (2019) investigated gold-palladium nanoparticles modified with quercetin, which help clear intracellular Aβ by stimulating autophagy, thereby reducing Aβ-induced neurotoxicity. Although quercetin is a powerful natural antioxidant, its clinical application is hindered by limited blood-brain barrier (BBB) penetration and rapid clearance. Nevertheless, recent research shows quercetin can enhance autophagy in brain cells, speeding up the removal of abnormal Aβ. Liu et al. (2019) confirmed that these MNPs are non-toxic in both in vitro and in vivo settings and can successfully cross an in vitro model of the BBB (Cano *et al*., 2021).

Sonawane et al. (2019) investigated the impact of MNPs on Tau-related pathology by creating two protein-capped nanoparticles: iron oxide NPs and cadmium sulfide NPs. These were biologically synthesized using fungi species Fusarium oxysporum and Verticillium sp. Iron oxide NPs, which exhibit transient ferromagnetic behavior, were coated with hydrolytic proteins, while cadmium sulfide NPs were capped with sulfate-reducing enzymes. Both types effectively inhibited Tau aggregation, with cadmium sulfide NPs notably disassembling Tau neurofibrillary tangles (NFTs) without harming cell viability (Cano *et al*., 2021; Sonawane *et al*., 2019).

Zhang et al. (2019) introduced hydrogen-doped palladium NPs designed to counteract oxidative stress-induced mitochondrial dysfunction in AD models. These nanoparticles facilitated self-catalyzed, sustained release of bio-reductive hydrogen, selectively scavenged hydroxyl radicals, prevented Aβ aggregation, reversed synaptic impairments and enhanced cognitive function in transgenic AD mice (Cano *et al*., 2021; Zhang *et al*., 2019).

Cai et al. (2020) developed ultrasmall superparamagnetic iron oxide nanoparticles (USPIONs) linked to a phenothiazine-based near-infrared dye for combined diagnostic and therapeutic applications. These USPIONs inhibited Aβ self-aggregation, broke down preformed fibrils and increased fluorescence upon binding aggregated Aβ proteins. Their small size also allowed them to reduce circulating Aβ by adsorbing amyloidogenic peptides onto their surfaces (Cano *et al*., 2021; Cai *et al*., 2020).

4.3. Metal-Based Nanozymes in Oxidative Stress Management

This section focuses on metal-based nanomaterials that help reduce oxidative stress by scavenging reactive oxygen species (ROS) and nitric oxide (NO), functioning similarly to important antioxidant enzymes involved in the oxidative stress response. These materials include metal oxides and redox-active nanozymes, which mimic enzymes like catalase and superoxide dismutase (SOD). Nanozymes are nanomaterials that exhibit enzyme-like activities, with tunable catalytic functions, high stability and the ability to imitate several enzymes simultaneously. In Parkinson's disease (PD) models, Ruotolo et al. (2020) studied the effects of cerium oxide nanoparticles (CeO_2 NPs) using a yeast cell model that overexpresses human α-synuclein. Their results showed that CeO_2 NPs significantly decreased α-synuclein toxicity in a dose-dependent fashion by inhibiting the

formation of cytoplasmic α-synuclein aggregates and reducing α-synuclein-induced mitochondrial damage (Li *et al*., 2021; Ruotolo *et al*., 2020).

4.4. Nanocarriers for Drug Delivery in Neurodegenerative Diseases

Nanoparticles (NPs) show great promise as therapeutic carriers to improve blood-brain barrier (BBB) penetration. Their ability to enhance Parkinson's disease (PD) treatment is exemplified by lipoic acid, a mitochondrial molecule with potent antioxidant and anti-inflammatory effects that helps reduce oxidative stress. However, lipoic acid's clinical application is limited due to its short half-life and low bioavailability caused by rapid liver metabolism. Nanoparticles can overcome these limitations by facilitating better intracellular delivery. Piersimoni et al. (2020) demonstrated that gold nanoparticles capped with lipoic acid (GNPs-LA) were biocompatible, effectively entered cells and improved drug delivery in vitro (Ahmadkhani *et al*., 2017). These GNPs-LA inhibited reactive oxygen species (ROS) production and restored mitochondrial function, helping to normalize cellular conditions (Li *et al*., 2021; Piersimoni *et al*., 2020).

Recent research has also investigated hydrogel-nanomaterial composites or nanogels as platforms for enhancing antioxidant drug delivery in Alzheimer's disease (AD). For example, Rajput et al. (2018) developed xanthan and gellan gum-based gels combined with nanostructured lipid carriers to solubilize resveratrol (RES) for nasal administration in AD treatment. Similarly, Elnaggar et al. (2015) utilized chitosan nanogels to enable intranasal delivery of the neuroprotective compound piperine. Thanks to their mucoadhesive properties, these gels allowed effective delivery at significantly reduced doses in AD rat models. Cardia et al. (2019) applied chitosan hydrogel nanoparticles for intranasal delivery of progesterone, achieving increased progesterone levels in treated rats (Li *et al*., 2021; Rajput *et al*., 2018; Elnaggar *et al*., 2015).

4.5. Nanomaterials Targeting α-Synuclein Aggregation

Approaches to reduce α-synuclein (α-syn) aggregation focus on either directly targeting the misfolded α-syn fibrils or preventing their excessive production. This section highlights the use of graphene quantum dots (GQDs) and cerium oxide nanoparticles (CeO_2 NPs), which can break down α-syn fibrils, alongside a modified exosome system designed to deliver α-syn siRNA to the central nervous system to block α-syn protein synthesis. GQDs are nanoscale graphene-based materials, roughly 100 nm in size. Kim et al. (2018) showed that GQDs are capable of crossing the blood-brain barrier, binding to α-syn fibrils and effectively inhibiting fibril formation while also breaking down existing fibrils in a time-dependent way. In models where α-syn preformed fibrils (PFFs) induced synaptic dysfunction and mitochondrial injury, treatment with GQDs restored synaptic protein levels, reduced mitochondrial damage and decreased the formation of Lewy bodies and neurites. Notably, GQDs exhibited no significant long-term toxicity in both in vitro and in vivo studies (Li *et al*., 2021; Kim *et al*., 2018).

4.6. Nanodrugs approved by the FDA and those undergoing clinical trials

Evaluating the long-term accumulation of nanoparticles, immune system activation, hepatotoxicity and nephrotoxicity is essential for mitigating these risk factors. For example, certain metal-based nanoparticles (e.g., AuNPs, AgNPs, Fe_3O_4 NPs) can persist in the body without degradation and induce oxidative stress. Moreover, the neurotoxicity risk of nanomaterials capable of crossing the blood–brain barrier must also be assessed.

Accordingly, the FDA and EMA require a thorough characterization of the safety profile prior to clinical approval.

However, compared to conventional approaches, nano-based methods offer several advantages. These benefits are summarized in the table below.

Table 1. Comparison of Conventional and Nano-Based Methods

Feature	Conventional Drugs	Nano-Based Drugs
Distribution	Non-specific; affects both healthy and diseased tissues.	Targeted delivery via passive (EPR effect) and active (ligand-mediated) targeting.
Side Effects	Often high and systemic toxicity.	Reduced and localized; lower immunogenicity.
Bioavailability	Low; limited tissue exposure due to metabolism and degradation.	High; controlled release ensures optimal tissue concentrations.
Clinical Success	Long-standing use; efficacy varies with disease and drug.	Growing; several approved (Doxil®, Abraxane®, Onpattro®), many under clinical evaluation.
Pharmacokinetics	Short half-life; rapid clearance.	Prolonged half-life; stable transport and enhanced tissue accumulation.
Drug Stability	Sensitive to oxidation and hydrolysis.	Nanoparticles protect drugs from degradation.
Drug Loading Capacity	Usually carries a single drug; combination therapy limited.	Multifunctional carriers can deliver multiple drugs or imaging agents.
Patient Compatibility	Limited dosing routes; mainly oral or via intravenous (IV).	Drugs can be administered in a targeted and controlled manner via intravenous (IV), subcutaneous or local delivery.
Combination Therapy Potential	Higher risk; side effects increase.	Suitable for drug, gene and immunotherapy combinations; enables synergistic effects.

Currently, more than 50 nano-based drugs have been approved by the FDA and EMA and these agents have found clinical application in oncology, genetic disorders and other serious diseases. For instance, Doxil®, in its liposomal doxorubicin formulation, is used for the treatment of metastatic ovarian cancer and certain hematologic malignancies; the liposomal form enhances selective accumulation in tissues, thereby improving the toxicity profile. Abraxane®, an albumin-bound formulation of paclitaxel, is employed in the treatment of breast cancer and non-small cell lung cancer (NSCLC); this nanotechnology-based approach improves drug solubility and reduces the risk of infusion-related reactions. In the field of genetic disorders, Onpattro® (patisiran) - the first siRNA-based drug delivered via lipid nanoparticles - has demonstrated groundbreaking results in the treatment of hereditary transthyretin amyloidosis.

Simultaneously, numerous novel nanoplatforms are currently under clinical evaluation, including nanoparticle delivery systems combined with CAR-T cells, as well as multifunctional and targeted nanoparticles, whose efficacy and safety profiles are actively investigated during the transition from preclinical models to the clinical setting. These advancements demonstrate that nanodrugs not only optimize drug delivery but also have the potential to improve therapeutic outcomes and reduce adverse effects in patients.

Table 2. Nanomaterials: Applications and Clinical Status

Nanomaterial	Application Area	Clinical Status
Liposome (Doxil®)	Metastatic ovarian cancer, hematologic malignancies	FDA approved
Albumin-bound nanoparticles (Abraxane®)	Breast cancer, non-small cell lung cancer (NSCLC)	FDA approved
Lipid nanoparticles (Onpattro®)	siRNA therapy, hereditary transthyretin amyloidosis	FDA approved
Superparamagnetic iron oxide nanoparticles (SPIONs)	MRI contrast agent, some therapeutic carriers	Clinical trials
Gold nanoparticles (AuNPs)	Cancer diagnostics and therapy, photothermal therapy	Preclinical and clinical trials
CAR-T cells (can be combined with nanocarriers)	Targeted immunotherapy, hematologic malignancies and some solid tumors	Clinical trials and FDA approval for specific formulations; nanocarrier combinations are in preclinical/early clinical research stage

The FDA and EMA monitor the quality, safety and efficacy of nanodrugs more rigorously than conventional pharmaceuticals. Challenges such as standardizing production, limited long-term toxicological data and high manufacturing costs hinder commercialization. Global harmonization and production in compliance with Good Manufacturing Practice (GMP) are essential to address these challenges.

5. Conclusion

Nanotechnology-based biomaterials have led to significant advancements in medicine, particularly in the early diagnosis and targeted treatment of cancer and neurodegenerative diseases. Through smart nanocarrier systems, functional hydrogels and various types of nanoparticles, more precise, localized and minimally invasive interventions have become possible. Moreover, innovative nanoplatforms capable of crossing the blood-brain barrier have enhanced therapeutic potential in conditions such as Alzheimer's and Parkinson's diseases. Future research will focus on improving the biostability and safety of these technologies, as well as facilitating their integration into clinical practice. Thus, nanotechnology is expected to play a foundational role in the development of personalized and highly effective medical approaches in the near future. Future research will focus particularly on multifunctional nanocarriers, which can simultaneously deliver drugs, gene therapies and imaging agents, enabling synergistic and targeted therapeutic strategies. In parallel, the development of nanotherapeutic approaches tailored to personalized medicine - based on the patient's genetic profile, disease stage and tissue characteristics - will be a priority. Optimization of biostability, toxicological safety and pharmacokinetic properties will also remain central directions of research. As a result, in the future, nanotechnology is expected to play a key role not only in early disease diagnosis and targeted treatment but also in the development of personalized, minimally invasive and highly effective medical strategies.

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