MS.ID-IJPBS-2895
International Journal of Pharmacy and Biological Sciences-IJPBS™ (2024) 14 (4): 62-69
Online ISSN: 2230-7605, Print ISSN: 2321-3272
Review Article | Pharmaceutical Sciences | OA Journal | MCI Approved | Index Copernicus

Polymeric Nanoparticles Drug Delivery System

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Received:22 Jul 2024/ Accepted: 6 Aug 2024 / Published online: 1 Oct 2024
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Abstract

The recent emergence of nanomedicine has revolutionized the therapeutic landscape and necessitated the creation of more sophisticated drug delivery systems. Polymeric nanoparticles sit at the forefront of numerous promising drug delivery designs, due to their unmatched control over physiochemical properties such as size, shape, architecture, charge, and surface functionality. Furthermore, polymeric nanoparticles have the ability to navigate various biological barriers to precisely target specific sites within the body, encapsulate a diverse range of therapeutic cargo and efficiently release this cargo in response to internal and external stimuli. However, despite these remarkable advantages, the presence of polymeric nanoparticles in wider clinical application is minimal. This review will provide a comprehensive understanding of polymeric nanoparticles as drug delivery vehicles. The biological barriers affecting drug delivery will be outlined first, followed by a comprehensive description of the various nanoparticle designs and preparation methods, beginning with the polymers on which they are based. The review will meticulously explore the current performance of polymeric nanoparticles against a myriad of diseases including cancer, viral and bacterial infections, before finally evaluating the advantages and crucial challenges that will determine their wider clinical potential in the decades to come.

Keywords

Drug Delivery, Nanomedicine, Therapeutics, Nanoparticles, Personalized Medicine

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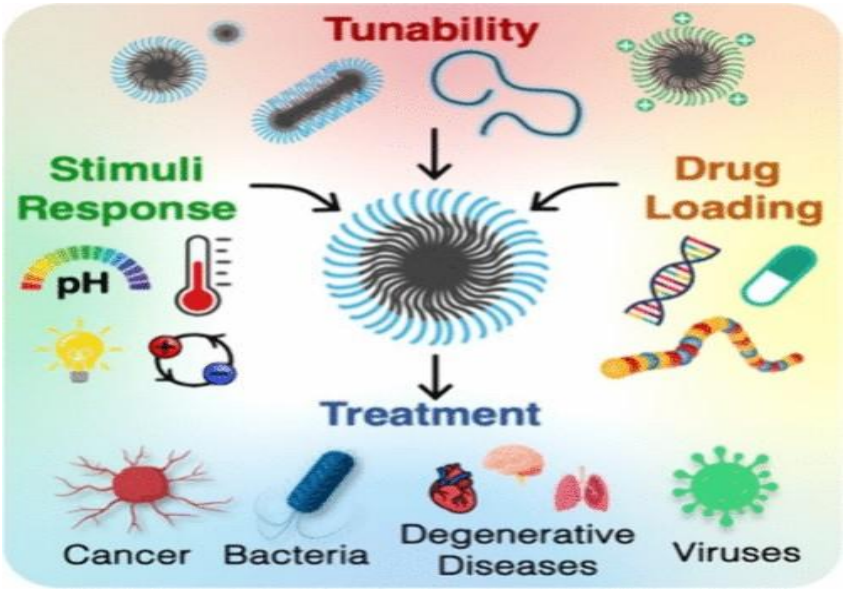

Fig 01: Treatment

INTRODUCTION:

Modern drug delivery technology began in 1952 with the advent of the Spansule® sustained-release capsule technology, which can deliver a drug for 12 hr after oral administration through an initial immediate dose followed by the remaining released gradually. Until the 1980s, oral and transdermal formulations providing therapeutic durations up to 24 hr for small molecules dominated the drug delivery field and the market.[1] In recent times, Polymer Nanoparticles [PNPs] are extensively employed as biomaterials because of their favourable characteristics in terms of simple elaboration and design, good biocompatibility, a broad structures variety and noticeable bio-imitative characteristics. Expressly in smart drug delivery discipline, PNPs had a marked role as they are able to bring therapeutics right into the purposed position in human body, with excellent efficiency. Advantages and characteristics of
PNPs

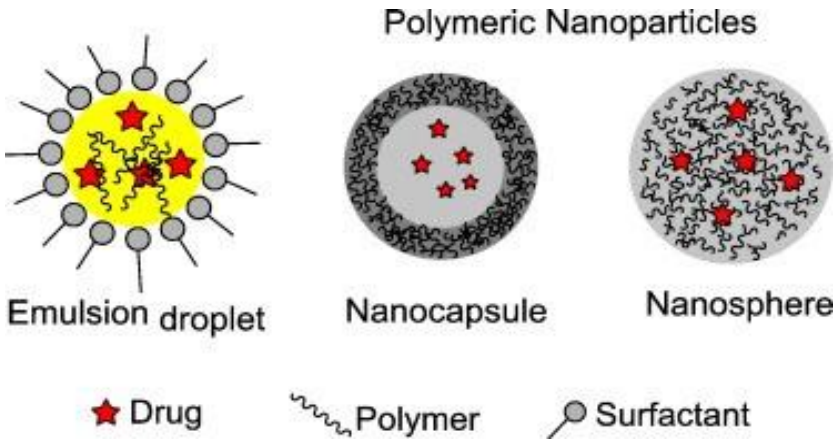

Fig 02: Polymeric Nanoparticles

Polymer nanoparticles (NPs):

These are a class of nanoscale drug delivery systems that have attracted considerable attention in the field of pharmaceuticals and biotechnology. These nanoparticles are composed of natural or synthetic polymers and are designed to encapsulate therapeutic agents such as small molecules, proteins, peptides, nucleic acids, or vaccines to enhance their efficacy, stability, and targeted delivery. Polymer NPs offer a promising approach to overcome many challenges associated with conventional drug delivery systems, such as poor solubility, rapid metabolism, non-specific distribution, and toxicity.

Nanomedicine has rapidly grown to treat certain diseases like brain cancer, lung cancer, breast cancer, cardiovascular diseases, and many others. These

nanomedicines can improve drug bioavailability and drug absorption time, reduce release time, eliminate drug aggregation, and enhance drug solubility in the blood. Nanomedicine has introduced a new era for drug carriage by refining the therapeutic directories of the energetic pharmaceutical elements engineered within nanoparticles. In this context, the vital information on engineered nanoparticles was reviewed and conferred towards the role in drug carriage systems to treat many ailments. All these nanocarriers were tested in vitro and in vivo. In the coming years, nanomedicines improve human health more effectively by adding more advanced techniques into the drug delivery system.[2]

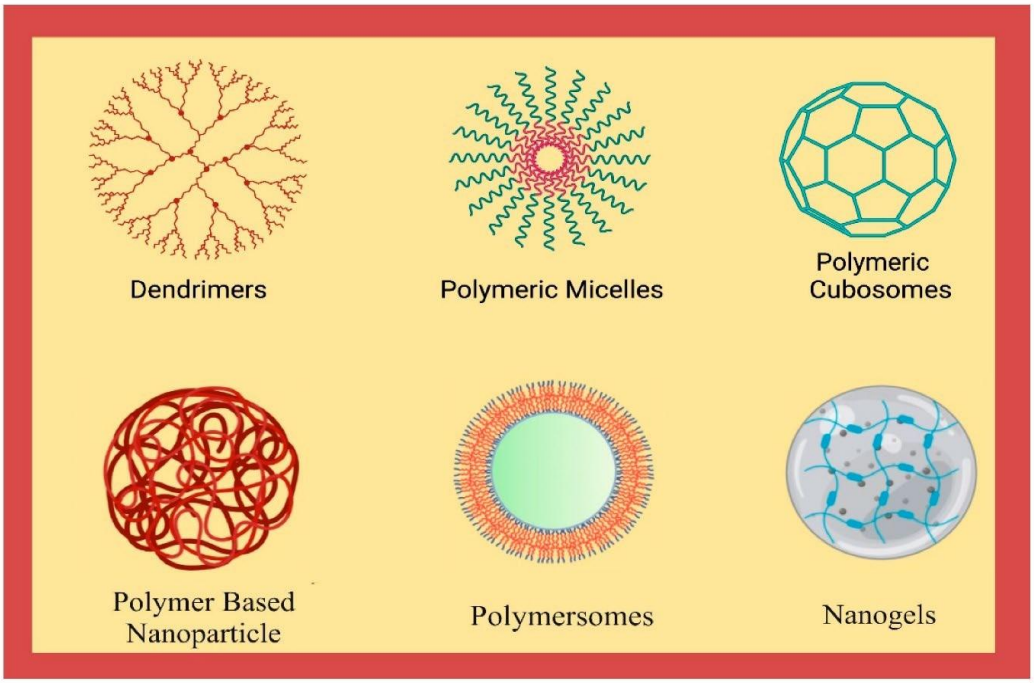

Fig 03: Polymers used in Nanoparticles

Types of Polymers Used in Nanoparticles

1.Dendrimers: -Dendrimers are highly branched, tree-like polymer structures. They have a well-defined, nanoscale size and a high degree of surface functionality, which can be easily modified for various applications.

- **Properties:**
  - High surface area, allowing functional groups to be attached for targeting. o Monodispersity (narrow size distribution).
  - Well-defined architecture, enabling precise control over the drug release mechanism.
- **Applications:**
  - Drug delivery (can carry small molecules, proteins, and nucleic acids). o Gene delivery and nucleic acid encapsulation. o Imaging agents for diagnostic purposes.[3]

2. Polymeric Micelles: -Polymeric micelles are self-assembled nanostructures formed by amphiphilic block copolymers in aqueous solutions. The hydrophilic blocks interact with water, while the hydrophobic blocks aggregate to form the core.

- **Properties:**
  - Nanometer-sized (typically 10–100 nm).
  - Ability to solubilize hydrophobic drugs in their core.
  - Stable in aqueous media and can be designed for controlled drug release.
- **Applications:**
  - Drug delivery for hydrophobic drugs.
  - Tumor targeting (due to enhanced permeability and retention effect).
  - Diagnostic imaging agents.[4]

3.Polymeric Cubosomes:-Polymeric cubosomes are bicontinuous cubic-phase nanostructures formed from amphiphilic copolymers. These structures are similar to liposomes but offer better stability and a unique structure with multiple interconnected channels.

- **Properties:**
  - High internal surface area for drug loading.
  - Excellent stability in aqueous media.
  - Controlled release properties due to the distinct internal structure.

- **Applications:**
  - Controlled drug delivery systems.
  - Bioactive agent encapsulation.
  - Topical drug delivery.[5]

4. Nanogels: -Nanogels are highly hydrated, cross-linked polymeric networks. These can swell in aqueous media and are capable of encapsulating both hydrophobic and hydrophilic drugs.

- **Properties:**
  - High water content (hydrophilic).
  - Biocompatible and biodegradable.
  - Can respond to environmental stimuli (pH, temperature, ionic strength) for controlled drug release.
- **Applications:**
  - Drug delivery (especially for proteins and nucleic acids).
  - Tissue engineering.
  - Targeted delivery and gene therapy.

5. Polymerosomes: Polymerosomes are vesicles made from amphiphilic block copolymers, similar to liposomes but composed of synthetic polymers. These structures have a bilayer membrane and can encapsulate both hydrophobic and hydrophilic substances.

- **Properties:**
  - Stable in biological environments.
  - High drug-loading capacity.
  - Ability to encapsulate both hydrophilic and hydrophobic drugs.
- **Applications:**
  - Drug delivery systems (cancer therapy, gene delivery).
  - Diagnostic imaging.
  - Vaccine delivery.[7]

6. Polymer-based Nanoparticles: -Polymer-based nanoparticles are small, solid, spherical particles formed from synthetic or natural polymers. These particles can be fabricated to carry drugs, proteins, or genetic materials.

- **Properties:**
  - Size range typically from 10 to 200 nm.
  - High drug-loading capacity.
  - Can be functionalized for targeting (active or passive).
  - Biodegradable and biocompatible.
- **Applications:**
  - Drug delivery (chemotherapeutics, antibiotics, and vaccines).
  - Gene delivery.
  - Diagnostic agents (imaging and sensing) [8]

➢ **Carriers Polymeric:** Polymeric carriers are the most widely used in nanoparticle drug delivery systems. They are made from natural or synthetic polymers and are often preferred due to their biodegradability, biocompatibility, and ability to control drug release.

Examples of Polymeric Carriers: -

- Poly (lactic-co-glycolic acid) (PLGA)
- Poly (lactic acid) (PLA)
- Polycaprolactone (PCL)
- Chitosan
- Albumin [9]

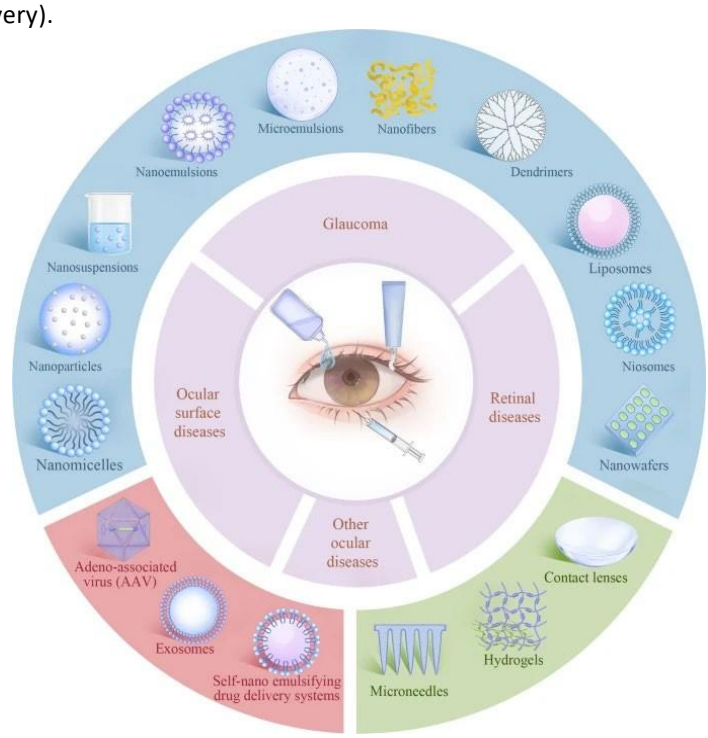

Fig 04: Polymeric Nanocarriers in Ocular Drug Delivery

➢ **Polymeric Nanocarriers in Ocular Drug Delivery: -**

- **Polymeric Nanoparticles (NPs):**
  Description: Polymeric nanoparticles are solid, submicron-sized particles made from biodegradable polymers like PLGA (Poly (lactic-co-glycolic acid)), PLA (Poly (lactic acid)), and PCL (Polycaprolactone). These nanoparticles can encapsulate hydrophilic and hydrophobic drugs and can be engineered to release drugs in a sustained and controlled manner.
  - **Applications**: Nanoparticles are used for the delivery of anti-inflammatory agents, antibiotics, anti-glaucoma drugs, and drugs for retinal diseases.
- **Nanocapsules**
  Description: - Nanocapsules are a type of nanoparticle where the drug is encapsulated in a polymeric shell, allowing for the controlled release of the drug over time. The polymeric shell also protects the drug from degradation.
  - **Applications**: Useful for delivering a wide variety of drugs, including those used for treating uveitis, glaucoma, and age-related macular degeneration (AMD).
- **Polymeric Micelles**
- **Description: -**Polymeric micelles are self-assembled nanoparticles composed of amphiphilic block copolymers. They have a hydrophobic core for drug loading and a hydrophilic outer shell to improve stability in aqueous environments.
  - **Applications**: These are particularly effective for delivering poorly water-soluble drugs in the treatment of retinal diseases and ocular infections.
- **Hydrogels**
  - **Description:** Polymeric hydrogels are three-dimensional networks of hydrophilic polymers that can hold large amounts of water or biological fluids.
    They are used to form ocular inserts or contact lenses for sustained drug release. o **Applications**: Hydrogels are used in drug delivery for conditions like dry eye syndrome, corneal wounds, and other surface ocular diseases.
    - **Dendrimers**
      - **Description:** Dendrimers are highly branched, tree-like macromolecules that can be functionalized for specific targeting. Their structure offers high surface area for drug loading and the potential for surface modification to improve ocular bioavailability.
      - **Applications**: Dendrimers are used for delivering antiviral drugs, antibiotics, and anti-inflammatory agents to the ocular tissues.[10]
      - **Polymeric Nanoparticles in Cancer Diagnosis**
- **Imaging and Molecular Diagnostics:** Polymeric nanoparticles can encapsulate imaging agents for magnetic resonance imaging (MRI), positron emission tomography (PET), computed tomography (CT), ultrasound, and fluorescence imaging. These particles can target specific tumor markers or the tumor microenvironment, improving the accuracy of imaging techniques and enabling early detection of cancer.
- **Targeted Diagnostic Delivery: -**Surface modification of polymeric nanoparticles with targeting ligands (e.g., antibodies, peptides, or small molecules) enables them to selectively bind to cancer cells or tumor vasculature. This targeting allows for the precise localization of imaging agents at the tumor site, reducing the risk of false positives and enhancing diagnostic accuracy.
- **Multimodal Imaging:**
  Polymeric nanoparticles can carry multiple imaging agents or have multiple functionalities, allowing for multimodal imaging. For example, a nanoparticle may contain both fluorescent probes for optical imaging and magnetic nanoparticles for MRI, providing complementary information that improves diagnostic sensitivity and resolution.
- **Detection of Circulating Tumor Cells (CTCs):** Polymeric nanoparticles can be functionalized with antibodies or aptamers that recognize and bind to specific markers on circulating tumor cells (CTCs) in the bloodstream. This facilitates the non-invasive detection of cancer at early stages, monitoring of metastasis, and assessment of treatment response.
- **Biosensors**: Nanoparticles can be designed as part of biosensors that detect molecular biomarkers associated with cancer. These biosensors can be used in a point-of-care setting for rapid and sensitive detection of

cancer biomarkers in bodily fluids like blood, saliva, or urine.[11]

Approaches for Nanoparticle-Based Drug Delivery Across the BBB

- **Size and Surface Modification**:
  - The ideal size for nanoparticles to cross the BBB is usually below 100 nm. Nanoparticles larger than this are typically cleared by the body, while smaller nanoparticles may not have sufficient interaction with the BBB. By modifying the surface of nanoparticles with certain molecules (e.g., PEG (polyethylene glycol), ligands, or peptides), their ability to pass through the BBB can be enhanced.
  - **Surface functionalization** can improve the BBB crossing efficiency by allowing the nanoparticles to interact with specific receptors or transporters on the endothelial cells of the BBB.
- **Active Targeting**:
  - Active targeting involves the attachment of targeting ligands to the surface of nanoparticles, which interact with specific receptors expressed on the BBB or on cells involved in transcytosis (e.g., transferrin receptor, low-density lipoprotein receptor, insulin receptor). o Ligands such as transferrin, apolipoproteins, opioid peptides, and R8 peptides are commonly used to enhance the targeting and uptake of nanoparticles by the brain.
- **Transcytosis and Endocytosis**:
  - **Receptor-mediated transcytosis** (RMT) and adsorptive-mediated transcytosis are key mechanisms through which nanoparticles can cross the BBB. In these processes, nanoparticles are absorbed by endothelial cells and transported across the BBB in vesicles.
  - **Endocytosis** (clathrin-mediated or caveolae-mediated) is another mechanism by which nanoparticles, especially those functionalized with targeting ligands, are internalized into cells and translocated across the BBB.
- **Nanocarrier Types for BBB Penetration**:
  - **Liposomes**: Liposomes are lipid-based nanoparticles capable of encapsulating both hydrophilic and lipophilic drugs. When functionalized with ligands (e.g., transferrin or antibodies), liposomes can cross the BBB efficiently.
  - **Polymeric Nanoparticles**: Nanoparticles made from biodegradable and biocompatible polymers such as **PLGA** (poly (lactic-co-glycolic acid)), **PLA** (poly (lactic acid)), and **PEG** can encapsulate drugs and cross the BBB through receptor-mediated mechanisms.
  - **Solid Lipid Nanoparticles (SLNs)** and Nanostructured Lipid Carriers (NLCs): SLNs and NLCs are alternatives to liposomes that are used to improve drug stability and increase the delivery of lipophilic drugs to the brain.[12]

➢ **Improved Drug Delivery and Targeting**

- **Advantage**: Polymer nanoparticles can be engineered to improve the solubility, stability, and controlled release of drugs, enhancing drug bioavailability and reducing side effects.[13] **2. Controlled Release Properties**
- **Advantage**: Polymer nanoparticles can provide sustained and controlled release of active compounds, ensuring prolonged therapeutic effects.[14]

3. Biocompatibility and Biodegradability

- **Advantage**: Polymers such as PLGA (Poly (lactic-co-glycolic acid)) are biodegradable, making them suitable for medical applications as they do not accumulate in the body.[15] **4. Versatility in Functionalization**
- **Advantage**: The surface of polymer nanoparticles can be easily modified with targeting ligands, antibodies, or other molecules to improve specificity for target cells or tissues.[16] **5. Enhanced Cellular Uptake**
- **Advantage**: Due to their small size, polymer nanoparticles can easily penetrate biological barriers, enabling enhanced cellular uptake and intracellular delivery.[17]

➢ **Significance of polymeric nanoparticles**

1. Enhanced Drug Delivery and Bioavailability

- **Significance**: Polymer nanoparticles can significantly improve the bioavailability of poorly soluble drugs, enabling efficient delivery and improving the therapeutic effects of drugs. By encapsulating drugs, they prevent early degradation and enhance absorption at target sites.[18]

2. Targeted and Controlled Drug Delivery

- **Significance**: Polymer nanoparticles can be designed for targeted drug delivery by modifying their surface properties with ligands, antibodies, or other targeting molecules, allowing them to direct drugs to specific cells or tissues (e.g., tumor cells).[19]

➢ **Challenges associated with nanoparticle drug delivery systems:**

1 Toxicity and Biocompatibility

o **Nanotoxicity**: The small size and large surface area of nanoparticles may lead to unexpected interactions with biological systems, causing cellular damage, oxidative stress, or inflammation. Nanoparticles can accumulate in vital organs such as the liver, kidneys, and spleen, causing toxicity and disrupting normal cellular functions. This poses a significant barrier to their clinical use.[20]

2. Manufacturing and Scalability

o **Production Challenges**: The synthesis of nanoparticles with uniform size, shape, and surface properties is technically difficult and costly. Scaling up the production process from laboratory to industrial scale while maintaining the quality of nanoparticles remains a significant hurdle.[21]

3. Regulatory and Safety Concerns

o **Regulatory Approval**: Regulatory agencies such as the FDA require comprehensive preclinical and clinical data on the safety and efficacy of nanoparticles, which can be challenging to generate due to the complexity of nanoparticles and their behaviour in biological systems.[22]

4. Drug Release Control

o **Unpredictable Release Profiles**: The controlled and sustained release of drugs from nanoparticles can be difficult to achieve due to variations in the environment (e.g., pH, temperature) and the properties of the drug. The instability of the drug or nanoparticle can also affect the release profile.[23]

5. Immune Response

o **Immunogenicity and Clearance**: Nanoparticles are often recognized as foreign bodies by the immune system, triggering the formation of a protein corona and leading to rapid clearance by the reticuloendothelial system (RES).

This limits their circulation time and reduces their therapeutic effectiveness.[24]

6. Targeting and Specificity

o **Achieving Effective Targeting**: While nanoparticles can be engineered to target specific cells or tissues, achieving precise and selective targeting remains a major challenge. Nanoparticles often accumulate non-specifically in other organs, such as the liver and spleen, leading to off-target effects.[25]

7. Pharmacokinetics and Biodistribution

o **Biodistribution Variability**: The distribution of nanoparticles within the body can be unpredictable, with significant variations depending on their surface characteristics, size, and shape. This can result in uneven distribution in target tissues and unintended accumulation in non-target organs.[26]

8. Cost and Affordability

o **High Production Costs**: The complex processes involved in nanoparticle synthesis, functionalization, and scale-up contribute to the high costs of nanoparticle-based drug delivery systems. This can limit their commercial viability, especially for diseases that require affordable treatments.[27]

9. Environmental and Ethical Considerations

o **Environmental Impact**: The disposal and degradation of nanoparticles in the environment is a growing concern. The release of nanoparticles into the environment can have unforeseen consequences on ecosystems, necessitating the development of biodegradable or environmentally friendly materials for their synthesis.[28]

CONCLUSION:

Polymeric nanoparticles are highly significant in modern medicine and pharmaceutical applications due to their versatility, biocompatibility, and ability to enhance drug delivery. They enable controlled release, targeted therapy, and improved stability of therapeutic agents, offering solutions for challenging diseases such as cancer and genetic disorders. Their customization potential and low toxicity make them a promising tool for personalized medicine and diagnostics, shaping the future of healthcare.

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