



International Journal of Research in Pharmacy and Life Sciences
 Home Page: <https://pharmaresearchlibrary.org/journals/index.php/ijrpls>
 CODEN (USA): IJRPL | e-ISSN: 2321-5038 | Publisher: Pharma Research Library
 Int. J. Pharm. Natural Med., 2025, 13(2): 58-64
 DOI: <https://doi.org/10.30904/j.ijrpls.2025.4857>



Polymer Based Nanocarriers: A Promising Platform for Targeted Drug Delivery

Katta Sai Manu¹, Sarvepalli Revathi*², Battala Divya³, Kunda Varalakshmi³, K Charunya³, Ediga Vardhan³, Yerikala Ramesh⁴, Penabaka Venugopalaiah⁴, Yadala Prapurna Chandra⁵

¹IV-year B Pharmacy, Ratnam Institute of Pharmacy, Pidathapolur (V&P), Muthukur (M), SPSR Nellore-524 346.

²Associate Professor, Department of Pharmaceutics, Ratnam Institute of Pharmacy, Pidathapolur (V&P), Muthukur (M), SPSR Nellore- 524 346.

³IV-year B Pharmacy, Ratnam Institute of Pharmacy, Pidathapolur (V&P), Muthukur (M), SPSR Nellore - 524 346.

⁴Professor, Department of Pharmaceutics, Ratnam Institute of Pharmacy, Pidathapolur (V&P), Muthukur (M), SPSR Nellore - 524 346.

⁵Professor and Principal, Ratnam Institute of Pharmacy, Pidathapolur (V&P), Muthukur (M), SPSR Nellore-524 346.

ABSTRACT

Polymer-based nanocarriers have revolutionized modern drug delivery by offering precise control over therapeutic release, enhanced bioavailability, and reduced off-target effects. Owing to their tunable physicochemical properties, biocompatibility, and structural versatility, these nanocarriers provide an adaptable platform for the delivery of a wide range of drugs, including small molecules, peptides, and nucleic acids. Various polymeric systems such as micelles, dendrimers, nanogels, and polymeric nanoparticles have been designed to respond to specific biological or environmental stimuli, including pH, temperature, redox potential, and enzymatic activity, thereby ensuring site-specific and controlled drug release. Both natural (e.g., chitosan, alginate, gelatin) and synthetic (e.g., PEG, PLGA, polylactic acid) polymers have been explored to fabricate nanocarriers with desirable mechanical strength, degradation profiles, and surface functionality. However, despite these advances, challenges related to large-scale synthesis, reproducibility, stability, and long-term safety remain key hurdles for clinical translation.

Keywords: Polymer-based nanocarrier, drug delivery system, polymeric nano particles, targeted delivery, micelles, dendrimers.

ARTICLE INFO

Corresponding Author

Sarvepalli. Revathi
 Associate Professor, Department of Pharmaceutics
 Ratnam Institute of Pharmacy
 Pidathapolur (V&P), Muthukur (M), SPSR Nellore- 524 346.

Article History

Received : 25 July 2025
 Revised : 31 Aug 2025
 Accepted : 29 Sep 2025
 Published : 20 Oct 2025

E-Mail ID: revathisarvepalli1990@gmail.com | Mobile no: 7780760442 | ORCID: <https://orcid.org/0009-0009-4339-2693>

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Citation: Katta Sai Manu, *et al.* Polymer Based Nanocarriers: A Promising Platform for Targeted Drug Delivery. Int. J. Res. Pharm, L. Sci., 2025, 13(2): 58-64.

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1. Introduction

In recent times, the use of nanotechnology aimed at developing cancer medicines and nanocarriers has increased fleetly. Nanotechnology has a very wide range of applications and also has the potential to make a significant impact in bio-technology, healthcare, drug delivery,

electronics, storage systems, and industries. For example, in nanomedicine, there is an increasing research interest in the development of various systems, such as nano-carriers for drug delivery to targeted cells such as cancer cells or infections/neurodegenerative disorders⁽¹⁾. The integration

and co-delivery of both drugs and photo absorbers with double cargo nanocarriers are feasible:[1]nanocarriers have plenty space to accommodate both agents ⁽²⁾ ;[2] some nanoscale photothermal materials per se can load drugs to constitute nanocarriers ; [3] photo absorbers produce heat that can trigger the release of drugs ⁽³⁾ ;[4] the hydrophilic moiety of the polymer improves the bioavailability, stability and security of nanocarriers. In summary, the in vivo route and action of the double-cargo nanocarriers are illustrated in Figure1.

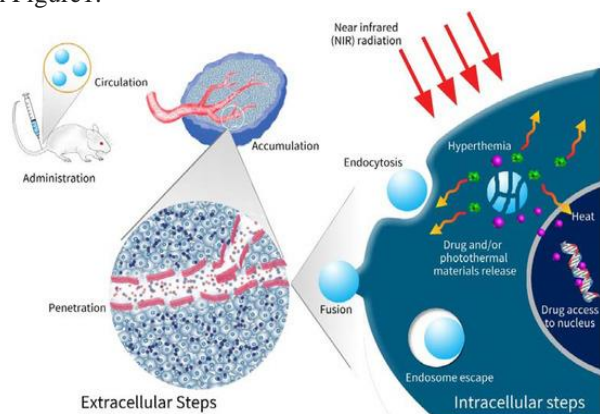


Fig.1: Schematic illustration of nanocarriers exerting therapeutic effects in vivo.

After administration, the drug-loaded photothermal nanocarriers navigate to tumors through the blood circulation. Owing to the enhanced permeability and retention (EPR) effects, the nanocarriers penetrate tumor tissues across vessel walls of tumor vasculature, leading to accumulation within tumors.

A large number of studies have concentrated on nanocarriers as effective individual or remedial tools for serious conditions, similar as cancer, contagious or neurodegenerative conditions. Besides, nanocarriers could not only ameliorate the solubility of hydrophobic nutraceuticals more efficiently, but also, they've nearly no effect on the appearance of final food products, similar as, drinks and potable ⁽⁴⁾. In general, nanocarriers are colloidal in size with diameters ranging from 1 to 1,000 nm. Further research into the pathogenesis of cancer has led to new treatment options, including targeted therapy and immune therapy. Targeted chemotherapy substantially uses molecular targeted medicines to block specific moles and metabolic pathways in excrescence cell growth and proliferation. In particular, the more targeted the drug, the lower the possibility of drug resistance. The clinical success of immunotherapy has revolutionized the treatment of a variety of advanced malignant tumors ⁽⁵⁾.

2. Classification

Table 1: Classification of Polymer-Based Nanocarriers

Basis of classification	Types	Description	Examples
Polymer source	Natural polymers	Biodegradable, biocompatible, less toxic	Chitosan, Alginate, Gelatin, Dextran
	Synthetic polymers	Tunable properties, controlled synthesis, may require surface modifications	PLA, PLGA, PEG, PCL
Structural Organization	Polymeric nanoparticles	Solid colloidal systems: nanospheres (matrix type) and nanocapsules	PLGA nanoparticles, chitosan nanocapsules
	Polymeric micelles	Amphiphilic copolymers self-assemble into core-shell structures	PEG-PLA micelles, PEG-PCL micelles
	Dendrimers	Highly branched, nanosized polymers with modifiable surface groups	PAMAM dendrimers, PLL dendrimers
	Polymersomes	Vesicle-like nanocarriers from block copolymers, encapsulate hydrophilic & hydrophobic drugs	PEG-PLA polymersomes
	Hydrogels/Nanogels	Crosslinked hydrophilic networks, swell in water, responsive release	PEG-based nanogels, chitosan nanogels
Stimuli Responsiveness	pH-responsive	Release triggered in acidic microenvironments	Poly(histidine)-PEG micelles
	Temperature-responsive	Drug release at hyperthermic conditions	PNIPAAm-based carriers
	Enzyme-responsive	Degradable by disease-associated enzymes	MMP-sensitive hydrogels
	Redox/ROS-responsive	Triggered by GSH or ROS in pathological tissues	Disulfide-crosslinked nanogels
	Multi-stimuli responsive	Combination of pH, redox, enzyme, or	Dual pH/ ROS-sensitive

		temperature	micelles
Drug Release Mechanism	Diffusion-controlled	Drug diffuses through polymer matrix	PLGA nanospheres
	Degradation-controlled	Polymer degradation governs release	PLGA nanoparticles
	Swelling-controlled	Swelling in aqueous environment leads to release	Hydrogel nanogels
	Stimuli-controlled	Internal/external stimuli trigger release	Magnetic/ultrasound-sensitive carriers

2.1 Polymeric Micelles:

The most common and stable nanostructures of amphiphilic macromolecules in aqueous media are polymeric micelles and vesicles^(6,7). Various types of polymeric micelles can be obtained via the self-assembly of amphiphilic copolymers and are broadly studied for drug delivery⁽⁸⁾. Exploiting the inter-molecular interactions, these micelles can also be designed as mixed, flower-like, multicompartamental, star-like, and dendritic micelles Figure2. Their sizes may vary from 20 to 200 nm⁽⁹⁾.

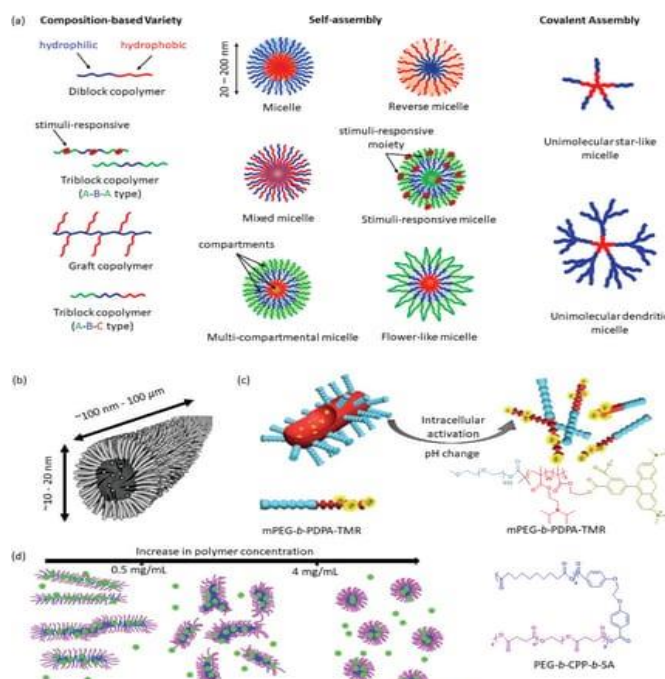


Fig.2: a) Various polymeric nanomicelles that can be fabricated depending on the architectures of copolymers and inter-chain interactions. b) Schematic donation of a wormlike micelle having hydrophobic core girdled by hydrophilic blocks of amphiphilic polymers. Reproduced with permission. Copyright 2003, American Chemical Society. c) Intracellular pH-activated drug release from wormlike micelle composed of dye-tagged diblock copolymer. Copyright 2010, Royal Society of Chemistry. d) Concentration dependent self-assembly mechanism of micelle formation composed of triblock biodegradable copolymer poly (ethylene glycol)-b-1,3-bis(p-carboxy phenoxy) propane-b-sebacic acid (PEG-b-CPP-b-SA).

2.2 Polymeric Dendrimers:

Dendrimers are other starburst macromolecules that belong to the nanoscale drug delivery regime. The idea of

dendrimers was first proposed by Flory, who was first synthesized by Voegtle⁽¹⁰⁾ in 1978. The word 'Dendrimer' is derived from the Greek words 'dendron' and 'meros', which mean tree and part, respectively⁽¹¹⁾. Figure3 shows a diagrammatic representation of the dendrimer structure. The inner core builds coops and channels' to insure the easy creation of raying units, thereby accommodating bioactive principles.

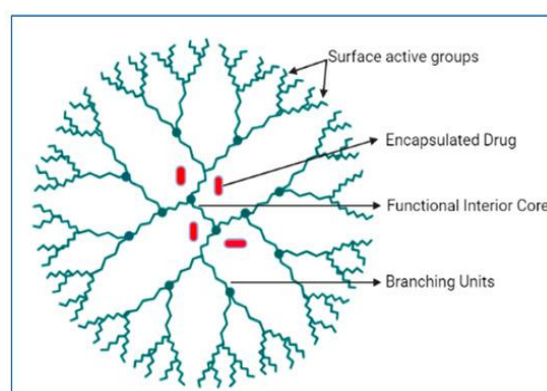


Fig.3: Diagrammatic representation of the dendrimer structure (created with BioRender.com, accessed on 25 August 2022).

Thus, polymeric dendrimers are being progressively used in the delivery of bioactive agents such as drugs, oligonucleotides, enzymes, vaccines, and genes⁽¹²⁾. They have also been found to be suitable for drug-specific, as well as, site-specific nanocarrier design in anticancer therapy⁽¹³⁾.

2.3 Polymeric Nanogels:

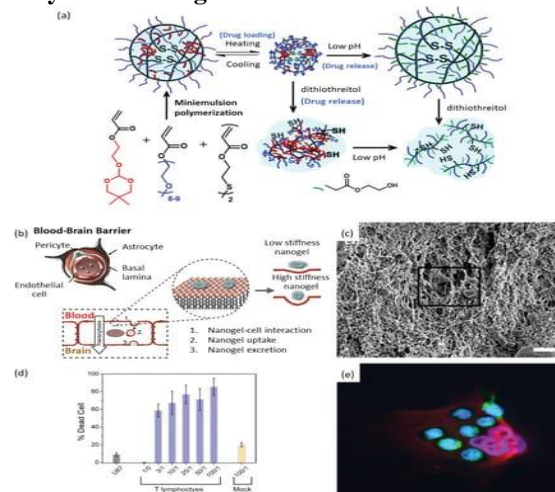


Fig.4: a) A schematic presentation of nanogel synthesis by miniemulsion polymerization and its pH-responsive drug

release phenomena for cancer therapy. Reproduced with permission. Copyright 2011, Elsevier. b) Nanogel transcytosis across an in vitro blood- brain hedge eased by low nanogel stiffness. Reproduced under the terms of a Creative Commons Attribution 4.0 International License. Copyright 2021, The Authors. published by Elsevier. c) The scanning electron microscopic image of T lymphocyte invading through the poly (ethylene glycol)-g-chitosan gel. d) Percent of tumor cell death caused by T lymphocyte treatment at various T lymphocyte/U87 ratios (1/0, 3/1, 100/1). e) Fluorescence image of T lymphocytes (green) attached to U-87 MG cells (red) after crossing through the trans well membrane mimicking the blood-brain barrier under in vitro test condition.

In recent years, nanogels have got popularized due to their high loading capacity and improved stability⁽¹⁴⁾. They are polymeric 3D nanostructures, and their properties can be tailored. These nanogels can be designed in various structures, such as, simple nanogel sphere, core-shell, hollow, functionalized, hairy, multilayer, etc⁽¹⁵⁾. Nanogels can be prepared as stimuli-responsive for drug delivery. Nanogels can be prepared as stimuli-responsive for drug delivery. They are responsive to temperature, pH, light, magnetic field, biomolecule recognition, Figure4⁽¹⁶⁾.

2.4 Polymeric Vesicles:

Polymeric vesicles, also known as polymersomes, are PNCs that have a bilayer membrane composed of a hydrophobic layer trapped between hydrophilic core and hydrophilic shell Figure5⁽¹⁷⁾. The size of vesicles plays important roles in regulating circulation time, RES recognition, biodistribution, and process of cellular uptake. Considering these processes, the optimum sizes of vesicles are expected to be in the range of 80–150 nm⁽¹⁸⁾.

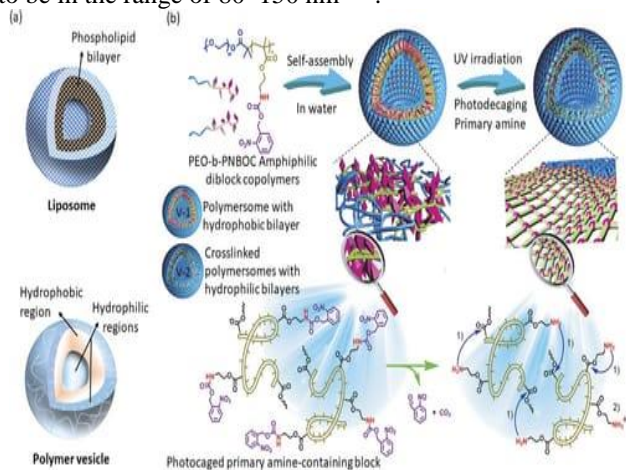


Fig.5: a) Schematic presentation of liposome and polymer nanovesicle. b) A novel photo-responsive polymersome capable of co-loading both the hydrophilic and hydrophobic drugs. Reproduced with permission.

Two main strategies of loading vaccine antigens or nucleic acid cargoes onto the nanovesicles are: i) Loading on the surface, and ii) encapsulation at the core. Having these cargoes loaded on the nanocarrier surface can lead to potent immunogenicity, while the encapsulated active agents at the

core can stay protected and thereby demonstrate controlled delivery⁽¹⁹⁾.

3. Design and Structural Features

3.1 Structure-Based Variety of Polymeric Nanocarriers:

Researchers interest in the study of PNCs emerged mainly due to the advantages of personalized drug administration, increased bioavailability, sustained release from a single dose, and capability of safe carriage until delivered to the targeted site. Traditional medication has numerous challenges like continuous administration of the medicine with a shorter half-life, diminished patient consistency, high and ordinary peak-valley plasma concentration-time profile, and so on. They can load drugs, proteins, DNA, or RNA and defend them from denaturation and carry to targeted cells or tissue. To the matrix of polymer nanoparticles, the medicine or any other composites can get dissolved, attached, entangled, or reprised, counting on different lading ways.

3.2 Biodegradable Polymeric Nanocarriers:

A concern about the use of non-biodegradable polymeric nanostructures is that they may lead to problems like chronic toxicity and high immunological response. There has been great potential of BPNCs in medical applications as they can play significant role in diagnosis for the treatment of different types of diseases, in medical imaging, biomarkers, biosensors, nanomachines, nano-robots, and nano drug delivery systems low cytotoxicity^(20,21). BPNCs are being chemically engineered to develop highly selective and stable properties for advanced applications Figure6. Examples of some biodegradable polymers used for designing PNCs polyesters, polyamides, polysaccharides, proteins, polyphosphorous, and polyanhydrides⁽²²⁻²⁴⁾.

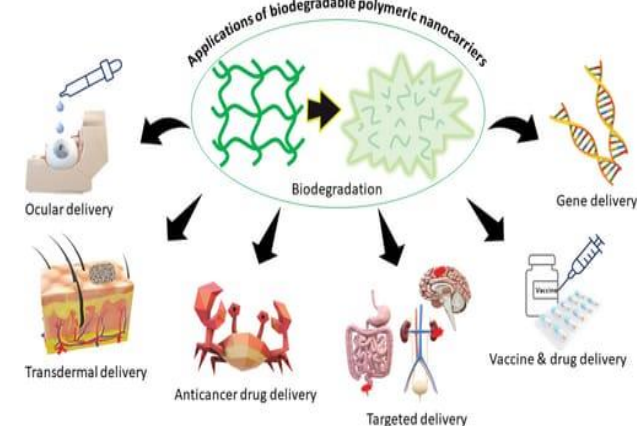


Fig.6: Examples of some advanced applications of biodegradable polymers and their nanostructures in disease treatment.

3.3 Shape and Architecture:

Recently, nanocarriers of colorful shapes and infrastructures are being precipitously delved to explore their influences on efficacy of medicine transport. However, the use of elongated or filament-like morphologies are also being increasingly studied as they can offer extended lifetime in the circulatory system along with higher efficacy of cargo carriage⁽²⁵⁾. The dynamic

micelle was formed by the tone- assembly of amphiphilic polymer motes while the unimolecular micelle was covalently bound amphiphilic macromolecular micelle. It's observed that, in the unicellular and dynamic micelles the efficacy of lading depended primarily on the hydrodynamic volume of medicines. Here, the unimolecular micelle exhibited higher loading capacity in comparison to the dynamic micelle. Still, their release did not show strong dependence on the infrastructures of micelle.

3.4 Surface Properties:

Surface parcels of a nanocarrier can greatly impact its continuance in several ways. Once the nanocarrier is administered via intravenous pathway, its commerce with the mucus, epithelia etc can determine the continuance in the circulatory system. Latterly, high viscosity of cut defied the dissociation of the micelle in the media having the serum protein.

Therefore, face property of nanomicelle can regulate the stability and thereby achieve bettered targeted delivery. face charge also influences the colloidal stability of nanocarrier-grounded medicine phrasings which thereby impacts the shelf- life of several drugs. For illustration, PNCs having their face decorated with amphiphilic polymers favors cell piercing pathway.

3.5 Core Shell Structured Nanocarriers:

Different platforms of nanocarriers have different structures, coupled with different medication styles. According to their structures, we classify utmost of nanocarriers into two introductory orders core- shell structured bones and frame- fleece structured bones . Core-shell Structured Nanocarriers Figure7 commonly have a hydrophobic core where drug molecules are encompassed and a hydrophilic shell which has a direct contact with the outside world, e.g., aqueous solutions or mice blood.

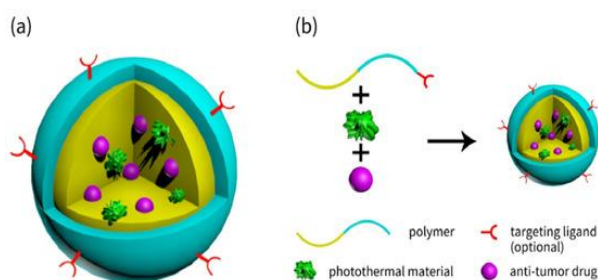


Fig.7: Schematic illustration of (a) the core-shell structured nanocarriers and (b)the preparation process of such nanocarriers.

4. Mechanism of Polymer Based Nanocarriers

Understanding the fate of nanoparticles in cells constituting the intestinal epithelium is critical for development of new efficient oral nanocarriers. To study the mechanisms of nanoparticle transport across the intestinal hedge, *in vitro* models have been used. They can act directly or indirectly on tight junction component. The pathway used for internalization of nanoparticles will depend on physicochemical characteristics of the particle and the cell type ⁽²⁶⁾. Human M-like cells *in vitro* model has been well described ⁽²⁷⁾ and allows quantitative and mechanistic transport studies of particles.

4.1 Stimuli Responsive Nanocarriers:

A major area of the recent research in drug delivery science is focused on developing stimuli-responsive nanocarriers by exploiting the availability of various natural, as well as, synthetic polymers which are extremely sensitive to their environmental changes. This is a promising approach of delivering weight to a specific point at the asked time, that is, the targeted delivery. Production of temperature-sensitive drug delivery carrier is typically demanding and requires the selection of a polymer that is both safe and responsive to minor changes in temperature around the normal physiological body temperature (37°C). Other internal stimuli like hypoxia and glucose have also been widely studied for their suitability in nanomedicine formulation ⁽²⁸⁾.

5. Applications

5.1 Chemotherapy Based on Polymer Nanocarrers:

Chemotherapy is the most common treatment for cancer ⁽²⁹⁾. As is well-established, chemotherapeutic medicines can be divided into alkylating agents ⁽³⁰⁾, antimetabolites ⁽³¹⁾, antitumor antibiotics ⁽³²⁾, antitumor factory and beast constituents ⁽³³⁾, antitumor hormones etc. Unfortunately, the current clinical application of antitumor chemotherapeutic drugs has led to unforeseen toxicity and side effects, thus limiting the drug dosage and use. When they kill tumor cells, they also damage normal tissue cells ^(34,35).

5.2 Gene Therapy Based on Polymer Nanocarriers:

Gene therapy is a technology that treats or cures diseases by modifying a person's genes. Gene therapy can work through the following mechanisms:(i) replacing disease-causing genes with healthy genes;(ii) inactivating disease-causing genes;(iii) introducing new or modified genes into the body to help treat diseases ⁽³⁶⁾. In addition, NDDSs can maintain their functions while improving the bioavailability of drugs and reducing off-target effects. Among existing nanocarriers, polymer nanocarriers are attracting a great deal of attention due to their non-toxicity, low immunogenicity, and high biocompatibility.

5.3 Combination therapy Based on Polymer Nanocarriers:

Cancer is a complex disease driven by multiple gene mutations, and its progression involves interaction between cancer cells and their microenvironment ⁽³⁷⁾. Compared to single-agent therapy, combination chemotherapy has shown better clinical treatment effects, especially in delaying the development of cancer chemotherapy resistance. In order to solve this problem, the use of two or more drugs with different pharmacological mechanisms for combined therapy is a promising treatment strategy ⁽³⁸⁾.

6. Future Perspectives

Polymer-based nanocarriers hold immense promise for the future of advanced drug delivery and precision medicine. Ongoing research is directed toward creating safer, biodegradable, and biocompatible systems that can overcome biological barriers while minimizing toxicity. The focus is increasingly on smart nanocarriers that respond to internal or external stimuli, enabling controlled and site-specific release of drugs. Their potential extends beyond

conventional therapeutics, as they are being explored for gene and protein delivery, cancer immunotherapy, and regenerative medicine. Integration of therapeutic and diagnostic functions within a single platform is also opening opportunities for personalized treatment approaches. Despite these advancements, challenges related to large-scale production, stability, and regulatory approval must be addressed before their full clinical potential can be realized, making polymer-based nanocarriers an exciting yet evolving field in biomedical research.

7. Conclusion

Polymer-based nanocarriers represent a pivotal advancement in the design of next-generation drug delivery systems. Their ability to encapsulate diverse therapeutic agents, provide controlled and stimuli-responsive release, and enhance pharmacokinetic profiles makes them superior to conventional formulations. By integrating smart polymers, surface modification techniques, and nanotechnological principles, these systems can achieve targeted delivery, minimize systemic toxicity, and improve patient compliance. Recent developments in multifunctional and biomimetic polymer systems have expanded their applications to areas such as cancer therapy, neurodegenerative disorders, vaccine delivery, and gene therapy. Nevertheless, translation from laboratory to clinical settings demands overcoming challenges related to large-scale manufacturing, stability during storage, regulatory approval, and long-term biocompatibility. Interdisciplinary collaborations combining polymer science, nanotechnology, materials engineering, and pharmacology are crucial to bridge this gap. Looking forward, polymer-based nanocarriers hold immense promise as a foundation for precision medicine, personalized therapeutics, and sustainable healthcare innovations.

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Source of Support: Nil.