



Paper Type: Original Article

## Biopolymers As Smart Drug Carriers in Cancer Therapy: Innovations and Perspectives

Nazanin Malek Mohammadi\* 

Mechanical Engineering Department, Morvarid Intelligent Industrial Systems Research Group, Iran;  
malekmohammadii.nazanin@gmail.com.

### Citation:

Received: 16 November 2024

Revised: 22 March 2025

Accepted: 06 May 2025

Malek Mohammadi, N. (2025). Biopolymers as smart drug carriers in cancer therapy: Innovations and perspectives. *Biocompounds*, 2(3), 138–150.

### Abstract

Cancer continues to pose a major global health burden, largely due to the limitations of conventional therapies, including non-specific drug distribution, systemic toxicity, and the emergence of multidrug resistance. Biopolymer-based smart drug delivery systems have emerged as promising platforms that can enhance tumor selectivity and therapeutic efficacy while reducing adverse effects. Natural and synthetic biopolymers offer key advantages, including biocompatibility, controlled biodegradability, tunable surface functionality, and the ability to form diverse nanoscale architectures that enable precise drug loading and targeted release. Recent advances have demonstrated the potential of biopolymer-derived nanoparticles, micelles, hydrogels, nanogels, and polymer-drug conjugates to respond to tumor-specific stimuli, including pH gradients, enzymatic activity, hypoxia, and external triggers. This review highlights major classes of biopolymers, design strategies for targeted and stimuli-responsive delivery, and their therapeutic applications across chemotherapy, gene delivery, and immunomodulation. Key challenges such as scalability, stability, and clinical translation are critically examined, and future perspectives are provided to guide the development of next-generation biopolymer-based smart carriers for precision cancer therapy.

**Keywords:** Biopolymer, Drug delivery, Nanoparticles, Cancer, Hydrogel.

## 1 | Introduction

Cancer is one of the leading causes of mortality worldwide. Despite major therapeutic advances, conventional treatments such as chemotherapy continue to face major limitations, including non-specific biodistribution, systemic toxicity, and unintended damage to healthy tissues [1]. Many commonly used chemotherapeutic agents, such as doxorubicin, exert cytotoxic effects on rapidly dividing normal cells, leading to adverse outcomes including alopecia, bone marrow suppression, and dose-dependent cardiotoxicity [2]. Furthermore, intrinsic and acquired tumor drug resistance driven by genetic mutations, overexpression of efflux pumps, alterations in intracellular signaling, and changes in metabolic pathways remains a significant barrier to successful therapy [3]. These challenges underscore the urgent need for more selective and efficient drug-

 Corresponding Author: malekmohammadii.nazanin@gmail.com

 <https://doi.org/10.48313/bic.vi.41>

 Licensee System Analytics. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).

delivery strategies. Targeted drug delivery systems aim to deliver therapeutic agents specifically to tumor tissue while minimizing off-target effects. By enhancing drug accumulation at the tumor site, these systems can increase therapeutic efficacy, reduce required dosages, and improve patient safety profiles [4]. Advances in nanotechnology have enabled the fabrication of nanoparticles smaller than 200 nm that exploit the Enhanced Permeability and Retention (EPR) effect to pass through leaky tumor vasculature and accumulate in tumor interstitium [5]. However, the EPR effect is highly heterogeneous across tumor types. It is influenced by factors such as vascular density, interstitial fluid pressure, stromal composition, and the overall complexity of the Tumor Microenvironment (TME) [6]. Consequently, passive targeting alone may not be sufficient for effective drug delivery.

Biopolymers have emerged as highly promising materials for the design of targeted drug delivery systems due to their excellent biocompatibility, predictable biodegradability, structural versatility, and broad chemical modifiability [7]. Natural biopolymers, including chitosan, alginate, Hyaluronic Acid (HA), gelatin, and synthetic biodegradable polymers such as Polylactic Acid (PLA), Polylactic-co-Glycolic Acid (PLGA), and Polycaprolactone (PCL), can encapsulate a wide range of therapeutic payloads, including hydrophilic and hydrophobic small-molecule drugs, nucleic acids, and proteins [8]. Their functional groups enable surface conjugation with targeting ligands such as folic acid, RGD peptides, antibodies, or aptamers, thereby enhancing selective uptake by cancer cells [9]. Moreover, some biopolymers possess innate targeting capabilities. For example, HA binds naturally to CD44 receptors, which are overexpressed in many tumors, providing an additional mechanism for active targeting [10]. Given the expanding role of biopolymers in cancer nanomedicine, a comprehensive assessment of their categories, targeting strategies, nano architectures, and translational challenges is essential [11]. This review aims to provide an updated and systematic overview of natural and synthetic biopolymers used in targeted anticancer drug delivery, evaluate their design principles and therapeutic potential, and highlight emerging concepts such as stimuli-responsive smart carriers and multifunctional hybrid platforms [12], [13]. These advancements are expected to contribute significantly to the development of next-generation precision therapeutics.

## 2 | Structure of Biopolymers

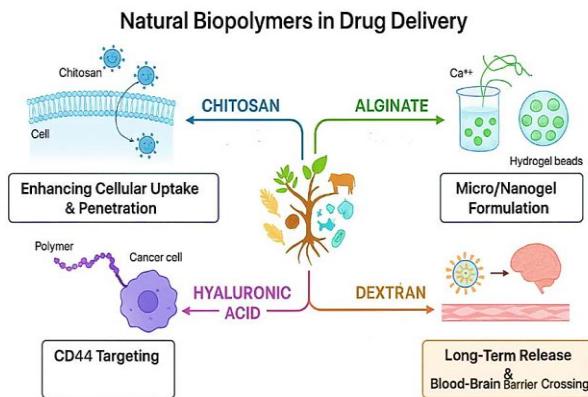
### 2.1 | Natural Biopolymers

Natural biopolymers are derived from biological sources, including animals, plants, and microorganisms. Owing to their inherent biocompatibility, low toxicity, and high biodegradability, they are among the most attractive candidates for next-generation drug delivery systems [14]. This class encompasses polysaccharides and proteins such as chitosan, alginate, gelatin, HA, and dextran, all of which can be engineered into various nano and microstructured platforms such as nanoparticles, nanogels, and hydrogels to enable efficient encapsulation and controlled release of therapeutic agents (*Fig. 1*) [15], [16].

- I. Chitosan is one of the most widely utilized natural polymers in drug delivery. Produced through the deacetylation of chitin, it carries a positive surface charge under physiological conditions, allowing electrostatic interactions with negatively charged cell membranes. These interactions enhance cellular adhesion, improve internalization, and facilitate deeper drug penetration. Additionally, chitosan's pH responsiveness makes it particularly advantageous for TME-activated release [17].
- II. Alginate is an anionic polysaccharide known for its excellent gel-forming ability. In the presence of divalent cations such as calcium, alginate undergoes ionic crosslinking to form stable hydrogel networks. This property makes it highly suitable for designing microgels and nanogels with high encapsulation efficiency and tunable mechanical stability for drug and gene delivery applications [18].
- III. HA is another key natural biopolymer, largely due to its specific affinity for the CD44 receptor, which is overexpressed in many cancer types. This intrinsic targeting capability enables HA-based nanocarriers to accumulate preferentially in tumor tissues and enhances active uptake via receptor-mediated endocytosis.

HA can also be chemically modified via methacrylation, thiolation, or conjugation to improve stability and stimulus responsiveness [19].

IV. Dextran is a linear polysaccharide that has been widely used in pharmaceutical formulations due to its high water solubility and ease of chemical functionalization [20]. Its hydroxyl-rich backbone enables conjugation to drugs, targeting moieties, or stimuli-responsive groups, allowing the construction of versatile nanosystems with controlled release profiles [21]. Dextran-based nanocarriers have shown promising results in enhancing tumor penetration, prolonging systemic circulation, and, in some cases, enabling delivery across the blood-brain barrier [22].



**Fig. 1. Major natural biopolymers used in anticancer drug delivery systems.**

## 2.2 | Synthetic Biopolymers

Synthetic biopolymers have emerged as key materials in advanced anticancer drug delivery systems due to their tunable physicochemical properties and the ability to precisely engineer parameters such as Molecular Weight (Mw), composition, architecture, and degradation rate [23]. These polymers are designed to achieve optimal biocompatibility while providing controlled, sustained, or stimuli-responsive release of therapeutic agents during circulation and within tumor tissues. Among the most widely applied synthetic biopolymers are poly PLGA, PLA, PCL, and Polyethylene Glycol (PEG), each offering distinct advantages in terms of biodegradability, stability, safety, and regulatory approval [24]. PLGA and PLA degrade into non-toxic metabolic byproducts, making them ideal for implantable or injectable systems, whereas PCL offers slower degradation, suitable for long-term delivery. PEG, on the other hand, remains essential due to its hydrophilicity, stealth properties, and ability to reduce opsonization and prolong circulation time. Synthetic biopolymers can be engineered into diverse nanostructures, including nanoparticles, micelles, nanocapsules, polymer-drug conjugates, and smart hydrogels, depending on the physicochemical properties of the therapeutic agent and the desired release profile [25]. Moreover, through advanced surface engineering techniques such as PEGylation, ligand conjugation (including folate, antibodies, and peptides), and charge modulation, these systems can enhance tumor-specific accumulation, reduce immune clearance, and improve the therapeutic index [26]. Recent advancements also highlight the development of stimuli-responsive synthetic polymers capable of responding to pH, redox potential, enzymes, hypoxia, or external triggers such as temperature, ultrasound, and light, enabling precise, on-demand drug release in the TME. *Fig. 2* depicts synthetic biopolymers, which are precisely engineered for applications such as targeted anticancer drug delivery. Also, *Table 1* provides a comparative overview of commonly used biopolymers, highlighting their biocompatibility, active targeting capabilities, ability to penetrate the blood brain barrier, and primary applications in anticancer drug delivery.

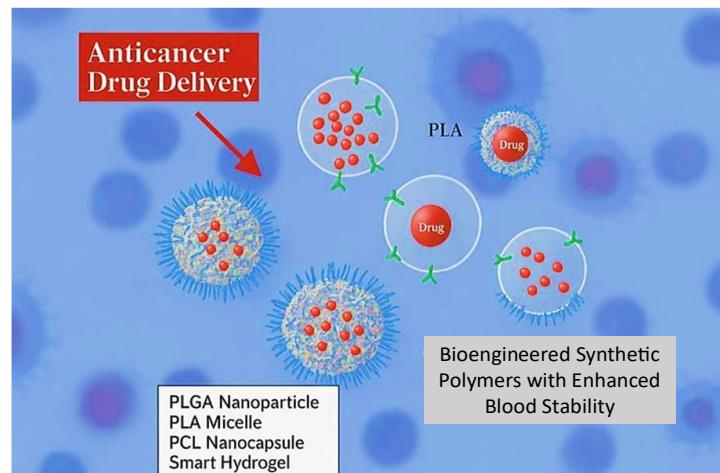


Fig. 2. Synthetic biopolymers designed for targeted anticancer drug delivery.

Table 1. Comparison of common biopolymers for targeted anticancer drug delivery.

Biopolymer	Biocompatibility	Active Targeting	Blood Brain Barrier Penetration	Main Anticancer Application	Sources
Chitosan	High	Folate, RGD	Yes (with modification)	Gene therapy, doxorubicin	[1]
Alginate	Medium	None	Limited	Colorectal therapy, Injectable nanogels	[7]
HA	High	CD44	Yes	Tumor cell targeting	[12]
Dextran	High	Chemical modification	Yes	Nanocarriers, CNS drugs	[24]
PLA/PLGA/PCL	High	PEG, Antibodies	Yes	Controlled drug release, Paclitaxel, Cisplatin	[25]

### 2.3 | Semi-Synthetic/Chemically Modified Biopolymers

Semi-synthetic or chemically modified biopolymers are derived from natural polymers but are structurally altered to enhance their physicochemical and biological properties. These modifications aim to improve solubility, mechanical stability, circulation time, drug-loading efficiency, and stimuli responsiveness, bridging the gap between natural biopolymers and fully synthetic polymers. Such hybrid systems combine the biocompatibility of natural polymers with the tunable performance of synthetic materials, making them highly versatile for advanced drug delivery applications [27], [28].

Common semi-synthetic biopolymers include:

- I. Carboxymethyl Chitosan (CMC): improved water solubility and pH responsiveness compared to native chitosan, enabling enhanced drug release in TMEs.
- II. Methacrylated Gelatin (GelMA): provides tunable mechanical properties and crosslinking ability for hydrogel-based drug carriers.

- III. Modified HA derivatives: conjugation with PEG, drugs, or targeting ligands improves stability, circulation time, and tumor-specific accumulation.
- IV. Oxidized or acetylated dextran: facilitates chemical conjugation of therapeutic molecules or stimuli-sensitive groups for controlled release.
- V. Cellulose derivatives (e.g., CMC, HEC): water-soluble polymers suitable for encapsulation of hydrophilic drugs and responsive formulations.

These semi-synthetic polymers can be engineered into a wide range of nanostructures, including nanoparticles, nanogels, micelles, and hydrogels, often with stimuli-responsive features such as pH, redox potential, enzymes, or temperature sensitivity. Such modifications enhance tumor targeting, improve drug bioavailability, and enable on-demand release in response to the TME (Fig. 3) [29], [30].

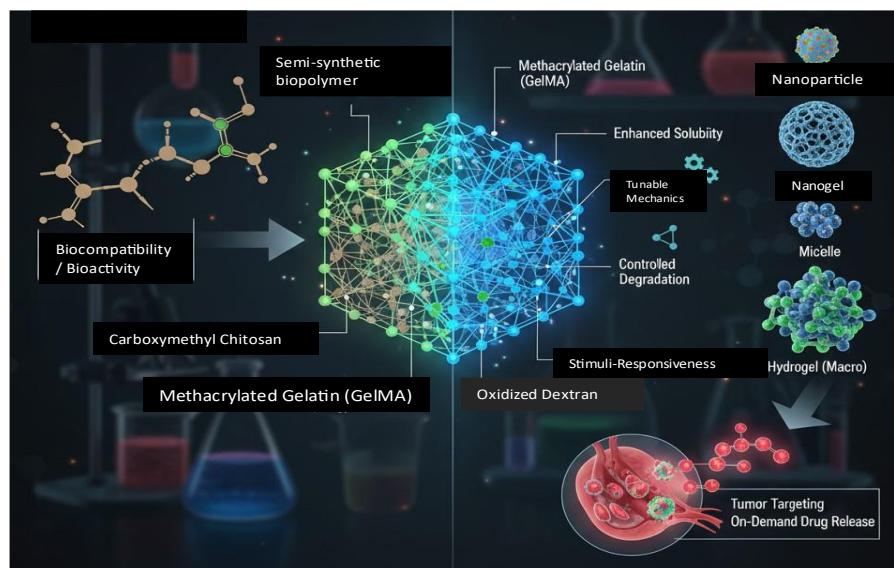


Fig. 3. Stimuli-responsive semi-synthetic biopolymers for drug release in tumor microenvironment.

### 3 | Classification of Biopolymers Based on Structure

Biopolymers can be classified according to the arrangement and organization of their polymer chains, which strongly influence their drug-loading capacity, release kinetics, mechanical properties, and overall performance in drug delivery systems. Understanding these structural classes allows researchers to tailor carriers for specific therapeutic applications [27]–[30].

#### 3.1 | Linear Polymers

Linear polymers consist of polymer chains arranged in a straight, unbranched fashion. This simple architecture facilitates the physical or chemical encapsulation of both hydrophilic and hydrophobic drugs. Linear polymers are widely used to fabricate conventional nanoparticles or micelles with relatively rapid release profiles. Examples include linear PEG, PLA, and chitosan derivatives [27]. Their simplicity allows easy functionalization, but drug release is often faster and less controllable compared to more complex architectures.

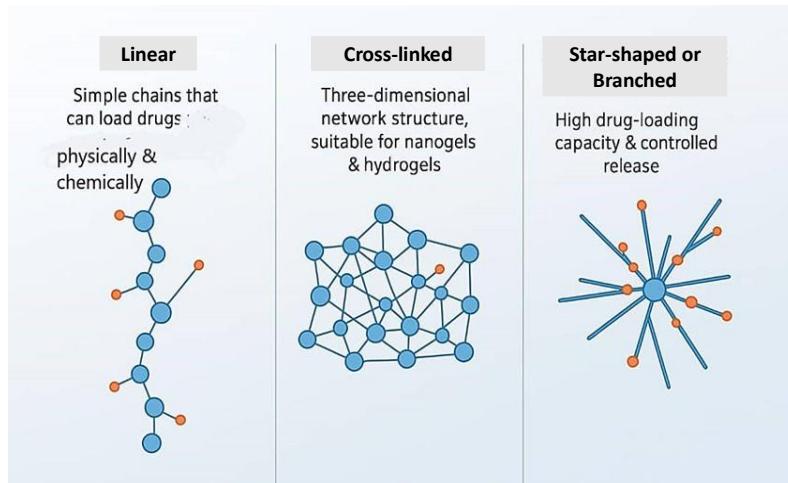
#### 3.2 | Crosslinked Polymers

Crosslinked polymers form stable three-dimensional networks through either chemical or physical crosslinking. This structure imparts high mechanical stability, swelling capacity, and the ability to provide sustained or stimuli-responsive drug release. Crosslinked networks are the basis for nanogels, hydrogels, and microgels, which can retain therapeutic agents and release them in a controlled manner in response to pH,

temperature, or enzymatic stimuli [28]. The degree and type of crosslinking directly affect porosity, diffusion rate, and degradation kinetics.

### 3.3 | Star-Shaped or Branched Polymers

In star-shaped or branched polymers, multiple polymer chains radiate from a central core. This architecture significantly increases the effective surface area and the number of functional end groups, enabling higher drug loading capacity, multidrug encapsulation, and finely controlled release kinetics. Dendrimers, star-shaped PEGs, and branched polysaccharides exemplify this category [29]. Such structures are particularly suitable for advanced drug delivery applications, including targeted therapy, combination therapy, and stimuli-responsive systems. *Fig. 4* illustrates three primary structural classifications of biopolymers relevant to their applications.



**Fig. 4. Classification of biopolymers based on structure: linear, crosslinked, and branched/star-shaped.**

## 4 | Physical and Chemical Properties Affecting Drug Delivery

The physicochemical characteristics of biopolymers critically influence the transport, release, and biodistribution of encapsulated drugs. Among the most important factors are:

- I. MW: Polymers with higher Mw generally exhibit greater stability in systemic circulation but may have limited penetration into tumor tissues. Conversely, lower Mw polymers penetrate tissues more effectively but are cleared more rapidly *in vivo* [31]. The Polydispersity Index (PDI) also affects uniformity and release kinetics of the drug.
- II. Surface charge: surface potential dictates interactions with cell membranes and the immune system. Positively charged particles tend to enter cells more efficiently due to electrostatic attraction to negatively charged membranes, but are also cleared more rapidly by the reticuloendothelial system. Neutral or negatively charged particles exhibit enhanced systemic stability, albeit at the expense of reduced cellular uptake [32].
- III. Hydrophilicity/hydrophobicity: the polarity of the polymer determines drug compatibility and release kinetics. Hydrophobic polymers are suitable for encapsulating lipophilic drugs, while hydrophilic polymers better accommodate water-soluble drugs, peptides, and proteins [33]. The balance between hydrophilic and hydrophobic domains also affects self-assembly into micelles or nanogels, drug loading efficiency, and release profiles.
- IV. Additional physicochemical factors: crystallinity versus amorphous state, glass transition temperature (T<sub>g</sub>), and chemical functionality influence mechanical properties, swelling behavior, and stimuli-responsiveness. Surface chemistry also affects protein adsorption, opsonization, and circulation time [34], [35].

## 5 | Mechanisms of Targeted Drug Delivery

Targeted drug delivery aims to maximize therapeutic efficacy while minimizing systemic toxicity by directing drugs specifically to tumor tissues. Mechanistically, targeted delivery can be classified into passive, active, and stimuli-responsive strategies (Fig. 5) [36]–[40].

### 5.1 | Passive Targeting

Passive targeting exploits the EPR effect inherent to tumor tissues. Leaky vasculature, irregular blood flow, and inefficient lymphatic drainage allow nanoparticles, typically smaller than 200 nm, to extravasate and accumulate within tumors [36], [37]. The main advantage of this approach is increased intratumoral drug concentration with reduced exposure to healthy tissues, thus lowering systemic toxicity [38]. However, EPR efficiency varies across tumor types and is influenced by vascular density, tumor size, and microenvironmental heterogeneity [39].

### 5.2 | Active Targeting

Active targeting involves functionalizing nanoparticle surfaces with ligands that specifically bind to receptors overexpressed on cancer cells, enhancing receptor-mediated endocytosis [40]. Common ligands include folic acid, RGD peptides, HA, and monoclonal antibodies, each providing selective recognition for specific tumor types [29]. Incorporating these ligands into nanocarriers such as PLGA-PEG or chitosan has been shown to significantly increase cellular uptake and intratumoral drug accumulation, significantly improving therapeutic efficacy while minimizing off-target effects [4], [23].

### 5.3 | Stimuli-Responsive Drug Delivery

Stimuli-responsive drug delivery is a hallmark of smart biopolymers, enabling spatiotemporal control of release in response to internal or external triggers [30].

- I. pH-sensitive polymers: exploit the slightly acidic TME. Polymers with pH-responsive linkers (e.g., hydrazone or imine bonds) remain stable at physiological pH but degrade or change conformation in acidic conditions, triggering drug release [30].
- II. Enzyme-responsive polymers: designed to degrade in the presence of tumor-specific enzymes, such as matrix metalloproteinases, allowing site-specific release [11].
- III. Thermo-responsive polymers: respond to localized hyperthermia, undergoing structural transitions that release the drug selectively. Examples include PNIPAM and thermoresponsive PEG-based systems [33].
- IV. Externally triggered polymers: light, magnetic fields, or ultrasound can induce conformational or chemical changes, providing precise external control over drug release [34].

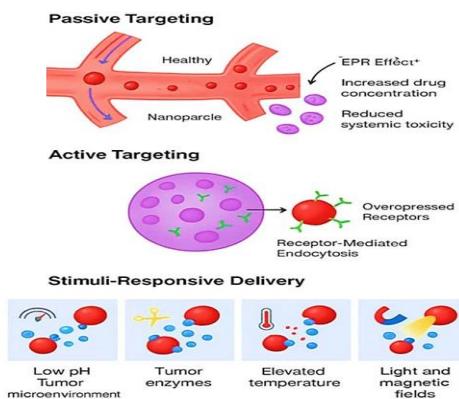


Fig. 5. Mechanisms of targeted drug delivery: passive (EPR), active, and stimuli-responsive.

## 5.4 | Combination of Mechanisms

Recent advancements in drug delivery have led to the development of hybrid nanocarriers that integrate multiple targeting strategies within a single system to maximize therapeutic efficacy. In these designs, passive accumulation via the EPR effect is often combined with active targeting via ligands that recognize tumor-specific receptors. Furthermore, stimulus-responsive features, such as pH-, enzyme-, or temperature-sensitivity, are incorporated to ensure site-specific drug release [3], [35]. Preclinical studies demonstrate that such multifunctional nanocarriers, particularly those coated with polymers such as PEG or HA and engineered for pH responsiveness, can significantly suppress tumor growth, including in breast and ovarian cancer models. By combining passive, active, and stimuli-responsive mechanisms, these systems not only improve drug accumulation and retention within tumors but also reduce off-target toxicity.

## 6 | Biopolymeric Nanostructures and Types of Carriers

Biopolymeric nanostructures represent versatile platforms for targeted and controlled drug delivery in cancer therapy, offering tunable physicochemical properties, high biocompatibility, and the potential for surface modification.

### 6.1 | Polymeric Nanoparticles

Polymeric Nanoparticles (NPs) are among the most widely utilized nanocarriers, designed primarily as nanocapsules or nanospheres [24], [27]. In nanocapsules, the therapeutic agent is confined within a liquid or semi-solid core, surrounded by a polymeric shell that protects the drug and regulates its release. Nanospheres, in contrast, consist of a homogeneous polymer matrix with the drug dispersed throughout, providing sustained, gradual release [8]. Biodegradable polymers such as PLGA, PLA, and PCL are commonly employed due to their favorable biocompatibility, adjustable degradation rates, and ability to carry a wide range of therapeutics, including small molecules, proteins, and nucleic acids [41]. Modulation of nanoparticle size, surface charge, and coating, particularly PEGylation, enhances circulation half-life, reduces immune clearance, and increases tumor accumulation via the EPR effect [23]. Overall, PNs offer engineering flexibility, controlled release, and compatibility with diverse therapeutics, making them reliable carriers for cancer treatment.

### 6.2 | Micelles and Nanomicelles

Micelles and nanomicelles, derived from amphiphilic polymers, self-assemble in aqueous environments with hydrophobic cores that encapsulate lipophilic drugs and hydrophilic shells that stabilize the particles in biological media [36], [37]. PEGylation of the micelle surface reduces immune recognition, prolongs systemic circulation, and facilitates tumor accumulation. Surface functionalization with ligands, such as antibodies or peptides, enables active targeting of cancer cells [10]. Polymers such as PEG-PLA form stable nanomicelles with high drug-loading efficiency and effective tumor penetration, thereby significantly enhancing intratumoral drug concentration while minimizing systemic toxicity [10]. Critical Micelle Concentration (CMC) and particle size are key parameters governing stability and biodistribution.

### 6.3 | Nanogels

Nanogels are three-dimensional, hydrophilic networks with tunable porosity, high water content, and stimulus-responsive properties, making them ideal for hydrophilic drugs, proteins, and other macromolecules [15], [38]. Their swelling and deswelling in response to pH or enzymatic activity enable precise and selective drug release within TMEs. Nanogels based on HA or chitosan can actively target tumors via interaction with CD44 receptors, enhancing cellular uptake and intratumoral drug distribution. Biocompatibility and biodegradability further reduce potential side effects. By combining high loading capacity, stimulus

responsiveness, and targeting capability, nanogels are leading platforms for controlled and targeted anticancer therapy [26].

## 6.4 | Multifunctional Nanocapsules and Hybrid Systems

Multifunctional nanocapsules represent the next generation of nanocarriers, integrating multiple functionalities within a single system [11]. Typically, these consist of a protected drug-containing core surrounded by functional layers, such as PEG coatings, targeting ligands, and stimuli-responsive components. These systems simultaneously employ passive (EPR), active (ligand-mediated), and stimuli-responsive mechanisms, enhancing penetration into tumor tissue while reducing off-target distribution [12]. They are also capable of co-delivering multiple therapeutics, including chemotherapeutic agents, nucleic acids, and immunomodulators, facilitating combination and multimodal therapies that can overcome drug resistance and strengthen anticancer efficacy [3], [7].

# 7 | Current Challenges in Biopolymeric Drug Delivery

Despite significant advances, biopolymeric drug-delivery systems continue to face several limitations [39]. One of the most critical issues is the heterogeneous distribution of nanoparticles within tumors. While the EPR effect underlies many passive delivery strategies, its extent varies across tumor types, and uniform penetration throughout the tumor mass is often not achieved, limiting therapeutic efficacy [5]. Another common challenge is the accumulation of nanoparticles in non-target organs such as the liver, spleen, and kidneys, which reduces drug availability at the tumor site and may induce off-target toxicity [1]. Additionally, the stability of nanoparticles in systemic circulation is crucial; premature degradation, disassembly, or aggregation can compromise drug delivery efficiency and controlled release mechanisms [28]. Collectively, these challenges underscore the need for further optimization to ensure stable, safe, and tumor-targeted performance [39].

## 7.1 | Biological and Safety Challenges

Biopolymeric nanocarriers face significant biological and immunological hurdles. Rapid recognition and clearance by the immune system shorten circulation time and reduce therapeutic efficacy [7]. Some polymers can also trigger inflammatory responses or antibody production, contributing to immunogenicity [2]. Polymer biodegradability and biocompatibility are critical considerations; certain synthetic polymers may generate toxic degradation byproducts [4]. Furthermore, discrepancies between preclinical (animal) and clinical (human) outcomes highlight that successful *in vivo* models do not always translate into human outcomes [3]. Strategies such as PEGylation, surface modification, and careful polymer selection can mitigate some of these challenges, but further research is needed to improve safety and efficacy [7].

## 7.2 | Manufacturing and Scalability Challenges

Large-scale production of biopolymeric nanoparticles presents technical and economic challenges [24]. Maintaining consistent particle size and uniform distribution is essential, as even minor variations affect drug loading, stability, and targeting efficiency [25]. Long-term stability is another critical concern, as many nanoformulations undergo physical or chemical changes during storage, necessitating specialized formulation and storage conditions [26]. High production costs are also a limiting factor. Many advanced fabrication techniques that allow precise control over nanoparticle properties are not economically feasible for industrial-scale manufacturing. Therefore, developing simpler, cost-effective, and scalable methods, including microfluidics, self-assembly optimization, and advanced biofabrication techniques, is essential for the commercialization of biopolymeric drug-delivery systems [22].

## 8 | Future Perspectives and Strategies

Despite the existing challenges, the future of targeted biopolymeric drug delivery appears highly promising [41–43]. A key direction is the development of multifunctional nanocarriers that integrate active targeting, responsiveness to tumor-specific stimuli, and features that enhance drug accumulation, thereby maximizing therapeutic efficacy [35]. Concurrently, the design of smart nanostructures capable of sensing and responding to biochemical and physical tumor conditions ,such as pH gradients, enzyme activity, and local temperature variations ,represents one of the most promising research avenues [3]. Recent advances in nanotechnology have also enabled the integration of drug delivery with gene therapy and immunotherapy. These hybrid systems can simultaneously carry drugs, genes, or immune-modulating molecules, providing coordinated combination therapies capable of overcoming drug resistance and tumor heterogeneity [44]. An emerging and critical trend is the shift toward personalized medicine, where patient-specific genetic information, biomarkers, and molecular profiles are used to design customized nanoparticles. This approach enables more precise, targeted, and low-toxicity therapies, paving the way for next-generation cancer treatment strategies [45].

## 9 | Conclusion

Biopolymers, as an emerging generation of drug carriers, have established a prominent role in targeted cancer therapy. With attributes such as high biocompatibility, controllable degradation, cellular targeting, and responsiveness to environmental stimuli, these materials offer a promising strategy to enhance the efficacy of anticancer drugs while minimizing side effects. Their use enables drugs to reach tumor sites more precisely, improving therapeutic outcomes and reducing damage to healthy tissues. Despite these advancements, several challenges remain, including limited stability of certain nanocarriers, premature drug leakage, heterogeneous tumor penetration, safety concerns, and challenges in large-scale industrial production. Addressing these issues requires further research, the development of smarter polymer systems, and extensive clinical evaluation. Future perspectives suggest that combining multifunctional biopolymers with imaging technologies, gene therapy, and stimuli-responsive systems could usher in a new era of personalized and precision cancer treatments. This approach has the potential not only to improve therapeutic outcomes but also to shift cancer therapy from conventional methods toward low-toxicity, patient-tailored medicine.

## References

- [1] Yadav, N., Singh, D., Rawat, M., & Sangwan, N. (2022). Novel archetype in cancer therapeutics: exploring prospective of phytonanocarriers. *3 biotech*, 12(11), 324. <https://doi.org/10.1007/s13205-022-03372-3>
- [2] da Silva Feltrin, F., Agner, T., Sayer, C., & Lona, L. M. F. (2022). Curcumin encapsulation in functional PLGA nanoparticles: A promising strategy for cancer therapies. *Advances in colloid and interface science*, 300, 102582. <https://doi.org/10.1016/j.cis.2021.102582>
- [3] Dong, S., Guo, X., Han, F., He, Z., & Wang, Y. (2022). Emerging role of natural products in cancer immunotherapy. *Acta pharmaceutica sinica b*, 12(3), 1163–1185. <https://doi.org/10.1016/j.apsb.2021.08.020>
- [4] Feng, L., Liu, R., Zhang, X., Li, J., Zhu, L., Li, Z., ... , & Zhang, A. (2021). Thermo-gelling dendronized chitosans as biomimetic scaffolds for corneal tissue engineering. *ACS applied materials & interfaces*, 13(41), 49369–49379. <https://pubs.acs.org/doi/10.1021/acsami.1c16087?goto=supporting-info>
- [5] Ashrafizadeh, M., Delfi, M., Zarabi, A., Bigham, A., Sharifi, E., Rabiee, N., ... , & Makvandi, P. (2022). Stimuli-responsive liposomal nanoformulations in cancer therapy: Pre-clinical & clinical approaches. *Journal of controlled release*, 351, 50–80. <https://doi.org/10.1016/j.jconrel.2022.08.001>
- [6] Xin, Y., Quan, L., Zhang, H., & Ao, Q. (2023). Emerging polymer-based nanosystem strategies in the delivery of antifungal drugs. *Pharmaceutics*, 15(7). <https://doi.org/10.3390/pharmaceutics15071866>
- [7] Bhatia, S. N., Chen, X., Dobrovolskaia, M. A., & Lammers, T. (2022). Cancer nanomedicine. *Nature reviews cancer*, 22(10), 550–556. <https://doi.org/10.1038/s41568-022-00496-9>

[8] Mu, W., Chu, Q., Liu, Y., & Zhang, N. (2020). A review on nano-based drug delivery system for cancer chemoimmunotherapy. *Nano-micro letters*, 12(1), 142. <https://doi.org/10.1007/s40820-020-00482-6>

[9] Quader, S., & Kataoka, K. (2017). Nanomaterial-enabled cancer therapy. *Molecular therapy*, 25(7), 1501–1513. <https://doi.org/10.1016/j.ymthe.2017.04.026>

[10] Moghaddam, F. D., Zare, E. N., Hassanpour, M., Bertani, F. R., Serajian, A., Ziae, S. F., ... , & Xu, Y. (2024). Chitosan-based nanosystems for cancer diagnosis and therapy: Stimuli-responsive, immune response, and clinical studies. *Carbohydrate polymers*, 330, 121839. <https://doi.org/10.1016/j.carbpol.2024.121839>

[11] Zhu, H., Loh, X. J., Ye, E., & Li, Z. (2022). Polymeric matrix-based nanoplatforms toward tumor therapy and diagnosis. *ACS materials letters*, 4(1), 21–48. <https://doi.org/10.1021/acsmaterialslett.1c00558>

[12] Khan, H., Mirzaei, H. R., Amiri, A., Kupeli Akkol, E., Ashhad Halimi, S. M., & Mirzaei, H. (2021). Glyco-nanoparticles: New drug delivery systems in cancer therapy. *Seminars in cancer biology*, 69, 24–42. <https://doi.org/10.1016/j.semcan.2019.12.004>

[13] Abulataefeh, S. R. (2023). Long-acting injectable PLGA/PLA depots for leuprolide acetate: Successful translation from bench to clinic. *Drug delivery and translational research*, 13(2), 520–530. <https://doi.org/10.1007/s13346-022-01228-0>

[14] Thakkar, S., Sharma, D., Kalia, K., & Tekade, R. K. (2020). Tumor microenvironment targeted nanotherapeutics for cancer therapy and diagnosis: A review. *Acta biomaterialia*, 101, 43–68. <https://doi.org/10.1016/j.actbio.2019.09.009>

[15] Liu, J., Li, M., Luo, Z., Dai, L., Guo, X., & Cai, K. (2017). Design of nanocarriers based on complex biological barriers in vivo for tumor therapy. *Nano today*, 15, 56–90. <https://doi.org/10.1016/j.nantod.2017.06.010>

[16] Dutta, B., Barick, K. C., & Hassan, P. A. (2021). Recent advances in active targeting of nanomaterials for anticancer drug delivery. *Advances in colloid and interface science*, 296, 102509. <https://doi.org/10.1016/j.cis.2021.102509>

[17] Singh, A. K., Bahadur, S., Yadav, D., & Dabas, H. (2023). Pharmaceutical and pharmacokinetic aspects of nanoformulation based drug delivery systems for anti-cancer drugs. *Current pharmaceutical design*, 29(24), 1896–1906. <https://doi.org/10.2174/1381612829666230824144727>

[18] Zhou, M., Dong, J., Huang, J., Ye, W., Zheng, Z., Huang, K., ... , Zhang, J. (2022). Chitosan-gelatin-EGCG nanoparticle-mediated LncRNA TMEM44-AS1 silencing to activate the P53 signaling pathway for the synergistic reversal of 5-FU resistance in gastric cancer. *Advanced science*, 9(22), 2105077. <https://doi.org/10.1002/advs.202105077>

[19] Jia, X., Fan, X., Chen, C., Lu, Q., Zhou, H., Zhao, Y., ... , & Geng, H. (2024). Chemical and structural engineering of gelatin-based delivery systems for therapeutic applications: A review. *Biomacromolecules*, 25(2), 564–589. <https://doi.org/10.1021/acs.biomac.3c01021>

[20] Stevanovic, M. (2017). Polymeric micro-and nanoparticles for controlled and targeted drug delivery. In *Nanostructures for drug delivery*; elsevier: Amsterdam, the netherlands (pp. 355–378). Elsevier. <https://doi.org/10.1016/b978-0-323-46143-6.00011-7>

[21] He, B., Sui, X., Yu, B., Wang, S., Shen, Y., & Cong, H. (2020). Recent advances in drug delivery systems for enhancing drug penetration into tumors. *Drug delivery*, 27(1), 1474–1490. <https://doi.org/10.1080/10717544.2020.1831106>

[22] de La Torre, L. G., Sipoli, C. C., Oliveira, A. F., Eş, I., Pessoa, A. C. S. N., Vitor, M. T., ... , & F. Naves, T. (2017). Biopolymers for gene delivery applications. In *Biopolymer-based composites* (pp. 289–323). Woodhead Publishing. <https://doi.org/10.1016/B978-0-08-101914-6.00010-7>

[23] Madej, M., Kurowska, N., & Strzalka-Mrozik, B. (2022). Polymeric nanoparticles—tools in a drug delivery system in selected cancer therapies. *Applied sciences*, 12(19), 1–21. <https://doi.org/10.3390/app12199479>

[24] Tekade, R. K., Maheshwari, R., & Tekade, M. (2017). Biopolymer-based nanocomposites for transdermal drug delivery. In *Biopolymer-based composites* (pp. 81–106). Woodhead Publishing. <https://doi.org/10.1016/B978-0-08-101914-6.00004-1>

[25] Reddy, M. S. B., Ponnamma, D., Choudhary, R., & Sadasivuni, K. K. (2021). A comparative review of natural and synthetic biopolymer composite scaffolds. *Polymers*, 13(7), 1–51. <https://doi.org/10.3390/polym13071105>

[26] Gopi, S., Amalraj, A., Sukumaran, N. P., Haponiuk, J. T., & Thomas, S. (2018). Biopolymers and their composites for drug delivery: A brief review. *Macromolecular symposia*, 480, 1800114. <https://doi.org/10.1002/masy.201800114>

[27] Gheorghita, R., Anchidin-Noroel, L., Filip, R., Dimian, M., & Covasa, M. (2021). Applications of biopolymers for drugs and probiotics delivery. *Polymers*, 13(16), 1–32. <https://doi.org/10.3390/polym13162729>

[28] Dutta, R., Mohapatra, S. S., & Mohapatra, S. (2021). Biopolymeric systems for the delivery of nucleic acids. In *Tailor-made and functionalized biopolymer systems* (pp. 635–661). Woodhead Publishing. <https://doi.org/10.1016/B978-0-12-821437-4.00009-8>

[29] Herdiana, Y., Husni, P., Nurhasanah, S., Shamsuddin, S., & Wathoni, N. (2023). Chitosan-based nano systems for natural antioxidants in breast cancer therapy. *Polymers*, 15(13), 1–28. <https://doi.org/10.3390/polym15132953>

[30] Paul, P., Nandi, G., Abosheasha, M. A., & Bera, H. (2021). Alginate-based systems for protein and peptide delivery. In *Tailor-made and functionalized biopolymer systems* (pp. 85–113). Woodhead Publishing. <https://doi.org/10.1016/B978-0-12-821437-4.00011-6>

[31] Zahavi, D., & Weiner, L. (2020). Monoclonal antibodies in cancer therapy. *Antibodies*, 9(3), 1–20. <https://doi.org/10.3390/antib9030034>

[32] Le, T. M. D., Yoon, A. R., Thambi, T., & Yun, C. O. (2022). Polymeric systems for cancer immunotherapy: A review. *Frontiers in immunology*, 13, 826876. <https://doi.org/10.3389/fimmu.2022.826876>

[33] Makadia, H. K., & Siegel, S. J. (2011). Poly lactic-co-glycolic acid (PLGA) as biodegradable controlled drug delivery carrier. *Polymers*, 3(3), 1377–1397. <https://doi.org/10.3390/polym3031377>

[34] Lin, A., Giuliano, C. J., Palladino, A., John, K. M., Abramowicz, C., Yuan, M. Lou, . . ., & Sheltzer, J. M. (2019). Off-target toxicity is a common mechanism of action of cancer drugs undergoing clinical trials. *Science translational medicine*, 11(509), eaaw8412. <https://doi.org/10.1126/scitranslmed.aaw8412>

[35] Kamaly, N., Yameen, B., Wu, J., & Farokhzad, O. C. (2016). Degradable controlled-release polymers and polymeric nanoparticles: Mechanisms of controlling drug release. *Chemical reviews*, 116(4), 2602–2663. <https://doi.org/10.1021/acs.chemrev.5b00346>

[36] Alvi, M., Yaqoob, A., Rehman, K., Shoaib, S. M., & Akash, M. S. H. (2022). PLGA-based nanoparticles for the treatment of cancer: Current strategies and perspectives. *AAPS open*, 8(1), 12. <https://doi.org/10.1186/s41120-022-00060-7>

[37] Wei, R., Liu, S., Zhang, S., Min, L., & Zhu, S. (2020). Cellular and extracellular components in tumor microenvironment and their application in early diagnosis of cancers. *Analytical cellular pathology*, 2020(1), 6283796. <https://doi.org/10.1155/2020/6283796>

[38] Kim, S. M., Faix, P. H., & Schnitzer, J. E. (2017). Overcoming key biological barriers to cancer drug delivery and efficacy. *Journal of controlled release*, 267, 15–30. <https://doi.org/10.1016/j.jconrel.2017.09.016>

[39] Zhang, W., Mehta, A., Tong, Z., Esser, L., & Voelcker, N. H. (2021). Development of polymeric nanoparticles for blood-brain barrier transfer—strategies and challenges. *Advanced science*, 8(10), 2003937. <https://doi.org/10.1002/advs.202003937>

[40] Elmowafy, M., Shalaby, K., Elkomy, M. H., Alsaidan, O. A., Gomaa, H. A. M., Abdelgawad, M. A., & Mostafa, E. M. (2023). Polymeric nanoparticles for delivery of natural bioactive agents: Recent advances and challenges. *Polymers*, 15(5), 1–34. <https://doi.org/10.3390/polym15051123>

[41] Rostaminejad, B., Dinari, M., Karimi, A. R., & Hadizadeh, M. (2023). Oxidative cross-linking of biocompatible chitosan injectable hydrogel by perylene-dopamine to boost phototoxicity of perylene on in vitro melanoma and breast cancer therapy. *Journal of molecular liquids*, 386, 122553. <https://doi.org/10.1016/j.molliq.2023.122553>

[42] Tian, B., Hua, S., & Liu, J. (2023). Multi-functional chitosan-based nanoparticles for drug delivery: Recent advanced insight into cancer therapy. *Carbohydrate polymers*, 315, 120972. <https://doi.org/10.1016/j.carbpol.2023.120972>

[43] Wickens, J. M., Alsaab, H. O., Kesharwani, P., Bhise, K., Amin, M. C. I. M., Tekade, R. K., ... , & Iyer, A. K. (2017). Recent advances in hyaluronic acid-decorated nanocarriers for targeted cancer therapy. *Drug discovery today*, 22(4), 665–680. <https://doi.org/10.1016/j.drudis.2016.12.009>

[44] He, P., Dai, L., Wei, J., Zhu, X., Li, J., Chen, Z., & Ni, Y. (2022). Nanocellulose-based hydrogels as versatile drug delivery vehicles: A review. *International journal of biological macromolecules*, 222, 830–843. <https://doi.org/10.1016/j.ijbiomac.2022.09.214>

[45] Gholamali, I., & Yadollahi, M. (2020). Doxorubicin-loaded carboxymethyl cellulose/Starch/ZnO nanocomposite hydrogel beads as an anticancer drug carrier agent. *International journal of biological macromolecules*, 160, 724–735. <https://doi.org/10.1016/j.ijbiomac.2020.05.232>