

## Review article

# Nanomedicine and Veterinary Treatment

Basmala M. Ismael<sup>3</sup>, Somia A. Abdulhakim<sup>3</sup>, Salma R. Othman<sup>3</sup>, Hager A. Rabea<sup>3</sup> Rawan K.

Abdallah<sup>3</sup>, Adham R. Alyaan<sup>3</sup>, Habiba A. Helmy<sup>2</sup>, Marwa M. F. Atta<sup>1</sup>, Huda O. AbuBakr<sup>1</sup>

<sup>1</sup>Department of Biochemistry, Faculty of Veterinary Medicine Egyptian Chinese University.

<sup>2</sup>Department of Pharmacology, Faculty of Veterinary Medicine Egyptian Chinese University

<sup>3</sup>Student, Faculty of Veterinary medicine, Egyptian Chinese University

\*Corresponding author's Email: [huda.omar@cu.edu.eg](mailto:huda.omar@cu.edu.eg).

---

## Article History

Received: 03/08/2025, Received in revised form: 26/08/2025, Accepted: 27/08/2025, Available online: 31/08/2025

---

## Abstract

In recent decades, the concept of nanomedicine has undergone a significant transformation, utilizing the distinctive phenomenon known as the enhanced permeability and retention effect. By incorporating nanotechnology principles into medicine, this has enabled significant progress in individualized therapy, imaging, and targeted drug delivery. The treatment of diseases has been the focus of the development and application of numerous nanomedicines, with a particular emphasis on cancer therapy. Recently, nanomedicine has been employed in a variety of advanced disciplines, such as gene delivery, tissue engineering, immunotherapy, vaccines, and diagnosis. Moreover, nanomedicine has shown immense promise in treating complex conditions such as cardiovascular disease (CVD), diabetes, kidney cancer, and neurological disorders. Multifunctional nanomedicines enable the administration of medication, therapeutic monitoring, and imaging simultaneously, thereby enabling the development of personalized treatment plans and immediate responses. Beyond treatment, nanomedicine contributes to advanced diagnostics, tissue regeneration, antibacterial applications, and non-viral gene delivery. These benefits mark a significant step toward personalized and predictive medicine. Despite its immense promise, nanomedicine still faces challenges such as manufacturing scalability, limited targeting efficiency, safety concerns, and regulatory complexities. Therefore, this review article aimed to explore the latest advancements in nanomedicine for disease treatment, highlighting key innovations in nanoparticle design, therapeutic applications, and clinical translation challenges. We discussed in this review how nanomedicine is reshaping modern therapeutics and identified future directions for overcoming remaining barriers in this rapidly evolving field.

## Keywords:

Nanomedicine; Therapeutics; Tissue engineering; Gene therapy; Cancer; cardiovascular disease; CNS

## **Introduction**

Modern medicine has been transformed by the rapid advancement of nanotechnology, which has provided innovative solutions for therapeutic interventions, diagnostics, and drug delivery in a diverse array of diseases. Beyond infectious diseases, nanomedicine has shown immense promise in treating complex conditions such as cardiovascular disease (CVD)<sup>1</sup>, diabetes<sup>2</sup>, kidney cancer<sup>3</sup>, and neurological disorders<sup>4</sup>. In CVD, where traditional treatments often fall short cell-membrane-coated nanoparticles (CMCNCs) have emerged as a breakthrough strategy leveraging natural targeting mechanisms to improve drug delivery and reduce off-target effects<sup>1</sup>. Similarly, in diabetes nanotechnology offers solutions for continuous glucose monitoring and responsive insulin delivery, addressing the limitations of conventional therapies<sup>2</sup>.

Through the enhanced permeability and retention (EPR) effect, nanomedicine has revolutionized chemotherapy and immunotherapy in oncology by increasing drug accumulation in tumors, while minimizing systemic toxicity.<sup>5</sup> Multifunctional nanocarriers now enable combination therapies, overcoming multidrug resistance (MDR)<sup>5</sup>. Additionally, nanoparticles are being engineered to target the tumor microenvironment (TME) for precise immunomodulation<sup>6</sup>, boosting the response rates of cancer immunotherapy<sup>6</sup>.

Drug delivery across the blood-brain barrier (BBB) remains one of the most formidable

challenges in medicine, Parkinson's and Alzheimer's diseases are among the neurological disorders that are treated.<sup>4</sup>. Nanotechnology provides promising strategies, including ligand-functionalized nanoparticles and stimuli-responsive carriers, to enhance brain penetration while minimizing systemic side<sup>4</sup>.

This review explores the latest advancements in nanomedicine for disease treatment, highlighting key innovations in nanoparticle design, therapeutic applications, and clinical translation challenges, by examining successes in cancer therapy, CVD, diabetes, and neurological disorders.<sup>1,2,3,4,5,6</sup> We discuss how nanomedicine is reshaping modern therapeutics and identify future directions for overcoming remaining barriers in this rapidly evolving field.

## **Composition**

Nanomedicines typically comprise three core components:

### **1. Nanoparticle Core:**

This is the structural base of nanomedicine. Carbon-based nanostructures, such as carbon nanotubes, metals such as gold and iron oxide, and biodegradable polymers like poly (lactic-co-glycolic acid) (PLGA) are among the core materials. Lipids, which are employed in liposomes, are also included. The core is engineered to be biocompatible and often allows for controlled drug release.<sup>7</sup>

### **2. Therapeutic Payload:**

The drug or bioactive agent is either encapsulated in or conjugated to the nanoparticle. Common payloads include chemotherapeutics (e.g., doxorubicin), antibiotics, peptides, or nucleic acids like siRNA and mRNA. This component is

protected by the nanoparticle structure, which enhances stability and reduces degradation prior to reaching the target site.<sup>7</sup>

### 3. Surface Modifiers:

Polyethylene glycol (PEG) is frequently used to modify the nanoparticle's surface in order to enhance blood circulation or to conjugate it with targeting ligands such as antibodies, peptides, or aptamers to facilitate the active targeting of specific cells, such as cancer cells.<sup>7</sup>

A newer approach includes One-Component Nanomedicines (OCNs), where the therapeutic agent self-assembles into a nanostructure without needing additional carriers. This simplifies formulation and ensures high drug-loading efficiency with well-defined release kinetics.<sup>8</sup>

### Types of Nanomedicine:

#### 1. Diagnostic Nanomedicine:

Used for early detection and monitoring of diseases.

- Quantum Dots:

Fluorescent semiconductor nanoparticles provide stable, bright signals for cell tracking and cancer detection.

- Iron Oxide Nanoparticles:

Contrast agents are employed in magnetic resonance imaging (MRI).

- Gold Nanoparticles:

Due to their optical properties and biomarker binding capacity, they are utilized in diagnostic assays and imaging.<sup>9</sup>

#### 2. Therapeutic Nanomedicine:

Focused on treatment and drug delivery.

- Lipid-Based Nanocarriers:

Liposomes: Spherical vesicles used to deliver chemotherapy drugs.

Solid Lipid Nanoparticles (SLNs): Stable carriers for poorly water-soluble drugs.

- Polymeric Nanoparticles:

Made from biodegradable polymers like PLGA or PEG.

Used for sustained or targeted drug release.

- Dendrimers:

Tree-like, highly branched structures that carry drugs in their interior or on their surface.

- Nanocrystals:

Pure drug crystals in nano-size to improve solubility and bioavailability.

- Carbon-Based Nanoparticles:

Fullerenes and carbon nanotubes for drug delivery and gene therapy.

- Metal-Based Nanoparticles:

Gold, silver, or iron oxide particles for targeted therapy or hyperthermia treatment.<sup>10</sup>

#### 3. Regenerative Nanomedicine:

Used in tissue engineering and wound healing.

- Nanofibers and Scaffolds:

Mimic extracellular matrix for tissue growth.

- Hydrogels with Nanoparticles:

Maintain moisture and deliver growth factors for wound healing and cartilage repair.<sup>10</sup>

#### 4. Theranostic Nanomedicine:

Combination of therapy and diagnostics.

- Multifunctional Nanoparticles:

Carry medications and imaging agents.

Allow for the surveillance of therapeutic response and drug delivery in real time.<sup>9</sup>

#### 5. Immuno-Nanomedicine:

Enhances or modulates the immune system.

- Nano vaccines:

Use nanoparticles to deliver antigens more effectively.

- Immune Checkpoint Nanoparticles:

Deliver immune-modulating drugs directly to tumor sites.<sup>10</sup>

### **Applications:**

#### **1. Application: Nanomedicine Treatment for Cancer -Pure Paclitaxel Nanodrugs**<sup>13</sup>

Paclitaxel (PTX) is an effective chemotherapy drug used to treat solid tumors, but its hydrophobic nature limits its efficiency in conventional form. The cellular uptake and distribution of the nanoparticles are significantly improved when formulated at the nanoscale. This is due to the enhanced permeability and retention (EPR) effect, a property of tumor blood vessels that enables nanoparticles to enter and remain in tumor tissue more easily than in normal tissues. Additionally, the accumulation at tumor sites is increased.<sup>11</sup> To minimize side effects caused by carrier materials, the concept of self-delivery nanodrugs (SDNs) was introduced, allowing the production of pure PTX nanocrystals without additional components. This approach increases therapeutic efficacy while reducing potential toxicity.<sup>12</sup>

#### **• CO-ASSEMBLY OF PACLITAXEL AND OTHER DRUGS**

Additional developments involved the co-assembly of PTX with other drugs into single SDN structures, which has resulted in enhanced treatment outcomes and the surmounting of multidrug resistance (MDR)—a phenomenon in which cancer cells become resistant to multiple chemotherapy drugs, thereby complicating the treatment process.<sup>13</sup>

#### **2. Applications of Nanomedicine Treatment in Cardiovascular Diseases (CVD) Severe Hind limb Ischemia**<sup>15</sup>

Researchers have implemented bioengineering approaches aimed at boosting the functionality of nanocarriers (NCs) coated with stem cell membranes. Bioengineered Stem Cell Membrane-Coated Nanocarriers (BSMNCs) are these specialized carriers were specifically engineered to optimize the delivery of targeted drugs to ischemic tissues in the hindlimb.

To utilize the distinctive CXCR4 (C-X-C chemokine receptor type 4)-dependent targeting ability of stem cells, human adipose-derived stem cells (hASCs) were genetically modified to overexpress the CXCR4 receptor on their membranes. These modified cells (CXCR4- hASCs) were subsequently employed as coating material to functionalize nanocarriers composed of PLGA (poly(lactic-coglycolic acid)) and loaded with VEGF (vascular endothelial growth factor).

Following systemic administration of VEGF-loaded BSMNCs into mice models with induced hindlimb ischemia, researchers observed significant improvements in blood flow restoration (reperfusion), muscle tissue regeneration, and overall preservation of the affected limbs.<sup>14</sup>

#### **3. Applications of Nanoparticles in Tissue Engineering In tissue engineering**<sup>30</sup>

Injectable hydrogels act as supportive scaffolds and are developed as biodegradable biomaterials. These hydrogels are combined with nanoparticles like gold and silica, and stem cells, to enhance cell behavior and promote tissue regeneration. After injection into damaged tissues, the hydrogel gradually

biodegrades, aiding in the restoration of natural tissue.<sup>16</sup> The model is used in several applications, including:

### 1. Biological Property Enhancement

Nanoparticles can help improve how cells behave within the scaffold. For example:

- Gold nanoparticles (GNPs) are very small particles made of gold. They are safe for the body and can help stem cells develop into bone or fat cells. These effects happen because the gold nanoparticles activate specific internal processes, such as the MAPK pathway (a signaling system that tells cells how to grow or differentiate).<sup>17</sup>
- Also, GNPs may replace traditional bone growth proteins like BMPs (Bone Morphogenetic Proteins), which are expensive and may cause side effects like unwanted bone growth or inflammation.<sup>18,19</sup>
- Studies show that GNPs are most effective when sized between 30–50 nanometers (around 1,000 times smaller than the width of a human hair).<sup>20</sup>

#### Example:

In animal experiments, GNPs were mixed with gelatin to create a hydrogel. When this was implanted into bone defects in rabbit skulls, bone cells grew faster and stronger, especially at higher GNP concentrations.<sup>21</sup>

#### Also:

- GNPs have been used in heart tissue repair. They helped stem cells turn into cardiomyocytes (heart muscle cells) and improved heart function after injury.<sup>22</sup>
- Titanium dioxide (TiO<sub>2</sub>) nanoparticles were also used to support cardiomyocytes. When combined with PLGA (Polylactic-co-glycolic acid), they improved the surface of the scaffold, making it rougher, which helps cells attach and grow better. They also

reduced harmful acids released during scaffold breakdown.<sup>23,24</sup>

### 2. Antibacterial Applications

Because many bacteria are becoming increasingly resistant to antibiotics scientists are exploring the use of nanoparticles, especially silver—to prevent infections in tissue implants.<sup>25</sup>

- In laboratory experiments, nanofibrous scaffolds composed of silver nanoparticles and poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) exhibited exceptional compatibility with cells and potent antibacterial properties in one study. It is recommended that silver-loaded PHBV scaffolds be further investigated for their potential application in joint replacement surgeries (arthroplasty).<sup>26</sup>

### 3. Gene Delivery

Nanoparticles can also deliver genes into cells, which is essential for controlling cell behavior during tissue regeneration. Gene delivery can be viral or non-viral; this section focuses on the non-viral method using nanoparticles.<sup>22</sup>

Examples include:

- Magnetofection: A method where DNA is combined with magnetic nanoparticles (MNPs). A magnetic field guides these gene-loaded particles into specific cells, improving gene transfer efficiency—especially in hard-to-modify cells like stem cells and fibroblasts.<sup>27</sup>
- Iron oxide nanoparticles are another type of magnetic particle that can be used to deliver genes. They can be embedded into other materials or used to bind DNA on their surface, helping it enters the cells.<sup>22</sup>
- Other materials like carbon nanotubes (CNTs) and mesoporous silica nanoparticles

also show great promise. They carry genetic material into cells without triggering immune responses.<sup>28</sup>

These delivery systems increase accuracy, reduce toxicity, and improve the success of gene-based tissue repair.<sup>29</sup>

#### **4. Nanotechnology-Based Strategies to Overcome Antibiotic Resistance**<sup>33</sup>

Bacterial resistance to antibiotics is a growing problem, and nanomedicine has emerged as a promising solution. By using nanoparticles to target infection sites with precision, nanotechnology improves drug delivery, making treatments more effective while minimizing side effects.

One strategy involves using positively charged nanoparticles to target bacterial membranes. Since bacterial membranes are negatively charged, these nanoparticles can easily attach to the surface, enhancing drug delivery. For example, Hu et al. developed micelles (small spherical particles) loaded with a prodrug of triclosan (an antimicrobial agent) and a positively charged polymer called Poly (N,N-dimethylaminoethyl methacrylate) (PDMAEMA). The nanoparticles helped break down the bacterial membrane and released triclosan inside the bacterial cell. Methicillin-resistant *Staphylococcus aureus* (MRSA), a form of bacteria resistant to numerous standard antibiotics, was effectively inhibited by this method. It did this without causing resistance or harmful side effects.

Another approach is coating nanoparticles with cell membranes to improve targeted adhesion. These coated nanoparticles mimic natural cells, allowing them to bind specifically to bacteria. Zhang et al. coated

nanoparticles loaded with clarithromycin (an antibiotic used to treat infections like *Helicobacter pylori*) with gastric epithelial cell membranes. These coated nanoparticles specifically adhered to *Helicobacter pylori* bacteria, which cause stomach ulcers. This method provided better antibacterial performance than free clarithromycin or uncoated nanoparticles.<sup>31</sup>

A third strategy involves designing pH-responsive nanoparticles that activate drug delivery at infection sites, which typically have a lower pH than healthy tissues. This allows for targeted activation, improving the drug's effectiveness at the infection site.<sup>32</sup>

#### **5. Nanomedicine for Image-Guided Surgery**<sup>41</sup>

Surgical resection remains the primary approach for treating patients with renal cell carcinoma (RCC). Achieving maximal tumor removal is essential for effective long-term disease management, as it plays a key role in minimizing both recurrence and tumor progression.<sup>34</sup> Consequently, achieving precise visualization of tumor boundaries during surgery is critically important.<sup>38</sup>

Fluorescence-based intraoperative imaging offers a significant advantage by enabling accurate differentiation between malignant and healthy tissues. A near-infrared (NIR) peptide probe with a signal-to-noise ratio (SNR) of 2.5 was devised by Hongwei An et al. in a notable study.<sup>39</sup> The  $\alpha v \beta 3$  integrin, which is overexpressed in RCC cells, is the initial target of this probe. Subsequently, matrix metalloproteinases MMP-2/9 cleave it, enzymes that are frequently elevated in the tumor microenvironment. After cleavage, the

remaining fragments self-assemble into nanofibrous superstructures.

This dual mechanism of targeted recognition and enzymatic activation enabled the efficient and high-precision detection of RCC. This NIR peptide probe effectively identified small, sub-millimeter lesions (< 1 mm) that are otherwise invisible under standard bright-field conditions by utilizing the tumor excretion-retarded (TER) strategy. In comparison to conventional surgical techniques, this improved precision enabled the complete resection of the tumor and a significant reduction in postoperative recurrence.

The activated excretion retarded tumor imaging (AERTI) system was effectively accumulated at tumor sites in RCC xenograft models in follow-up studies, with sustained tumor retention lasting up to 72 hours, as demonstrated by the same research team.<sup>42</sup>

Additionally, lymphatic drainage in RCC does not always follow predictable pathways. As previously documented, sentinel lymph node identification using intraoperative lymphoscintigraphy has been shown to be a feasible method for accurately locating and sampling these nodes.<sup>35,36,37</sup>

## **6. Nanomedicines for Targeting CNS Diseases**<sup>43</sup>

Alzheimer's (AD), Parkinson's (PD), and amyotrophic lateral sclerosis (ALS) are neurodegenerative diseases that are distinguished by a protracted pathological degeneration process, which results in significant distress for both patients and their families. The technical challenges associated with nanomaterial research have been

resolved as a result of the progress made in nanotechnology since the 1990s. Nanomaterials have progressively captured the attention of neurodegenerative disease experts. Numerous nanomaterials have been implemented for research purposes, including inorganic nanoparticles, polymeric nanomaterials (such as micelles, dendrimers, nanocapsules, and nanospheres), and lipid-based nanomaterials (e.g., liposomes and solid lipid nanoparticles (SLN)). The primary objective of nanoparticle-based therapeutic approaches for CNS-related diseases is to facilitate the local release and targeted delivery of therapeutic agents to the afflicted areas of the brain after they have crossed the blood-brain barrier (BBB).<sup>42</sup>

## **7. Nanomedicine for Gene Therapy**<sup>45</sup>

Gene therapy has recently garnered significant attention due to its ability to regulate gene expression by targeting various components of the genome, including genomic DNA, messenger RNA (mRNA), microRNA (miRNA), and short-interfering RNA (siRNA), in the treatment of both malignant and non-malignant conditions. A diverse array of nucleic acid analogs has been created to regulate gene activity by targeting both coding and non-coding sequences of the human genome.<sup>44</sup> In principle, gene therapy is a simple treatment method that entails the replacement of a defective gene with a healthy one or the addition of an absent gene to facilitate the expression of the required protein.

## **8. Nanotechnology Applications in Monitoring**<sup>52</sup>

Conventional glucose meters are usually employed to monitor glucose levels in diabetes. Patients are required to manually

"prick" themselves multiple times throughout the day to monitor glucose fluctuations. Although this method has been extensively employed over time, it has several drawbacks, such as unreliable readings that are influenced by factors such as age, meal timing, and others, and poor patient compliance.<sup>46</sup> Furthermore, traditional glucose monitoring is not feasible during certain activities like sleeping or driving. Consequently, the intermittent nature of these methods implies that patients may overlook critical glycemic fluctuations between tests, thereby elevating the likelihood of severe complications.<sup>47,48</sup> In the past three decades, there have been numerous endeavors to create a more convenient method for glucose monitoring. The development of continuous glucose monitoring (CGM) systems, which can trace glucose levels continuously for up to 10 days, was made possible by the advent of implantable biosensors.<sup>49</sup> A measurable electric current is generated by amperometric sensors that are implanted beneath the skin in the initial iteration of CGM devices. This current is based on the glucose concentration.<sup>50</sup> Despite being a significant advancement in the field of CGM, these devices have a number of drawbacks, such as instability caused by signal latencies and sensor drift, the necessity for weekly subcutaneous calibration and implantation, and a high sensitivity to changes in physiological factors such as pH and temperature.<sup>50,51</sup> Nanotechnology-based biosensors offer potential solutions to overcome these challenges.

#### **Advantages and Disadvantages:**

##### **Advantages:**

#### **1. Better Drug Delivery**

Nanomedicine helps carry drugs exactly to the place where they are needed in the body. This makes the medicine work better and reduces harm to healthy cells.<sup>53</sup>

#### **2. Less Side Effects**

Since nanomedicine targets sick cells more directly, it can reduce side effects that usually happen with normal treatments like chemotherapy.<sup>54</sup>

#### **3. Helps in Many Diseases**

Nanomedicine is not just for cancer. It is also used in treating infections, brain diseases, and even helps with vaccines like the COVID-19 mRNA vaccines.<sup>55</sup>

#### **4. Smart Systems**

Some nanoparticles are made to respond to things like temperature or pH. This means they release medicine only in the right condition, which makes the treatment smarter and more effective.<sup>54</sup>

#### **5. Improves Old Treatments**

Old drugs that didn't work well can now be made better with nanomedicine. It gives them a better chance to work by improving how they move in the body.<sup>56</sup>

#### **6. Nanomedicine in cancer**

Cancer remains a highly lethal disease in the world. Currently, either conventional cancer therapies or modern immunotherapies are non-tumor-targeted therapeutic approaches that cannot accurately distinguish malignant cells from healthy ones, giving rise to multiple undesired side effects.

A series of nanocarriers has been developed in response to recent advancements in nanotechnology and our expanding



comprehension of cancer biology and nano-bio interactions. These nanocarriers are designed to enhance the therapeutic efficacy of encapsulated anticancer agents while simultaneously reducing off-target toxicity through tumor tissue-, cell-, or organelle-specific targeting.

In contrast, the therapeutic indices of the overwhelming majority of nanocarriers are frequently compromised by poor tumor accumulation, inefficient cellular internalization, or inaccurate subcellular localization, as they lack hierarchical targeting capability.<sup>57</sup>

### **6.1 Smart cancer nanomedicine for synergetic therapy:**

The second most common cause of mortality is cancer. No significant advancements in cancer therapy have been identified in the absence of Nanomedicine.

The diagnostic potential of nanomedicine has piqued interest due to its capacity to deliver therapeutic agents to malignancies with minimal adverse effects. Nanomedicines have become increasingly common in the treatment of cancer.

In this section, we provide four strategic recommendations for enhancing the functionality and application of nanomedicine:

1. The selection of intelligent drugs is a necessary condition for both commercial and medicinal success. The role of opportunistic decisions, which are contingent upon drug availability, should be taken into account when allocating resources to the advancement of modular (pro)drugs and nanocarrier design.

2. Nanomedicines that respond to stimuli are being developed for cancer therapy in order to dispense medications at precise locations.

3. Combination therapy is the foundation of clinical cancer treatment. Nanomedicines should be incorporated into multimodal combination therapy regimens more frequently, as they are valuable complement to pharmacological and somatic co-treatments.

4. Cancer therapy is being revolutionized by immune system regulation. Nanomedicines have the potential to enhance the efficacy of the immune system and regulate the behavior of anticancer immunity. The development of effective cancer nano-medicine treatments will be expedited and promoted by the implementation of these four strategies, both individually and in combination.<sup>58</sup>

### **6.2 Nanomedicine in the Treatment of Diabetes:**

The treatment of diabetes could be enhanced by nanomedicine by utilizing appropriate Nano formulations to leverage a variety of therapeutic mechanisms.

For instance, to simulate the physiological release of insulin, glucose-sensitive nanoparticles can release insulin in response to elevated glucose levels. Oral Nano-formulations for insulin uptake via the intestines are a long-awaited alternative to subcutaneous injections, which can result in pain, discomfort, and even local infection. In gene therapy and cell therapy, nanoparticles containing oligonucleotides can be employed to modulate the responses of T1DM-associated immune cells and stimulate insulin secretion in  $\beta$  cells or  $\beta$ -like cells

On the other hand, viral vectors do not elicit immunogenicity.

Lastly, the local delivery of Nano-formulations containing regenerative molecules can stimulate tissue repair in diabetic wound healing, thereby providing a valuable tool to treat this diabetic complication. In this section, we will elucidate the potential for clinical implementation of these various Nano-formulations -based diabetes treatment methods.<sup>59</sup>

### **Disadvantages:**

#### **1. Toxicity and Safety Concerns**

##### **Potential Risks of Nanoparticles**

Nanoparticles (NPs) used in drug delivery (e.g., liposomes, polymeric NPs, metallic NPs) may exhibit unintended toxicity due to:

- Reactive Oxygen Species (ROS) generation: Oxidative stress, DNA damage, and cell death.
- Biological accumulation: Long-term retention in the liver, spleen, and kidneys, leading to organ toxicity.
- Size-dependent effects: Very small NPs (<10 nm) may penetrate cell membranes unpredictably.<sup>60</sup>

#### **2. Poor Biocompatibility and Immune Reactions**

##### **Unwanted Immune System Activation**

- The body may recognize NPs as foreign, triggering:
- Complement activation as inflammation and rapid clearance from blood.
- Antibody production which reduced drug efficacy upon repeated dosing.
- Protein corona formation and blood proteins coat NPs, altering their function.<sup>61</sup>

#### **3. High Cost and Manufacturing Challenges**

### **Economic Barriers to Nanomedicine**

- Complex synthesis
- Requires specialized equipment (e.g., microfluidics, high-pressure homogenizers).
- Batch-to-batch variability
- Difficulty in maintaining consistency.
- Regulatory hurdles
- Lengthy and expensive approval processes (e.g., FDA, EMA).<sup>62</sup>

### **4. Regulatory and Ethical Issues**

#### **Lack of Standardized Guidelines**

- No global consensus on NP safety testing.
- Long-term effects unknown
- Potential risks like carcinogenicity are still under study.
- Ethical concerns
- Nanoparticles in the environment (e-waste, medical waste).<sup>63</sup>

### **5. Limited Clinical Success (In Vivo vs. In Vitro Gaps)**

#### **Why Many Nanodrugs Fail in Trials**

- Poor tumor penetration (in cancer nanomedicine).
- Rapid clearance by the liver and spleen (reducing circulation time).
- Lack of targeting precision                      Off-site toxicity.<sup>64</sup>

### **Challenges:**

Challenges in Nanomedicine-Based Treatments:

#### **1. Limited Clinical Translation**

Even though there's been a lot of progress in nanomedicine research, not many treatments have been actually used in patients. The big problems are how to make these treatments in large amounts, keep the same quality in every batch, and get approval from health organizations.<sup>65</sup>

## 2. Inefficient Targeting and Biodistribution

When you put nanoparticles in the body, they do not always end up where they should be. This happens because they often stick to proteins in the blood, creating a layer called a “protein corona.” This messes with how they move around in the body and makes it harder for them to reach the target.<sup>65</sup>

## 3. Toxicity and Long-Term Safety

Some of these medicines can build up in organs like the liver or spleen, and that can cause problems in the long term. We don’t know enough yet about the long-term effects, especially on the immune system.<sup>65</sup>

## 4. Challenges in Oral Nanomedicine Delivery

When you take nanomedicines by mouth, it’s hard for them to work properly. The acid in the stomach, digestive enzymes, and the way your body absorbs stuff through the intestines all reduce how effective they are. This makes it harder to ensure their functionality.<sup>66</sup>

## 5. Cancer Nanomedicine Delivery Limitations

Nanomedicine has definitely helped with cancer treatment, but getting the medicine into tumors is still a big challenge. Things like low oxygen and high pressure inside the tumor make it really hard for the medicine to reach the right place.<sup>67</sup>

## 6. Ethical, Regulatory, and Environmental Concerns

As nanomedicine becomes more common, there are more concerns about ethics, laws, and the environment. Issues like keeping patients safe, monitoring long-term effects, protecting privacy, and looking at how it affects the environment still need to be dealt

with. Plus, the rules for using these treatments are still being figured out.<sup>68</sup>

## Conclusion:

Nanomedicine represents one of the most revolutionary advancements in modern medicine, offering innovative approaches in diagnosis, treatment, and disease prevention. By utilizing smartly designed nanoparticles, it enables precise drug delivery, improved therapeutic efficiency, and reduced side effects—especially in complex conditions such as cancer, cardiovascular diseases, diabetes, and neurological disorders.

In cancer therapy, nanomedicine enhances drug targeting and helps overcome multidrug resistance. For cardiovascular diseases, cell membrane-coated carriers improve treatment precision and reduce immune reactions. In diabetes, nano-sensors and glucose-responsive insulin systems enable real-time monitoring and better glycemic control. Moreover, engineered nanoparticles can now cross the blood-brain barrier, offering new possibilities for treating neurological disorders like Alzheimer’s and Parkinson’s.

Beyond treatment, nanomedicine contributes to advanced diagnostics, tissue regeneration, antibacterial applications, and non-viral gene delivery. These benefits mark a significant step toward personalized and predictive medicine.

Despite its immense promise, nanomedicine still faces challenges such as manufacturing scalability, limited targeting efficiency, safety concerns, and regulatory complexities. Nevertheless, ongoing research and innovation continue to push the boundaries of what's possible, making nanomedicine a vital

pillar in the future of healthcare—one that brings safer, smarter, and more personalized treatment options to patients worldwide.

## References:

- 1 Bose, R. J., Ha, K., & McCarthy, J. R. Bio-inspired nanomaterials as novel options for the treatment of cardiovascular disease. *Drug discovery today*, 2021; 26(5), 1200–1211.
- 2 Lemmerman, L. R., Das, D., Higueta-Castro, N., Mirmira, R. G., & Gallego-Perez, D. Nanomedicine-Based Strategies for Diabetes: Diagnostics, Monitoring, and Treatment. *Trends in endocrinology and metabolism: TEM*, 2020; 31(6), 448–458.
- 3 Wu, R., Wang, K., Gai, Y., Li, M., Wang, J., Wang, C., Zhang, Y., Xiao, Z., Jiang, D., Gao, Z., & Xia, X. Nanomedicine for renal cell carcinoma: imaging, treatment and beyond. *Journal of nanobiotechnology*, 2023; 21(1), 3.
- 4 Kakinen, A., Jiang, Y., Davis, T. P., Teesalu, T., & Saarna, M. Brain Targeting Nanomedicines: Pitfalls and Promise. *International journal of nanomedicine*, 2024; 19, 4857–4875.
- 5 Wei, G., Wang, Y., Yang, G., Wang, Y., & Ju, R. Recent progress in nanomedicine for enhanced cancer chemotherapy. *Theranostics*, 2021; 11(13), 6370–6392.
- 6 Peng, S., Xiao, F., Chen, M., & Gao, H. Tumor-Microenvironment-Responsive Nanomedicine for Enhanced Cancer Immunotherapy. *Advanced science (Weinheim, Baden-Wurttemberg, Germany)*. 2022; 9(1), e2103836. <https://doi.org/10.1002/advs.202103836>.
- 7 Das R. A Comprehensive Review on Advanced Nano Biomaterials for Drug Delivery Application. *International Journal of Nanomaterials and Molecular Nanotechnology*. 2023. <https://www.pubtexto.com/journals/international-journal-of-nanomaterials-and-molecular-nanotechnology/fulltext/acomprensive-review-on-advanced-nano-biomaterials-for-drug-delivery-application>
- 8 Hu, Q., Katti, P. S., & Gu, Z. Enzyme-responsive nanomaterials for controlled drug delivery. *Nanoscale*, 2014; 6(21), 12273–12286.
- 9 Rizzo, L. Y., Theek, B., Storm, G., Kiessling, F., & Lammers, T. Recent progress in nanomedicine: therapeutic, diagnostic and theranostic applications. *Current opinion in biotechnology*, 2013; 24(6), 1159–1166.
- 10 Wang, C., Guo, M., Qi, R., Shang, Q., Liu, Q., Wang, S., Zhao, L., Wang, R., & Xu, Z. Visible-Light-Driven, Copper-Catalyzed Decarboxylative C(sp<sup>3</sup>)-H Alkylation of Glycine and Peptides. *Angewandte Chemie (International ed. in English)*, 2018; 57(48), 15841–15846.
- 11 Hu, Q., Shang, L., Wang, M., Tu, K., Hu, M., Yu, Y., Xu, M., Kong, L., Guo, Y., & Zhang, Z. Co-Delivery of Paclitaxel and Interleukin-12 Regulating Tumor Microenvironment for Cancer Immunotherapy. *Advanced healthcare materials*, 2020; 9(10), e1901858.
- 12 Wang, H., Zhu, W., Liu, J., Dong, Z., & Liu, Z. pH-Responsive Nanoscale Covalent Organic Polymers as a Biodegradable Drug Carrier for Combined Photodynamic Chemotherapy of Cancer. *ACS applied materials & interfaces*, 2018; 10(17), 14475–14482.
- 13 Zhou, M., Han, S., Aras, O., & An, F. Recent Advances in Paclitaxel-based Self-Delivery Nanomedicine for Cancer Therapy. *Current*

- medicinal chemistry*, 2021; 28(31), 6358–6374.
- 14 Bose, R. J., Ha, K., & McCarthy, J. R. Bio-inspired nanomaterials as novel options for the treatment of cardiovascular disease. *Drug discovery today*, 2021; 26(5), 1200–1211.
- 15 Bose, R. J., Ha, K., & McCarthy, J. R. Bio-inspired nanomaterials as novel options for the treatment of cardiovascular disease. *Drug discovery today*, 2021; 26(5), 1200–1211.
- 16 Esmaeili, H., Patino-Guerrero, A., Nelson, R. A., Jr, Karamanova, N., M Fisher, T., Zhu, W., Perreault, F., Migrino, R. Q., & Nikkhah, M. Engineered Gold and Silica Nanoparticle-Incorporated Hydrogel Scaffolds for Human Stem Cell-Derived Cardiac Tissue Engineering. *ACS biomaterials science & engineering*, 2024; 10(4), 2351–2366.
- 17 Suh, K. S., Lee, Y. S., Seo, S. H., Kim, Y. S., & Choi, E. M. Gold nanoparticles attenuates antimycin A-induced mitochondrial dysfunction in MC3T3-E1 osteoblastic cells. *Biological trace element research*, 2013; 153(1-3), 428–436.
- 18 Bessa, P. C., Casal, M., & Reis, R. L. Bone morphogenetic proteins in tissue engineering: the road from laboratory to clinic, part II (BMP delivery). *Journal of tissue engineering and regenerative medicine*, 2008; 2(2-3), 81–96.
- 19 Lim, Jin-Su, Kook, Min-Suk, Jung, Seunggon, Park, Hong-Ju, Ohk, Seung-Ho, Oh, Hee-Kyun, Plasma Treated High-Density Polyethylene (HDPE) Medpor Implant Immobilized with rhBMP-2 for Improving the Bone Regeneration, *Journal of Nanomaterials*, 2014, 810404-810411
- 20 Ko WK, Heo DN, Moon HJ. The effect of gold nanoparticle size on osteogenic differentiation of adipose-derived stem cells. *Journal of Colloid and Interface Science*, 2015; 438:68–76. ISSN 0021-9797.
- 21 Heo, D. N., Ko, W. K., Bae, M. S. Lee, J. B., ee, D. W., Byun, W., Lee, C. H., Kim, E. C., Jung, B. Y., Kwon, I. K. Enhanced bone regeneration with a gold nanoparticle-hydrogel complex. *Journal of materials chemistry. B*, 2014; 2(11), 1584–1593.
- 22 Hasan, A., Morshed, M., Memic, A., Hassan, S., Webster, T. J., & Marei, H. E. Nanoparticles in tissue engineering: applications, challenges and prospects. *International journal of nanomedicine*, 2018; 13, 5637–5655.
- 23 Jawad, H., Ali, N.N., Lyon, A.R., Chen, Q.Z., Harding, S.E. and Boccaccini, A.R. Myocardial tissue engineering: a review. *J Tissue Eng Regen Med*, 2007; 1: 327-342.
- 24 Liu, H., Slamovich, E. B., & Webster, T. J. Less harmful acidic degradation of poly(lactico-glycolic acid) bone tissue engineering scaffolds through titania nanoparticle addition. *International journal of nanomedicine*, 2006; 1(4), 541–545.
- 25 Patrascu, Jenel Marian, Nedelcu, Ioan Avram, Sonmez, Maria, Fikai, Denisa, Fikai, Anton, Vasile, Bogdan Stefan, Ungureanu, Camelia, Albu, Madalina Georgiana, Andor, Bogdan, Andronescu, Ecaterina, Rusu, Laura Cristina, Composite Scaffolds Based on Silver Nanoparticles for Biomedical Applications, *Journal of Nanomaterials*, 2015, 587989-17.
- 26 Pattnaik, S., Nethala, S., Tripathi, A., Saravanan, S., Moorthi, A., & Selvamurugan,

- N. Chitosan scaffolds containing silicon dioxide and zirconia nano particles for bone tissue engineering. *International journal of biological macromolecules*, 2011; 49(5), 1167–1172.
- 27 Scherer, F., Anton, M., Schillinger, U., Henke, J., Bergemann, C., Krüger, A., Gänsbacher, B., & Plank, C. Magnetofection: enhancing and targeting gene delivery by magnetic force in vitro and in vivo. *Gene therapy*, 2002; 9(2), 102–109.
- 28 Cai, D., Mataraza, J. M., Qin, Z. H., Huang, Z., Huang, J., Chiles, T. C., Carnahan, D., Kempa, K., & Ren, Z. Highly efficient molecular delivery into mammalian cells using carbon nanotube spearing. *Nature methods*, 2005; 2(6), 449–454.
- 29 Ito A, Kamihira M. Tissue engineering using magnetite nanoparticles. *Prog Mol Biol Transl Sci*. 2011;104:355–395.
- 30 Hasan, A., Morshed, M., Memic, A., Hassan, S., Webster, T. J., & Marei, H. E. Nanoparticles in tissue engineering: applications, challenges and prospects. *International journal of nanomedicine*. 2018; 13, 5637–5655.
- 31 Angsantikul, P., Thamphiwatana, S., Zhang, Q., Spiekermann, K., Zhuang, J., Fang, R. H., Gao, W., Obonyo, M., & Zhang, L. Coating nanoparticles with gastric epithelial cell membrane for targeted antibiotic delivery against *Helicobacter pylori* infection. *Advanced therapeutics*. 2018; 1(2), 1800016.
- 32 H. Chen, Y. Jin, J. Wang, Y. Wang, W. Jiang, H. Dai, S. Pang, L. Lei, J. Ji and B. Wang, *Nanoscale*. 2018, 10, 20946-20962.
- 33 Wang, S., , Gao, Y., , Jin, Q., , & Ji, J. Emerging antibacterial nanomedicine for enhanced antibiotic therapy. *Biomaterials science*. 2020; 8(24), 6825–6839.
- 34 Ljungberg, B., Albiges, L., Abu-Ghanem, Y., Bensalah, K., Dabestani, S., Fernández-Pello, S., Giles, R. H., Hofmann, F., Hora, M., Kuczyk, M. A., Kuusk, T., Lam, T. B., Marconi, L., Merseburger, A. S., Powles, T., Staehler, M., Tahbaz, R., Volpe, A., & Bex, A. European Association of Urology Guidelines on Renal Cell Carcinoma: The 2019 Update. *European urology*. 2019; 75(5), 799–810.
- 35 Bex, A., Vermeeren, L., de Windt, G., Prevoo, W., Horenblas, S., & Olmos, R. A. Feasibility of sentinel node detection in renal cell carcinoma: a pilot study. *European journal of nuclear medicine and molecular imaging*. 2010; 37(6), 1117–1123.
- 36 Kuusk, T., De Bruijn, R., Brouwer, O. R., De Jong, J., Donswijk, M., Grivas, N., Hendricksen, K., Horenblas, S., Prevoo, W., Valdés Olmos, R. A., Van Der Poel, H. G., Van Rhijn, B. W. G., Wit, E. M., & Bex, A. Lymphatic Drainage from Renal Tumors In Vivo: A Prospective Sentinel Node Study Using SPECT/CT Imaging. *The Journal of urology*. 2018; 199(6), 1426–1432.
- 37 Brouwer, O. R., Noe, A., Olmos, R. A., & Bex, A. Lymphatic drainage from renal cell carcinoma along the thoracic duct visualized with SPECT/CT. *Lymphatic research and biology*. 2013; 11(4), 233–238.
- 38 Cha, S. W., Sohn, J. H., Kim, S. H., Kim, Y. T., Kang, S. H., Cho, M.-Y., Kim, M. Y., and Baik, S. K. Interaction between the tumor microenvironment and resection

- margin in different gross types of hepatocellular carcinoma. *Journal of Gastroenterology and Hepatology*. 2020; 35: 648–653.
- 39 Hong-Wei An, Dayong Hou, Rui Zheng, Man-Di Wang, Xiang-Zhong Zeng, Wu-Yi Xiao, Tong-Da Yan, Jia-Qi Wang, Chang-Hao Zhao, Li-Ming Cheng, Jin-Ming Zhang, Lu Wang, Zi-Qi Wang, Hao Wang, and Wanhai Xu 2020: A near-infrared peptide probe with tumor-specific excretion-retarded effect for image-guided surgery of renal cell carcinoma ACS Nano. 2020; 14 (1), 927-936.
  - 40 Hou, D. Y., Wang, M. D., Hu, X. J., Wang, Z. J., Zhang, N. Y., Lv, G. T., Wang, J. Q., Wu, X. H., Wang, L., Wang, H., & Xu, W. An activated excretion-retarded tumor imaging strategy towards metabolic organs. *Bioactive materials*. 2021; 14, 110–119.
  - 41 Wu R, Wang K, Gai Y, Li M, Wang J, Wang C, Zhang Y, Xiao Z, Jiang D, Gao Z, Xia X. Nanomedicine for renal cell carcinoma: imaging, treatment and beyond. J Nanobiotechnology. 2023 Jan 3;21(1):3.
  - 42 Liu, H. L., Fan, C. H., Ting, C. Y., & Yeh, C. K. Combining microbubbles and ultrasound for drug delivery to brain tumors: current progress and overview. *Theranostics*. 2014; 4(4), 432–444.
  - 43 Guo, Z. H., Khattak, S., Rauf, M. A., Ansari, M. A., Alomary, M. N., Razak, S., Yang, C. Y., Wu, D. D., & Ji, X. Y. Role of Nanomedicine-Based Therapeutics in the Treatment of CNS Disorders. *Molecules (Basel, Switzerland)*, 2023; 28(3), 1283.
  - 44 Wirth, T., Parker, N., & Ylä-Herttuala, S. History of gene therapy. *Gene*. 2013; 525(2), 162–169.
  - 45 Zhang, Z., Wang, J., Liang, J., Zheng, Y., Wu, X., Tian, C., Sun, A., Huang, Y., Zhou, Z., Yang, Y., Liu, Y., Tang, C., Chen, Z. and Chen, C.-C. Organizing Uniform Phase Distribution in Methylammonium-Free 1.77 eV Wide-Bandgap Inverted Perovskite Solar Cells. 2023;19: 2303213. <https://doi.org/10.1002/sml.202303213>.
  - 46 American Diabetes Association. 2. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes-2021*. *Diabetes care*, 44(Suppl 1), S15–S33.
  - 47 Association A.D., 6. Glycemic targets: standards of medical care in diabetes—2019. *Diabetes Care*, 2019.
  - 48 Schulman, R. C., Moshier, E. L., Rho, L., Casey, M. F., Godbold, J. H., & Mechanick, J. I. Association of glycemic control parameters with clinical outcomes in chronic critical illness. *Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*. 2014; 20(9), 884–893.
  - 49 Edelman, S. V., Argento, N. B., Pettus, J., & Hirsch, I. B. Clinical Implications of Real-time and Intermittently Scanned Continuous Glucose Monitoring. *Diabetes care*. 2018; 41(11), 2265–2274.
  - 50 Hovorka, R., Nodale, M., Haidar, A., & Wilinska, M. E. Assessing performance of closed-loop insulin delivery systems by continuous glucose monitoring: drawbacks and way forward. *Diabetes technology & therapeutics*. 2013; 15(1), 4–12.



- 51 Schmid, C., Haug, C., Heinemann, L., & Freckmann, G. System accuracy of blood glucose monitoring systems: impact of use by patients and ambient conditions. *Diabetes technology & therapeutics*. 2013; 15(10), 889–896.
52. Lemmerman, L. R., Das, D., Higuera-Castro, N., Mirmira, R. G., & Gallego-Perez, D. Nanomedicine-Based Strategies for Diabetes: Diagnostics, Monitoring, and Treatment. *Trends in endocrinology and metabolism: TEM*. 2020; 31(6), 448–458.
53. Lammers, T., & Ferrari, M. The success of nanomedicine. *Nano today*. 2020; 31, 100853.
54. Rehan, F., Zhang, M., Fang, J., & Greish, K. Therapeutic Applications of Nanomedicine: Recent Developments and Future Perspectives. *Molecules (Basel, Switzerland)*. 2024; 29(9), 2073.
55. Zhang N. Promoting the bench-to-bedside translation of nanomedicines. *Medical review*. 2021; 3(1), 1–3.
56. Halwani A. A. Development of Pharmaceutical Nanomedicines: From the Bench to the Market. *Pharmaceutics*, 2022; 14(1), 106.
57. Fan, D., Cao, Y., Cao, M., Wang, Y., Cao, Y., & Gong, T. Nanomedicine in cancer therapy. *Signal transduction and targeted therapy*. 2023; 8(1), 293.
58. Kanungo, A., Mohanty, C., & Acharya, S. Smart Cancer Nanomedicine for Synergetic Therapy. *Current medicinal chemistry*. 2025; 32(2), 286–300.
59. Andreadi, A., Lodeserto, P., Todaro, F., Meloni, M., Romano, M., Minasi, A., Bellia, A., & Lauro, D. Nanomedicine in the Trans. Health Sci. Aug 2025, Vol (1), Issue (2), 69 – 85
- Treatment of Diabetes. *International journal of molecular sciences*. 2024; 25(13), 7028.
60. Zhang, Y. et al. Toxicity Mechanisms of Engineered Nanoparticles. *Nature Nanotechnology*. 2021; 16, 1150–1160.
61. Chen, F. et al. (2023). Immune Responses to Nanocarriers in Drug Delivery. DOI: [10.1126/scitranslmed.abo2200] <https://doi.org/10.1126/scitranslmed.abo2200>
62. Smith, A. et al. (2022). The Economics of Nanomedicine Production. DOI: [10.1038/s41578-022-00485-2] (<https://doi.org/10.1038/s41578-022-00485-2>).
63. Johnson, R. et al. (2023). Regulatory Gaps in Nanomedicine. DOI: [10.1021/acsnano.3c04567] (<https://doi.org/10.1021/acsnano.3c04567>).
64. Wang, L. et al. (2024). Barriers in Nanomedicine Translation. DOI: [10.1016/j.jconrel.2024.02.001] (<https://doi.org/10.1016/j.jconrel.2024.02.001>).
65. Metselaar, J. M., & Lammers, T. Challenges in nanomedicine clinical translation. *Drug delivery and translational research*. 2020; 10(3), 721–725.
66. Lou, J., Duan, H., Qin, Q., Teng, Z., Gan, F., Zhou, X., & Zhou, X. Advances in Oral Drug Delivery Systems: Challenges and Opportunities. *Pharmaceutics*. 2023; 15(2), 484.
67. Yao Y, Zhou Y, Liu L, Xu Y, Chen Q, Wang J. Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug



resistance. *Front Mol Biosci.* 2020;7:193.  
PMC7468194.

nanomedical innovations: a scoping  
review. *Frontiers in genetics.* 2023; 14,  
1163392.

68. Wasti, S., Lee, I. H., Kim, S., Lee, J. H., &  
Kim, H. Ethical and legal challenges in