

Nanorobots as novel drug delivery systems: A comprehensive pharmaceutical review

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Abstract

Nanorobots are emerging nanoscale systems in pharmaceutics designed for targeted drug delivery, overcoming limitations of conventional therapies such as poor specificity and systemic toxicity. This review includes the design and components of nanorobots, drug loading and stimuli-responsive release mechanisms, and their mechanism of action involving navigation, target recognition, and cellular internalization. Nanorobots enable precise drug delivery at the cellular level and show significant potential in applications such as cancer and other complex diseases.

Keywords: Nanorobots; Targeted Drug Delivery; Drug Loading; Stimuli-Responsive Release; Navigation; Target Recognition; Cellular Internalization; Cancer

1. Introduction

Nanorobots are emerging nanoscale devices in pharmaceutics designed to overcome limitations of conventional drug delivery systems such as poor targeting, low bioavailability, and systemic toxicity. Developed using principles of nanotechnology, biotechnology, and biomedical engineering, they enable controlled navigation, site-specific targeting, and precise drug release at the cellular level. These systems incorporate functional components for drug loading and stimuli-responsive release, triggered by factors such as pH, enzymes, temperature, or magnetic fields, thereby enhancing therapeutic efficacy and reducing side effects. Nanorobots show significant potential in applications such as cancer and other complex diseases; however, challenges related to biocompatibility, toxicity, large-scale manufacturing, and regulatory approval continue to limit their clinical translation.

2. Design and Components of Nanorobots

Nanorobots are complex nanoscale systems engineered with multiple functional components that enable targeted drug delivery, controlled navigation, and precise therapeutic action. Their design integrates biocompatible materials, targeting mechanisms, propulsion systems, and controlled release features.

2.1. Structural Framework (Body)

The structural framework forms the core of the nanorobot and provides mechanical stability. It is typically constructed from biocompatible materials such as polymers (e.g., PLGA), metals (gold, silica), or DNA-based structures. This framework protects the drug payload and ensures safe interaction within biological systems.

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2.2. Drug Payload (Therapeutic Core)

This component contains the active pharmaceutical ingredient (API). The drug may be encapsulated, conjugated, or embedded within the nanorobot matrix. The payload is designed to remain stable during circulation and to be released specifically at the target site.

2.3. Targeting Ligands

Targeting ligands are molecules attached to the surface of nanorobots that enable specific binding to receptors on diseased cells. These may include antibodies, peptides, aptamers, or small molecules such as folic acid. This component ensures site-specific delivery and enhances therapeutic efficiency.

2.4. Propulsion System

The propulsion system enables movement of nanorobots within biological fluids. Depending on the design, propulsion may be achieved through:

- Magnetic fields (externally controlled)
- Chemical reactions (self-propulsion)
- Biological mechanisms (e.g., bacteria-driven systems)

This allows nanorobots to navigate toward target tissues.

2.5. Sensors and Control Units

Nanorobots may incorporate nano sensors that detect environmental signals such as pH, temperature, or specific biomarkers. These sensors help in decision-making processes, enabling the nanorobot to release drugs only under specific conditions.

2.6. Drug Release Mechanism

This component controls the release of the drug at the target site. Release mechanisms are often stimuli-responsive, triggered by

- Internal stimuli (pH, enzymes, redox conditions)
- External stimuli (light, heat, magnetic field)
- This ensures controlled and localized drug delivery.

Surface Coating (Biocompatibility Layer)

Surface modification enhances stability, circulation time, and biocompatibility. Materials such as polyethylene glycol (PEG) are commonly used to avoid immune recognition and prolong systemic circulation (stealth effect).

2.7. Power Source

Nanorobots require energy for movement and functioning. Power sources may include

- External energy (magnetic fields, ultrasound)
- Internal biochemical reactions (glucose, enzymes)

3. Drug Loading Mechanisms

Nanorobots can incorporate drugs through various strategies depending on their design and material composition.

- **Encapsulation** involves entrapping the drug within the nanorobot matrix or core, providing protection from degradation during circulation.
- **Surface adsorption** allows drugs to bind onto the nanorobot surface via electrostatic or hydrophobic interactions.
- **Chemical conjugation** involves covalent attachment of drug molecules to the nanorobot structure, enhancing stability and controlled release.

4. Mechanism of Action of Nanorobots

The mechanism of action of nanorobots in targeted drug delivery involves a sequence of coordinated processes, including navigation through biological systems, target recognition, and cellular internalization, ultimately leading to precise drug release at the diseased site.

4.1. Navigation in Biological Systems

Nanorobots are designed to move through complex biological environments such as blood circulation and tissue matrices to reach target sites. Their navigation can be achieved through passive targeting, utilizing physiological factors like blood flow and enhanced permeability and retention (EPR) effect, or active propulsion mechanisms, such as magnetic guidance, chemical reactions, or biohybrid motility. These strategies enable nanorobots to overcome biological barriers and accumulate at the desired site.

4.2. Target Recognition (Ligand–Receptor Interaction)

Target specificity is achieved through surface functionalization of nanorobots with ligands such as antibodies, peptides, or aptamers. These ligands selectively bind to overexpressed receptors on diseased cells, such as cancer cell markers. The ligand–receptor interaction ensures precise localization of nanorobots at the target site, minimizing off-target effects and enhancing therapeutic efficiency.

4.3. Cellular Internalization

Following target recognition, nanorobots are internalized into cells primarily via endocytosis, including receptor-mediated endocytosis, phagocytosis, or pinocytosis. Once inside the cell, nanorobots can escape endosomal compartments and release the drug into the cytoplasm or specific intracellular organelles. This intracellular delivery enhances drug effectiveness, particularly for therapies requiring action at the molecular or genetic level.

5. Applications and Future Perspectives of Nanorobots

5.1. Applications

Nanorobots have demonstrated significant potential across various areas of pharmaceuticals and medicine due to their ability to deliver drugs with high precision and control.

- **Cancer Therapy:** Nanorobots enable targeted delivery of anticancer drugs directly to tumor cells, improving therapeutic efficacy while minimizing damage to healthy tissues.
- **Cardiovascular Diseases:** They can assist in targeted thrombolysis, plaque removal, and site-specific drug delivery in vascular disorders.
- **Neurological Disorders:** Nanorobots have the potential to cross the blood–brain barrier, enabling treatment of diseases such as Alzheimer's and Parkinson's.
- **Infectious Diseases:** Targeted delivery of antimicrobial agents enhances treatment efficiency and reduces drug resistance.
- **Gene Therapy:** Nanorobots can deliver genetic material (DNA/RNA) for precise gene modulation and treatment of genetic disorders.

5.2. Future Perspectives

The future of nanorobots in pharmaceuticals is highly promising, with ongoing advancements expected to enhance their clinical applicability and therapeutic performance.

- **Integration with Artificial Intelligence:** AI-driven nanorobots may enable real-time decision-making, adaptive drug release, and personalized therapy.
- **Personalized Medicine:** Tailoring nanorobot design based on individual patient profiles can improve treatment outcomes.
- **Improved Biocompatibility and Safety:** Development of biodegradable and non-toxic materials will enhance clinical acceptance.
- **Advanced Manufacturing Techniques:** Scalable and cost-effective production methods are essential for widespread use.

- **Regulatory Advancements:** Establishment of clear regulatory guidelines will facilitate clinical translation and commercialization.

6. Conclusion

Nanorobots represent a significant advancement in pharmaceuticals, offering precise and targeted drug delivery with improved therapeutic efficacy and reduced systemic toxicity compared to conventional systems. Their integrated design, controlled drug loading and release, and efficient mechanism of action enable site-specific treatment at the cellular level. Although challenges related to biocompatibility, scalability, and regulatory approval persist, ongoing research and technological advancements are expected to facilitate their clinical translation. Thus, nanorobots hold considerable promise as next-generation drug delivery systems in precision medicine.

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