

Chapter 3

Nanoparticles

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1 Introduction

Nanoparticles exhibit unique properties, such as excellent refractory characteristics, high mechanical resistance, and compatibility with sintering and reactions involving various oxides. These nanoscale materials, despite their robust mechanical and refractory qualities, can effectively interact with different oxides, making them highly versatile. Their applications have garnered significant attention from researchers across disciplines, ranging from material science to biotechnology and genetics.

Nanoparticles are defined as ultra-dispersed solid supramolecular structures with sizes ranging between 10 and 1000 nm. When encapsulated with specific drugs, these nanoparticles act as reservoirs within particulate systems, playing a vital role in drug delivery, particularly in oncology. Traditional drug formulations often rely on oral or injectable delivery routes, which may not always be the most efficient for certain therapies. Emerging biologic drugs, such as proteins and nucleic acids, necessitate innovative delivery technologies to reduce side effects and enhance patient compliance. Additionally, market demands drive the development of more effective drug delivery methods.

Polymeric nanoparticles and nanocapsules are widely used in drug delivery and are categorized as colloidal systems composed of solid polymers. These systems are typically submicron in size, with nanoparticles defined as particles smaller than 1 $\mu m.$ Nanocapsules consist of a polymeric shell surrounding a liquid core, where the drug is entrapped, while nanospheres feature a solid polymeric matrix in which the drug is dispersed. Active substances may be adsorbed onto the polymer's surface or encapsulated within the particle. These particles can be synthesized through polymerization of synthetic monomers or through dispersion of synthetic polymers or natural macromolecules.

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A wide range of nanoparticles has been developed, including polymeric and metallic nanoparticles, liposomes, solid lipid particles, micelles, quantum dots, dendrimers, microcapsules, cell-derived structures, lipoproteins, and various nanoassemblies. Recent advancements have focused on modernizing nanoparticle-based drug delivery systems to meet clinical needs.

Nanotechnology bridges the gap between physical and biological sciences by applying nanoscale structures and phases across various scientific domains. This is particularly true in nanomedicine and nanoparticle-based drug delivery systems, where these materials are of significant interest. In biomedicine, fields like nanobiotechnology, drug delivery, biosensors, and tissue engineering have been revolutionized by the use of nanoparticles, driving progress in innovative healthcare solutions.

NANOMEDICINE Types of Nanomedicines Viral Particles Polymeric Nanocarriers Nanomedicine Nanocarriers Nanoparticles Polymeric Nanocarriers Nanoparticles Nanoparticles Nanoparticles

Table:1 Summary of Nanoparticle Properties, Types, and Uses

Sr.No.	Property	Description	Examples	Applications	Key Benefit
1	Size	Typically 1-100 nm in diameter.	Quantum dots, Gold NPs	Drug delivery, imaging	High surface- to-volume ratio
2	Shape	Varies (spherical, rod-shaped, tubular, etc.).	Silver NPs, Nanorods	Catalysis, photothermal therapy	Shape-tunable properties
3	Surface Charge	Influences stability and interaction with cells.	Lipid nanoparticles	Colloidal stability, drug delivery	Enhances dispersion stability
4	Biocompatibility	Compatibility with biological systems.	Liposomes, PEGylated NPs	Implants, targeted therapies	Reduced adverse effects
5	Optical Properties	Size-dependent absorbance and fluorescence.	Quantum dots	Imaging, diagnostics	Bright, tunable emission
6	Chemical Composition	Made of metals, polymers, ceramics, or composites.	Gold NPs, Silica NPs	Drug carriers, coatings	Versatile for multiple uses
7	Magnetic Properties	Exhibit superparamagnetic behavior.	Iron oxide NPs	MRI contrast agents, hyperthermia therapy	Controlled targeting via magnets
8	Thermal Properties	Enhanced thermal conductivity and stability.	Carbon nanotubes, Au NPs	Heat dissipation, energy storage	Improved heat management
9	Reactivity	High chemical and catalytic activity.	Silver NPs, TiO2 NPs	Antimicrobial coatings, catalysis	Effective at low concentrations
10	Functionalization Potential	Ability to modify surface for specific uses.	PEGylated NPs, Ligand- coated NPs	Targeted drug delivery, diagnostics	Customizable for applications

2 Literature review

Over the past two decades, the availability of ultrafine, nanocrystalline oxide powders with characteristic length scales below 100 nm and high purity has significantly increased. These powders, when consolidated, display enhanced sintering activity due to their high surface-to-volume ratio, with a substantial number of atoms residing on particle surfaces. If these powders are processed and sintered to produce dense structures while maintaining a final grain size below 100 nm, they are classified as nanocrystalline ceramics or nanoceramics. However, processing these powders remains a complex task. Despite this, nanoceramics exhibit properties that are often superior to traditional coarse-grained ceramics, particularly in terms of mechanical, electrical, and thermal characteristics.

Nanoceramics demonstrate hardness and strength that are four to five times greater than those of conventional materials. For instance, nano-TiO₂ exhibits a microhardness of approximately 13,000 kN/mm² at 100°C, whereas standard titanium dioxide materials measure less than 2,000 kN/mm². Additionally, nanoceramics possess exceptional toughness. At room temperature, nano-titanium dioxide ceramics maintain their integrity even when compressed to one-quarter of their original length, highlighting their resilience compared to traditional ceramics. Ceramic nanoparticles and nanowhiskers are frequently integrated with other materials, such as polymers, to create nanostructured composite scaffolds for bone regeneration and drug delivery applications. Ceramic nanocoatings, on the other hand, are primarily utilized to enhance the biocompatibility and wear resistance of bone implants

The nanoparticles have various means through which it can enter the body. These are:

- > Accidentally
- > Deliberately introduced

There are two different approaches through which it enters the human cells. They are:

- ➤ In vivo
- ➤ In vitro
- > The in vivo exposure includes:
- > Intravenous
- > Intraperitonial
- Subcutaneous
- > Pulmonary
- Dermal
- > Oral
- > The in vitro exposure includes :

- ➤ GIT
- > Lung
- Dermal
- ➤ Cardiovascular
- > CNS
- > Liver
- ➤ Reproductive cell model

2 Properties of Nanoparticles

Nanoparticles exhibit unique properties due to their diminutive scale and molecular configuration. These properties often result in various electrical and magnetic behaviors, including:

Dielectric: This refers to the extent of electron movement within an electric current.

Ferroelectric: These are dielectric materials capable of polarization in multiple directions, allowing the negative and positive poles to be reversed through an electric field.

Piezoelectric: These materials generate an electrical charge in response to mechanical pressure.

Pyroelectric: This type of material can generate a temporary voltage when it experiences a change in temperature.

Ferromagnetic: Such materials are able to maintain a magnetic field following magnetization.

Magnetoresistive: These materials alter their electrical resistance when exposed to an external magnetic field.

Superconductive: Materials that demonstrate no electric resistance upon being cooled below a certain threshold temperature.

Electro-optical: Materials that modify their optical properties in response to an electric field.



2 Classification of Nanoparticles

Nanoparticles have been classified on the basis of nanofiller dimensionality:

- > zero-dimensional (e.g., nanoparticles (NPs) that include oxides, metals.
- > one-dimensional (e.g., nanofibers)
- > Two dimensional (e.g., nanolayers)
- > Three-dimensional (interpenetrating network that includes nanocomposites,
- ➤ hybrid nanograins, micro- and mesoporous hybrids, and organic-inorganic hybrids) systems.

Their architechtural style has been categorised into following:

- Nanoparticles
- Nanoscaffolds

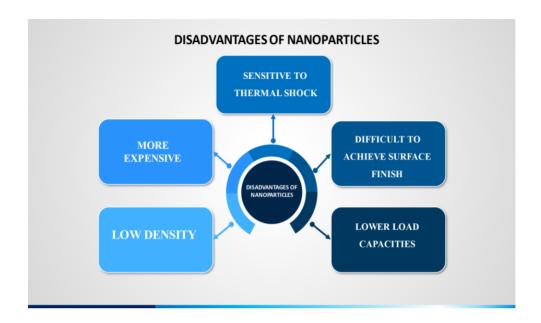
3 Advantages of Nanoparticles

- > Superplasticity
- ➤ Good refractory properties
- ➤ Good chemical resistance
- ➤ Good mechanical resistance
- Good Hardness
- ➤ Good fracture toughness
- > Excellent corrosion resistance



4 Disadvantages of Nanoparticles

- ➤ Low density
- > More expensive
- > Sensitive to thermal shock
- More difficult to achieve surface finish
- > Lower load capacities



5 Biopolymeric Nanoparticles

These materials and their properties are discussed below:

Chitosan

Nanomaterials derived from chitosan are extensively employed in sustained drug delivery systems across various epithelial tissues, such as buccal, intestinal, nasal, ocular, and pulmonary membranes.

Alginate

As an anionic mucoadhesive polymer, alginate features terminal carboxyl groups and exhibits superior mucoadhesive strength compared to neutral or cationic polymers.

Xanthan Gum

A polyanionic polysaccharide with excellent bioadhesive properties, xanthan gum is widely recognized as a non-toxic and non-irritating substance, making it a common pharmaceutical excipient.

Cellulose

Cellulose derivatives are modified to enhance solubility and control the gelation process, enabling better regulation of drug release profiles.

Liposomes

Discovered by Alec Bangham in the 1960s, liposomes are spherical vesicles formed from phospholipids and steroids, typically ranging in size from 50 to 450 nm.

Polymeric-Micelles

With sizes below 100 nm, polymeric micelles feature a narrow size distribution to minimize rapid renal clearance, facilitating accumulation in tumor tissues via the enhanced permeability and retention (EPR) effect. Their polymeric shell reduces nonspecific biological interactions, and their hydrophobic core enables efficient encapsulation, stabilization, and improved bioavailability of hydrophobic drugs.

Dendrimers

Dendrimers are globular structures with highly functionalized surfaces, making them excellent drug delivery candidates. However, their clinical applications are limited by the presence of amine groups.

Inorganic-Nanoparticles

While few inorganic nanoparticles have been approved for clinical use, many remain in the clinical trial phase. Drugs can be conjugated to the surfaces of gold nanoparticles (AuNPs) through ionic or covalent bonds or physical adsorption. These nanoparticles can control drug release through biological stimuli or light activation.

Nanocrystals

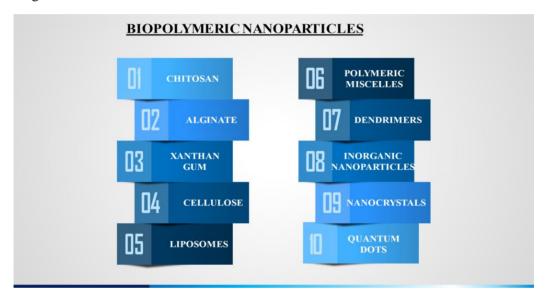
Nanocrystals consist of pure solid drug particles within a size range of up to 1000 nm. Free of carrier molecules, they are stabilized using polymeric steric stabilizers or surfactants. Their production methods include sono-crystallization, precipitation, high-gravity-controlled precipitation technology, multi-inlet vortex mixing, and limited impinging liquid jet precipitation techniques.

Metallic-Nanoparticles

Metallic nanoparticles are increasingly applied in fields such as bioimaging, biosensors, targeted or sustained drug delivery, hyperthermia, and photoablation therapy. Functionalization with specific groups enables binding to antibodies, drugs, and ligands, enhancing their potential for biomedical applications.

Quantum-Dots

Quantum dots (QDs) are semiconductor nanocrystals with diameters ranging between 2 and 10 nm, whose optical properties, such as photoluminescence and absorbance, are dependent on their size. These nanostructures have garnered significant attention in nanomedicine due to their distinct advantages over conventional organic dyes. Unlike traditional dyes, QDs emit light in the near-infrared region (<650 nm), a highly desirable characteristic for biomedical imaging because it minimizes tissue absorption and reduces light scattering. Furthermore, QDs with varying sizes or compositions can be excited using the same light source, producing distinct emission colors across a broad spectral range.



Protein and Polysaccharide-Nanoparticles

Proteins and polysaccharides, collectively referred to as natural biopolymers, are derived from biological sources, including plants, animals, microorganisms, and marine life. Protein-based nanoparticles are biodegradable, metabolizable, and can be easily functionalized to attach specific drugs or targeting ligands.

These nanoparticles are typically synthesized using two primary approaches: (a) from water-soluble proteins such as bovine or human serum albumin, and (b) from insoluble proteins like zein and gliadin.

The adaptability and unique properties of these biopolymers make them particularly valuable in nanomedicine and drug delivery. They can take on various forms, including soft gels, flexible fibers, and rigid shapes, with structures that may be porous or non-

porous. Additionally, their similarity to components of the extracellular matrix enables them to reduce the likelihood of triggering immunological reactions, further enhancing their therapeutic potential.

6 Nanocarriers for cancer immunotherapy

Nanodrug delivery systems (NDDS) enhance the solubility and bioavailability of medicinal agents, extend their circulation duration through passive or active targeting, and increase the concentration of these agents in tumor cells. Additionally, they improve in vivo pharmacokinetics, resulting in better therapeutic outcomes and fewer side effects (Algar et al., 2021; Altammar, 2023; Al-Thani et al., 2024; Anselmo & Mitragotri, 2021). The strengths and weaknesses of the three methods for delivering multiple agents in chemoimmunotherapy include:

The "Free drug + Nano" method offers benefits such as flexible dosing, manageable administration timing, straightforward preparation, and ease of scaling for industrial and clinical applications.

The "Nano + Nano" method provides flexibility in formulation, dosage adjustability, and harmonized distribution of dual agents. Our team has developed a pair of twin-like nanoparticles (TCNs) aimed at targeted delivery of sorafenib (SF) and IMD-0354 to enhance localized chemoimmunotherapy.

However, both the "Free drug + Nano" and "Nano + Nano" methods face challenges with mismatched pharmacokinetics in vivo and unpredictable activation times in tumor tissues. Numerous NDDS have been designed for the "coencapsulation" method in chemoimmunotherapy, including liposomes, polymer micelles, dendrimers, metallic and inorganic nanoparticles, nanogels, and biomimetic nanoparticles.

Nanoparticulate immunotherapy is an evolving field and introduces a new dimension to cancer treatment. Efficient and targeted delivery of immunomodulatory and costimulatory molecules to antigen-presenting cells (APCs) offers opportunities to advance nanocarrier-based immunotherapy (Chandrakala et al., 2022; Clogston et al., 2024; Gudkov et al., 2021; Hossain et al., 2023).

Regarding specific nanocarriers:

Liposomes made from hyperbranched poly(glycidol) derivatives demonstrate increased hydrophobicity and interaction with biomembranes as the polymerization degree increases, allowing them to bypass cellular acidic compartments and deliver antigens directly to the cytoplasm of dendritic cells.

Gold nanoparticles are valued for their adjustable surface chemistry, minimal cytotoxicity, and customizable sizes and shapes, critical for stimulating the immune response. Studies involving gold nanoparticles of varying sizes from 15 to 80 nm conjugated to OVA peptides or CpG ODN found that sizes 60 and 80 nm were most effective for antigen delivery.

PLGA nanoparticles are designed to include proteins or peptides of varying lengths, enhancing antigen presentation and anti-tumor T cell response, outperforming soluble antigens in vivo. These nanoparticles have been used to encapsulate lysates from head and neck squamous carcinoma for immunotherapy.

Exosomes are increasingly viewed as potential therapeutic agents due to their ability to provoke robust cellular responses both in vitro and in vivo. Tumor-derived exosomes carrying antigens have shown promise in triggering anti-tumor immune responses.

Micelles designed to respond to pH changes offer an innovative approach for improving antigen delivery through the MHC I pathway.

Solid lipid nanoparticles (SLNs) consist of a lipoidal matrix core solid at room temperature, incorporating various lipids and surfactants that enhance drug stability and delivery while minimizing efflux from cells. Despite these benefits, SLNs struggle with low drug-loading capacities and potential drug loss over time.

New-generation nanolipid carriers (NLCs) address issues such as low drug capacity and uneven distribution seen in traditional SLNs. Surface modifications of NLCs help overcome drug resistance and mitigate dose-related toxicity.

Carbon nanotubes, cylindrical structures with a hexagonal carbon atom network, offer a high drug payload due to their structure, ranging from a few nanometers to several millimeters in diameter (Hosseingholian et al., 2023; Janjua et al., 2021; Khan et al., 2022; Liu et al., 2023).

Nanoliposomes, prepared with cholesterol and various phospholipids, are utilized for their enhanced stability and targeted delivery capabilities, including folate-receptor targeting in tumors and antibody-mediated cell surface antigen recognition.

Hydrogels, hydrophilic polymers dispersed in water, create a gel-like network that can encapsulate and release drugs effectively. An example includes a thermosensitive and mucoadhesive sol-gel system developed for the targeted delivery of paclitaxel to treat oral squamous cell carcinoma, improving drug solubility and cytotoxic effects.

LIPOSOMES PH sensitive liposome will be a good candidate for induction of cellular immunity the loaded antigen can be released into cytoplasm by destabilizing with endosomal membrane. MISCELLES Exogenous antigens prefer lysosomal degredation wereas pendogenous antigens antigens and gereated in the properties with endosomal membrane. SOLID LIPID NANOPARTICLES They can be formulated to incorporate protein which facilitate antigen cross presentation and antitumor T.Cell response. SOLID LIPID NANOPARTICLES They possess lipodal matrix core that solubilizes lipophilic drugs. WANOLIPID CARRIERS They are the first class nanoparticles developed.Nanoliposomes are one of the most widely used delivery systems.

Cyclodextrin-Based Systems Cyclodextrins (CDs) are circular, doughnut-like structures consisting of at least six glucose molecules. CDs comprising fewer than six glucose units display reduced efficacy in drug encapsulation and take on a cone-like shape with a central cavity that entraps drugs. Natural variants such as α , β , and γ CD are utilized to create inclusion complexes with drugs, enhancing their solubility and permeability. These complexes help mitigate the inherent limitations of drugs. The CDs feature a lipophilic inner cavity and a hydrophilic outer surface, facilitating the delivery of lipophilic drugs. Moreover, chemical modifications of CDs allow them to encapsulate both lipophilic drugs and polar conjugates effectively.

Liquid Crystals Liquid crystals exist in a thermodynamically stable state that is intermediate between solid and liquid. They offer benefits such as the incorporation of insoluble drugs, reduced drug toxicity, and enhanced efficacy and release patterns. Based on their preparation methods, liquid crystals are categorized into different classes: For

instance, authors utilized glycerides in lamellar liquid crystals to embed paclitaxel. Using a BrijTM-based lamellar system with 20% medium-chain mono/diglycerides enhances the delivery of paclitaxel while mitigating its side effects like hypersensitivity, thrombocytopenia, and neutropenia. This approach is particularly promising for treating oral cancers (Maťátková et al., 2022; Mitchell et al., 2021; Plucinski et al., 2021; Saravanan et al., 2021).

Surface-Engineered Particulate Systems Surface engineering in particulate systems involves altering the surface chemistry to target tumors, extend circulation half-life, and reduce bodily clearance (Sun et al., 2023; Vijayaram et al., 2024). These modifications significantly affect the biodistribution, toxicity, and immunogenicity of nanoparticles. The changes typically include adjustments to the surface hydrophilicity and may also involve the addition of targeting agents like antigens, monoclonal antibodies, peptides, aptamers (short synthetic nucleic acid strands), or small molecules such as folic acid, EGF, and transferrin.

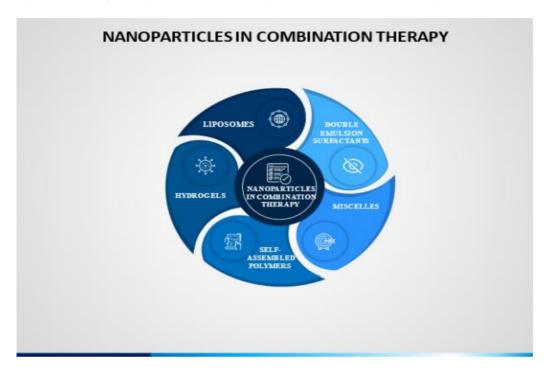
7 Nanoparticles in Combination Therapy

Nanomaterials have proven to be highly effective in the simultaneous delivery of various chemotherapeutic drugs, with dynamic materials facilitating optimal therapeutic outcomes via multi-modal cancer therapies. Examples of micro- and nano-scale delivery systems commonly employed include liposomes, double emulsion surfactants, micelles, self-assembling polymers, and hydrogels. A nano-scale coordination polymer, created through the self-assembly of polydentate bridging ligands and metal ions/clusters, has been recently utilized as an innovative means to concurrently transport oxaliplatin (30 wt.%) and gemcitabine (12 wt.%).

Nano-sized particles (NPs) with enhanced selectivity for cancer cells, along with targeted drug release triggered by unique tumor microenvironment traits such as a mildly acidic pH or elevated receptor expression, can reduce the necessary dosage of therapeutic agents. For instance, "nano-cocoons" have been developed using a single strand of self-assembled DNA featuring an acid-sensitive core that encapsulates DOX and DNase.

In a similar fashion, nanodevices have been engineered to activate only in the presence of two distinct proteases, showcasing precise control over drug release in specific conditions and targeting proteases that are prevalent in tumor environments. Furthermore, the overexpression of matrix-metalloproteinase in lung cancers has been exploited to trigger

the release of cisplatin and bortezomid from avidin-coated mesoporous silica NPs. The release of multiple agents from these nanocarriers can occur simultaneously or sequentially, depending on the desired drug release dynamics and timing.



8 Green synthesised nanoparticles for wound healing activity

Persistent bacterial and fungal infections in wound areas often lead to delays in the healing process, further complicating recovery. Integrating nanoparticles (NPs) with antimicrobial properties can enhance wound repair and inhibit bacterial colonization at the wound site. The potential of metal nanoparticles in addressing other wound healing challenges should also be explored to uncover their full therapeutic potential. Nanoparticles with strong antimicrobial activity against common pathogens, high woundhealing efficiency, and excellent biocompatibility are key to their practical application in medicine.

Silver nanoparticles (Ag NPs) synthesized using *Cassia auriculata L.* demonstrated significant effectiveness in both incision and excision wound models in Wistar albino rats. While the wound-healing properties of *C. auriculata* extract alone are well-documented,

the Ag NPs derived from it exhibited superior performance compared to the extract and Povidone-iodine ointment.

In addition to silver nanoparticles, other green-synthesized nanoparticles, such as titanium dioxide, gold, and copper oxide, have shown promise as wound-healing enhancers. These materials promote rapid wound closure, minimize infections, and reduce post-treatment side effects. For instance, gold nanoparticles synthesized using *Coleus forskohlii* root extract accelerated the re-epithelialization of excision wounds in rats, increased connective tissue formation, and stimulated the proliferation and migration of epidermal cells.

The mechanism underlying wound healing facilitated by green-synthesized metal- and carbon-based nanoparticles can be understood in the context of microbial interference. Bacteria and fungi are among the factors that can hinder the complex wound-healing process. Chronic wounds are often associated with bacterial colonies, which contribute to elevated proinflammatory cytokines and delayed healing.

Nanotechnology has introduced new possibilities for advancing the treatment and diagnosis of various diseases, including wound healing. Kumar et al. demonstrated the efficacy of nanoparticles in wound care through studies on albino rats. Cream-based formulations containing different concentrations of nanoparticles enhanced fibroblast and collagen synthesis while activating a significant number of macrophages in the wound area, thereby accelerating the healing process.

9 Preparation and Characterisation of Nanopaarticles

Size Distribution

The size of nanoparticles can be confirmed through mass spectrometry analysis. It was observed that the particle size of mannose-modified lactoferrin nanoparticles (Man-LF NPs) was slightly larger than that of unmodified LF NPs (150 nm vs. 110 nm, respectively) (Figure 1A). Both types exhibited a zeta potential of approximately 30 mV.

ZETA POTENTIAL MEASUREMENT

The apparent zeta potential (measured in mV) was determined by plotting the graph against nanoparticle intensity (105). For instance, studies have shown that nanoparticles

treated with mannose demonstrated a higher zeta potential compared to unmodified nanoparticles.

Stability

Stability tests were conducted using serum-containing PBS. Compared to unmodified nanoparticles, mannose-modified lactoferrin nanoparticles exhibited enhanced stability when immersed in serum-containing PBS.

In vitro release

In vitro studies revealed that nanoparticles with higher binding efficiency demonstrated greater cumulative release compared to standard nanoparticles. Fluorescence imaging of the biodistribution of nanoparticles showed efficient uptake in organs such as the liver, heart, lungs, and spleen.

10 Future Aspects and Challenges

Recent advancements in immunotherapy, such as anti-PD-1 checkpoint blockades, can be incorporated into cocktail therapies to achieve therapeutic goals. Additionally, a promising approach in camouflaging nanomedicine for cancer and infection treatment involves designing systems capable of adapting to the disease microenvironment, such as structural transformations that trigger the release of therapeutic cargo.

While these innovations have shown significant success, several unresolved challenges require attention to advance this field further. Maintaining the integrity of cell membranes remains a primary objective, as the functionality of the cell membrane is closely tied to its structural integrity.

Cancer immunotherapy has emerged as a pivotal area demonstrating the potential of camouflaging nanomedicine. Beyond its ability to target cancer cells, the cancer cell membrane, with its diverse antigen pool, makes nanoparticle camouflaging highly suitable for developing nanovaccines in immunotherapy. This strategy addresses the challenges of antigen specificity and simplifies the complex process of vaccine development. These advancements are poised to drive further progress in camouflaged immunotherapy, opening new possibilities in the fight against cancer.

Assessing the extent of integrity loss remains an open question. Advancements in minimizing cell membrane integrity loss could significantly enhance the effectiveness of this biomimetic approach. When considering clinical translation, several factors demand attention, with safety concerns surrounding the use of cancer cell or bacterial membranes being a primary focus.

A crucial aspect of successful immunotherapy is preventing tumor cells from evading immune surveillance. While checkpoint blockades combined with other therapies have shown promise in achieving durable cancer control, numerous obstacles hinder the widespread success of immunotherapy.



One challenge lies in the limitations of in vitro assays, which, although useful for intracellular evaluation, fail to replicate in vivo conditions due to the absence of critical elements, such as host and tumor-derived microenvironmental factors. Similarly, animal models provide valuable in vivo insights but are insufficient to mimic the intricate processes of human carcinogenesis, physiology, and disease progression.

Designing and optimizing delivery systems to achieve low systemic toxicity, high specificity, prolonged efficacy, and sustained bioavailability of therapeutic payloads is a significant clinical hurdle. Enhancing the efficacy of immunotherapy for cancer patients also requires targeting ligands that are highly specific to immune cells and remain stable in plasma.

Furthermore, the variation among different human cancers—such as the distinctions between liquid and solid tumor profiles and their associated therapies—must be accounted for when developing nanoparticle-based immunotherapies for clinical use. This effort necessitates collaboration among materials scientists, bioengineers, pharmaceutical experts, chemists, immunologists, vaccinologists, and clinicians.

Although liquid crystalline forms of anticancer drugs have been extensively studied for their ability to enhance antitumor activity, relatively little research has focused on their application in oral cancers. Given that the efficacy of liquid crystals in treating other cancer types has been well-documented, exploring their potential in the treatment of OSCC warrants further investigation.

Conclusion

Scientists working on the practical implementation of nano-drugs encounter numerous uncertainties, particularly the difficulty of defining these products with clarity and consistency. As a result, further investigation is essential to convert nanotechnology theories into practical solutions. This involves establishing precise drug dosages and refining controlled-release mechanisms to enhance the treatment of various cancers, each characterized by unique molecular and cellular pathways.

References

- Algar, W. R., Massey, M., Rees, K., Higgins, R., Krause, K. D., Darwish, G. H., ... & Kim, H. (2021). Photoluminescent nanoparticles for chemical and biological analysis and imaging. *Chemical Reviews*, 121(15), 9243-9358.
- Altammar, K. A. (2023). A review on nanoparticles: characteristics, synthesis, applications, and challenges. *Frontiers in microbiology*, *14*, 1155622.
- Altammar, K. A. (2023). A review on nanoparticles: characteristics, synthesis, applications, and challenges. *Frontiers in microbiology*, *14*, 1155622.
- Al-Thani, A. N., Jan, A. G., Abbas, M., Geetha, M., & Sadasivuni, K. K. (2024). Nanoparticles in cancer theragnostic and drug delivery: A comprehensive review. *Life sciences*, 122899.
- Anselmo, A. C., & Mitragotri, S. (2021). Nanoparticles in the clinic: An update post COVID-19 vaccines. *Bioengineering & translational medicine*, 6(3), e10246.
- Chandrakala, V., Aruna, V., & Angajala, G. (2022). Review on metal nanoparticles as nanocarriers: Current challenges and perspectives in drug delivery systems. *Emergent Materials*, 5(6), 1593-1615.

- Clogston, J. D., Crist, R. M., Dobrovolskaia, M. A., & Stern, S. T. (Eds.). (2024). *Characterization of nanoparticles intended for drug delivery* (pp. 63-70). Humana Press.
- Gudkov, S. V., Burmistrov, D. E., Serov, D. A., Rebezov, M. B., Semenova, A. A., & Lisitsyn, A. B. (2021). A mini review of antibacterial properties of ZnO nanoparticles. *Frontiers in Physics*, 9, 641481.
- Hossain, N., Mobarak, M. H., Mimona, M. A., Islam, M. A., Hossain, A., Zohura, F. T., & Chowdhury, M. A. (2023). Advances and significances of nanoparticles in semiconductor applications—A review. *Results in Engineering*, 19, 101347.
- Hosseingholian, A., Gohari, S. D., Feirahi, F., Moammeri, F., Mesbahian, G., Moghaddam, Z. S., & Ren, Q. (2023). Recent advances in green synthesized nanoparticles: From production to application. *Materials Today Sustainability*, 24, 100500.
- Janjua, T. I., Cao, Y., Yu, C., & Popat, A. (2021). Clinical translation of silica nanoparticles. *Nature Reviews Materials*, 6(12), 1072-1074.
- Khan, Y., Sadia, H., Ali Shah, S. Z., Khan, M. N., Shah, A. A., Ullah, N., ... & Khan, M. I. (2022). Classification, synthetic, and characterization approaches to nanoparticles, and their applications in various fields of nanotechnology: A review. *Catalysts*, *12*(11), 1386.
- Liu, R., Luo, C., Pang, Z., Zhang, J., Ruan, S., Wu, M., ... & Gao, H. (2023). Advances of nanoparticles as drug delivery systems for disease diagnosis and treatment. *Chinese chemical letters*, *34*(2), 107518.
- Maťátková, O., Michailidu, J., Miškovská, A., Kolouchová, I., Masák, J., & Čejková, A. (2022).
 Antimicrobial properties and applications of metal nanoparticles biosynthesized by green methods. *Biotechnology advances*, 58, 107905.
- Mitchell, M. J., Billingsley, M. M., Haley, R. M., Wechsler, M. E., Peppas, N. A., & Langer, R. (2021). Engineering precision nanoparticles for drug delivery. *Nature reviews drug discovery*, 20(2), 101-124.
- Plucinski, A., Lyu, Z., & Schmidt, B. V. (2021). Polysaccharide nanoparticles: From fabrication to applications. *Journal of Materials Chemistry B*, 9(35), 7030-7062.
- Saravanan, A., Kumar, P. S., Karishma, S., Vo, D. V. N., Jeevanantham, S., Yaashikaa, P. R., & George, C. S. (2021). A review on biosynthesis of metal nanoparticles and its environmental applications. *Chemosphere*, 264, 128580.
- Sun, L., Liu, H., Ye, Y., Lei, Y., Islam, R., Tan, S., ... & Cai, L. (2023). Smart nanoparticles for cancer therapy. *Signal transduction and targeted therapy*, 8(1), 418.
- Vijayaram, S., Razafindralambo, H., Sun, Y. Z., Vasantharaj, S., Ghafarifarsani, H., Hoseinifar, S. H., & Raeeszadeh, M. (2024). Applications of green synthesized metal nanoparticles—a review. *Biological Trace Element Research*, 202(1), 360-386.