REVIEW ARTICLE

Recent Advances and Future Prospects in Polymer-Mediated Drug Delivery Systems: A Comprehensive Review

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ABSTRACT

Polymer-based drug carriers have revolutionized the pharmaceutical landscape, providing innovative approaches for efficient drug delivery. These advanced systems have significantly mitigated traditional challenges, offering new avenues for targeted and controlled drug release. This paper aims to explore polymers, focusing on their classification, properties, drug release mechanisms, and pharmaceutical applications while emphasizing recent advancements and future prospects in the field. Polymers can be classified based on their origin, biodegradability, and physical properties. Their unique characteristics, such as biocompatibility, flexibility, and ability to modify surface properties, make them ideal for drug delivery applications.

The review delves into various drug release mechanisms employed by polymer-based systems, including diffusion, degradation, swelling, and stimuli-responsive release. These mechanisms ensure a controlled and sustained release of therapeutic agents, enhancing efficacy and reducing side effects. The pharmaceutical applications of polymer-based drug carriers are vast, encompassing targeted delivery to specific tissues or cells, sustained-release formulations, and the delivery of complex molecules like proteins and nucleic acids.

Despite their advantages, polymer-based drug delivery systems face limitations, including potential toxicity, stability issues, and manufacturing challenges. Addressing these limitations through continued research and development is crucial for advancing the field. Recent advancements, such as smart polymers and nanotechnology integration, hold promise for overcoming these challenges and improving drug delivery efficiency. In conclusion, polymer-mediated drug delivery systems represent a significant leap forward in pharmaceutical technology. This review highlights the importance of polymers in modern medicine, their potential to revolutionize drug delivery, and the ongoing efforts to optimize their use in clinical applications.

Keywords: Polymer-based drug carriers, Drug delivery systems, Biocompatibility, Controlled release, Targeted delivery, Smart polymers, Nanotechnology, Pharmaceutical applications, Drug release mechanisms, Biodegradable polymers.

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INTRODUCTION

A polymer is a macromolecule made up of repeating structural units known as monomers. Covalent bonds link these monomers together to create a lengthy chain or network structure. Polymers can have a wide range of sizes, from small molecules with just a few monomers to giant molecules with thousands or even millions of monomers[1]. Polymer-based drug carriers have revolutionized the pharmaceutical field by introducing efficient drug delivery methods. Utilizing the unique properties of polymers, these carriers improve drug efficacy and reduce side effects. Traditional drug delivery methods often face challenges such as poor solubility, stability, and bioavailability. Polymer-based systems have addressed these issues, enabling targeted and controlled drug delivery.[2]

There are two types of polymers used in medication delivery: synthetic and natural. Because proteins are compatible with biological systems, they are employed extensively in products like collagen, gelatin, and enzymes. Connective tissues mostly consist of collagen, which is frequently utilized in medication delivery systems to encourage tissue regeneration and wound healing. Collagen is the source of gelatin, which is used to make hydrogels that contain medications and release them

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gradually over time to provide continuous drug release. For regulated drug release, polysaccharides with a natural origin and the capacity to form gels—like hyaluronic acid, chitosan, and alginate are preferred.[3,4] Chitosan, derived from chitin in crustacean exoskeletons, is ideal for oral and nasal drug delivery due to its mucoadhesive properties. Alginate, from brown seaweed, forms gels with calcium ions and is used in controlled-release formulations. Hyaluronic acid, a part of the extracellular matrix, is utilized in targeted drug delivery for its interaction with cell surface receptors. Nucleic acids like DNA and RNA-based polymers are crucial in gene therapy and nucleic acid delivery. For instance, plasmid DNA encapsulated in polymeric nanoparticles is protected from degradation and aids in therapeutic protein expression in target cells. RNA-based polymers, such as siRNA and mRNA, are notable for gene silencing and therapeutic protein production, respectively[5].

Synthetic polymers offer enhanced control over properties and functionalities. Examples include polyethylene glycol (PEG), polylactic acid (PLA), polyglycolic acid (PGA), poly(lactic-co-glycolic acid) (PLGA), and polyvinyl alcohol (PVA). PEG is notable for its solubility and immune evasion, extending drug circulation time. PEGylation, attaching PEG to drugs or carriers, improves solubility, stability, and circulation, as seen in PEGylated interferon for hepatitis C, which has better pharmacokinetics and reduced immunogenicity. PLA and PGA are biodegradable, breaking down into lactic and glycolic acid, respectively, and are used to create drug-encapsulating microparticles and nanoparticles for controlled release. PLGA, a PLA and PGA copolymer, offers adjustable degradation rates for various applications, including cancer therapy and vaccine delivery. PVA is valued for its film-forming, emulsifying, and adhesive properties[6].

Polymer-based drug carriers use various mechanisms for effective delivery, such as encapsulation, which protects drugs from degradation and controls release over time. Surface modification with targeting ligands (antibodies, peptides) enables site-specific delivery, enhancing therapeutic efficacy and reducing off-target effects. Stimuli-responsive polymers release drugs in response to environmental changes like pH, temperature, or light, providing controlled, on-demand delivery. For example, pH-responsive polymers release drugs in acidic tumor environments, while temperature-sensitive polymers release drugs at specific temperatures[7]. Polymer-based drug carriers are promising for applications like cancer therapy, gene therapy, vaccines, tissue engineering, and oral drug delivery. In cancer therapy, they enhance drug delivery, reduce systemic toxicity, and improve accumulation at tumor sites. For example, PEGylated liposomal doxorubicin (Doxil) extends circulation time and accumulates in tumors via the EPR effect. Polymeric micelles, formed from amphiphilic block copolymers, encapsulate hydrophobic anticancer drugs, enhancing their solubility and therapeutic efficacy.[8].

In gene therapy, polymers like polyethyleneimine (PEI) and chitosan deliver nucleic acids (DNA, RNA), protecting them from degradation and facilitating cell entry. PEI, a cationic polymer, complexes with negatively charged nucleic acids to form protective nanoparticles that enhance cellular uptake. Chitosan is used for delivering plasmid DNA and siRNA due to its biocompatibility and ability to form complexes with nucleic acids. Chitosan-based nanoparticles, for example, deliver siRNA for cancer and genetic disorder treatment, protecting siRNA and enhancing uptake for effective gene silencing and therapeutic effects[9].

Polymer-based carriers enhance vaccine delivery and immune responses by using biodegradable polymers like PLGA for sustained antigen release, improving vaccine efficacy. PLGA nanoparticles encapsulate antigens and adjuvants, protecting them from degradation and promoting uptake by antigen-presenting cells, as seen in vaccines for influenza, hepatitis B, and HPV. In tissue engineering, polymers like collagen and PLA create scaffolds that support tissue regeneration, loaded with growth factors and drugs to promote healing. Collagen scaffolds mimic the extracellular matrix for cell attachment, while PLA scaffolds, used in bone and cartilage regeneration, provide structural support and biodegradability[10].

In oral drug delivery, polymers enhance bioavailability by protecting drugs from the harsh gastrointestinal environment and improving absorption. Enteric coatings like cellulose acetate phthalate prevent stomach degradation and dissolve in the intestines for targeted release. Polymers such as polyvinylpyrrolidone (PVP) increase the solubility of poorly water-soluble drugs. Recent advancements include multifunctional nanoparticles for theranostics, combining drug delivery and diagnostic imaging. Examples include polymer-coated magnetic nanoparticles for MRI and drug delivery, and gold nanoparticles for combined drug delivery and photothermal cancer therapy[11].

Advances in polymer chemistry have led to sophisticated drug delivery systems with improved targeting and controlled release. Block copolymers and dendrimers enable precise control over nanoparticle size, shape, and surface functionality, enhancing tissue targeting and controlled drug release. Block copolymers, composed of distinct polymer blocks, self-assemble into nanostructures like micelles and vesicles, encapsulating drugs for controlled release. Dendrimers, with their highly branched, tree-like structure, provide precise size and surface control, making them ideal for targeted drug delivery and gene therapy[12]. Despite significant advances, challenges remain in the development and clinical translation of polymer-based drug carriers. Ensuring biocompatibility and safety requires extensive preclinical studies to assess long-term effects and toxicity. The regulatory approval process is complex and lengthy, necessitating thorough documentation and clinical trials. Scalable manufacturing processes are needed to meet demand and lower costs. Future research should focus on developing safer polymers and improving manufacturing techniques. Innovations in nanotechnology, materials science, and bioengineering are expected to advance next-generation polymer-based drug carriers, enhancing personalized medicine and therapeutic outcomes.

Natural polymer over synthetic polymer

The use of natural polymers over synthetic polymers offers several advantages, making them increasingly important in various applications. Here are some key reasons why natural polymers are favored in many situations:

Biocompatibility

Natural polymers are often biocompatible, meaning they are well-tolerated by the human body and do not trigger adverse immune responses or toxicity. This property is crucial in medical and pharmaceutical applications, such as drug delivery, tissue engineering, and wound healing[13].

Renewable and sustainable

Natural polymers are derived from renewable resources, such as plants, animals, and microorganisms. This makes them more sustainable and environmentally friendly compared to some synthetic polymers, which are derived from non-renewable petrochemical sources[14].

Biodegradability

Many natural polymers are biodegradable, meaning they can break down into harmless compounds over time, reducing environmental pollution and waste. This is particularly important in single-use products and packaging[15].

Low environmental impact

The extraction and processing of natural polymers often have a lower environmental impact than the production of synthetic polymers. Natural polymers can also reduce greenhouse gas emissions[16].

Health and safety

Natural polymers are often considered safer for use in products that come into contact with food, pharmaceuticals, and cosmetics due to their biocompatibility and minimal risk of leaching harmful substances[17].

Enhanced functionality

Natural polymers can provide unique functionalities, such as mucoadhesion, bioactive compound delivery, and improved taste and texture in food products, which may not be easily replicated by synthetic polymers[18].

Regulatory approval

Natural polymers are widely accepted by regulatory authorities in many countries, making them easier to incorporate into products that require regulatory approval, such as pharmaceuticals and food items[19].

Reduced allergenic potential

Natural polymers are generally less likely to cause allergic reactions compared to certain synthetic polymers[20]. Acrylic polymer products are generally inert, but active monomer particles can trigger allergic responses, with high allergenic capacity in both monomeric and dimeric forms.

Wound healing and tissue regeneration

Natural polymers like alginate, collagen and chitosan are well-suited for wound healing and tissue regeneration applications for their biocompatibility and ability to promote cell growth and tissue repair[21].

Cultural and traditional practices

In some cases, natural polymers have cultural or traditional significance. For example, natural materials like agar, seaweed, and gels from plants are commonly used in Asian cuisine and traditional medicine[22]. Polymers, including small molecular weight drugs, proteins, and DNA, are used in tissue engineering, wound healing, and anticancer therapy due to chemical and morphological modifications.

Improved drug delivery

Natural polymers, such as alginate, chitosan and hyaluronic acid, can enhance drug delivery, increasing the bioavailability and effectiveness of medications[23]. Polymers have been transformed into colloidal particles, acting as carriers for drug molecules, improving their delivery properties for controlled, ocular, transdermal, or intranasal systems, gene therapy, and tissue engineering.

Pharmaceutical Polymer

Pharmaceutical polymers are specialized polymers used in drug formulation, delivery, and various healthcare products. They are designed to meet specific requirements for the safe and effective administration of pharmaceutical compounds. Key roles and applications include:

Drug delivery dystems

Pharmaceutical polymers are often used to form drug delivery systems that control the release of medications over time. These systems include drug-loaded nanoparticles, microparticles, and hydrogels, among others, which can be administered orally, intravenously, or topically. The controlled release of drugs helps maintain therapeutic levels and minimize side effects.[24,25]

Excipients

Polymers are used as excipients in pharmaceutical formulations to enhance the physical properties of drugs. For example, they can improve drug solubility, stability, and bioavailability. Common excipients include binders, fillers, disintegrants, and coatings.[26]

Oral dosage forms

Many pharmaceutical polymers are used in the production of oral dosage forms, such as tablets, capsules, and oral suspensions. They help bind and disintegrate tablets, encapsulate drugs in capsules, and improve the taste and texture of oral suspensions.[27]

Topical formulations

Polymers are used in topical pharmaceutical products such as creams, ointments, gels, and transdermal patches. They can enhance the consistency and stability of these products while controlling the release of drugs through the skin.[28]

Biodegradable implants

Polylactic acid and polyglycolic acid are used to create biodegradable implants that slowly release drugs, making them suitable for long-term therapeutic applications.[29]

Ophthalmic products

Polymers are utilized in ophthalmic products such as eye drops, gels, and contact lens materials. They help improve the viscosity, stability, and lubricating properties of these products.[30]

Intravenous and injectable formulations

Pharmaceutical polymers are employed in intravenous and injectable formulations to control drug solubility and release. They can also be used to create drug-loaded microspheres and nanoparticles for targeted drug delivery.[31]

Wound healing and tissue regeneration

Some pharmaceutical polymers are used in wound care products and tissue engineering to promote tissue repair and regeneration.[32]

Pharmaceutical polymers used in these applications include PVP, PEG, HPMC, PLA, PGA, and chitosan. These polymers proved to have certain activities with particular concentrations, as mentioned in Table 1.

Criteria for Polymer Selection

Chemical compatibility

Ensure the polymer is compatible with other ingredients in the formulation to prevent undesirable interactions or reactions that could affect stability or efficacy.[41]

Physical properties

Consider properties such as viscosity, solubility, elasticity, and adhesion to ensure the polymer aligns with the intended purpose of the formulation. For instance, a coating may require a polymer with good adhesion, while a gel might need a polymer with specific viscosity characteristics.[42]

Stability

Assess the polymer's stability under various conditions, including temperature, pH, and light exposure, to ensure the formulation's shelf life and performance are maintained[43].

Safety and regulatory compliance

Confirm that the polymer meets safety standards and regulatory requirements for its intended use. This includes considerations for potential allergens, toxicity, and environmental impact.[44]

Cost and availability

Evaluate the cost-effectiveness and availability of the polymer in the required quantity for the formulation. Sometimes, certain polymers might be expensive or in limited supply.

Processing compatibility

Consider how easily the polymer can be processed or manufactured into the desired formulation. Some polymers might require specific equipment or processing conditions.[45]

Performance requirements

Ensure the polymer meets the functional needs of the formulation, such as durability, flexibility, or specific chemical or physical properties necessary for the product to perform as intended.[46]

Table 1: Significant concentration of polymer for desirable treatment

Treatment	*Polymer*	*Concentration*	*Activity*
Cancer	Poly(lactic-co-glycolic acid) (PLGA)	10–40% w/w	PLGA nanoparticles are utilized to encapsulate chemotherapeutic agents, enabling controlled drug release for cancer treatment. They provide sustained drug delivery to tumor sites, reducing systemic toxicity.[33]
Oral Drug Delivery	Hydroxypropyl methylcellulose (HPMC)	2–10% w/w	HPMC serves as a binder, disintegrant, and controlled-release agent in oral drug formulations. It enhances drug solubility and release.[34]
Wound Healing	Chitosan	1–5% w/v	Chitosan is used in wound care to promote wound healing. It provides antibacterial properties, hemostasis, and tissue regeneration.[35]
Ophthalmic Treatment	Carbomer (Carbopol)	0.2–1% w/v	Carbomers are employed to enhance the viscosity of ophthalmic formulations, extending drug contact time with the eye's surface while maintaining isotonic conditions.[36]
Transdermal Patches	Acrylate-based adhesive	20–50% w/w	The adhesive polymer in transdermal patches provides skin adhesion while releasing drugs into the bloodstream.[37]
Orthopedic Implants	Polyethylene	10–30%w/w (Based on the specific application and design)	Polyethylene is used in joint replacements due to its durability and low wear rate, enhancing the longevity of the implant.[38]
Biodegradable sutures	Polyglycolic acid (PGA)	Based on suture size and intended use	PGA sutures are biodegradable and provide wound closure, after which the body is naturally absorbed by them.[39]
Dermal fillers	Hyaluronic acid	2–10% w/w	Hyaluronic acid-based dermal fillers are used for facial rejuvenation, adding volume to the skin, and reducing wrinkles.[40]

End-user experience

Consider factors that impact the end-user, such as texture, appearance, and feel. For instance, in cosmetics or pharmaceuticals, the sensory aspects of the formulation can significantly impact consumer acceptance.[47]

Environmental impact

Consider the environmental impact of the polymer, including its biodegradability and potential for recycling, especially as there's a growing emphasis on sustainable and eco-friendly formulations.[48]

Compatibility with manufacturing process

Assess whether the polymer is compatible with the manufacturing process without causing issues like clogging equipment or hindering production efficiency.[49]

Why does polymer act as a drug carrier

Polymers are frequently used as drug carriers in pharmaceutical formulations to rally the delivery of drugs, enhance their bioavailability, and provide controlled release. Various types of polymer-based drug carriers are employed for different applications. Here are some common polymer drug carriers and their uses:

Nanoparticles

Polymer nanoparticles are used to encapsulate drugs, protecting them from degradation, improving solubility, and allowing for controlled release. They are suitable for oral, intravenous, and topical drug delivery. Poly (lactic-co-glycolic acid) (PLGA) nanoparticles, chitosan nanoparticles, and albumin nanoparticles.[48]

Liposomes

Liposomes are lipid bilayer structures that can encapsulate both hydrophobic and hydrophilic drugs. They are used for drug delivery, particularly in cancer therapy, as well as for cosmetic and dermatological applications. Doxil (liposomal doxorubicin) for cancer treatment and various liposomal cosmetic products.[49]

Micelles

Micelles, formed by self-assembling amphiphilic polymers, can solubilize hydrophobic drugs and enhance their delivery. They are used in cancer therapy and targeted drug delivery. Pluronics (poloxamers) and polymeric micelles are notable examples used for drug delivery.[50]

Hydrogels

Hydrogels are three-dimensional networks of polymers that can absorb and retain a large amount of water. They are used for the controlled release of drugs, particularly in topical applications, wound care, and tissue engineering. PEG-based hydrogels, alginate hydrogels, and chitosan hydrogels.[51]

Polymeric microspheres

Polymeric microspheres are often used for controlled drug release. They can be injected locally to release drugs over an extended period. They are commonly used in conditions like osteoarthritis and cancer. Injectable microspheres for long-acting drug delivery.[52]

Dendrimers

Dendrimers are highly branched polymers that improve their solubility, and provide controlled release. They are used in drug delivery, imaging, and diagnostics. Polyamidoamine (PAMAM) dendrimers for drug delivery and imaging.[53]

Polymeric prodrugs

Polymeric prodrugs involve the covalent attachment of drug molecules to a polymer carrier. This strategy can enhance drug solubility, stability, and release. PEGylated prodrugs for improved pharmacokinetics.[54]

Nanogels

Nanogels are nanoscale hydrogels that can encapsulate drugs and bioactive compounds for drug delivery, particularly in cancer therapy and targeted delivery. Chitosan nanogels and PEG-based nanogels.[55]

Mucoadhesive polymers

Mucoadhesive polymers can adhere to mucous membranes, prolonging drug contact and enhancing absorption. They are used in oral, nasal, and ocular drug delivery: carbopol-based formulations and chitosan-based mucoadhesive drug delivery systems.[56]

The choice of polymer-drug carrier depends on the specific drug, route of administration, and desired drug release profile. These polymer-based drug carriers have revolutionized drug delivery, offering improved therapeutic outcomes, reduced side effects, and better patient compliance in many medical treatments (Figure 1).

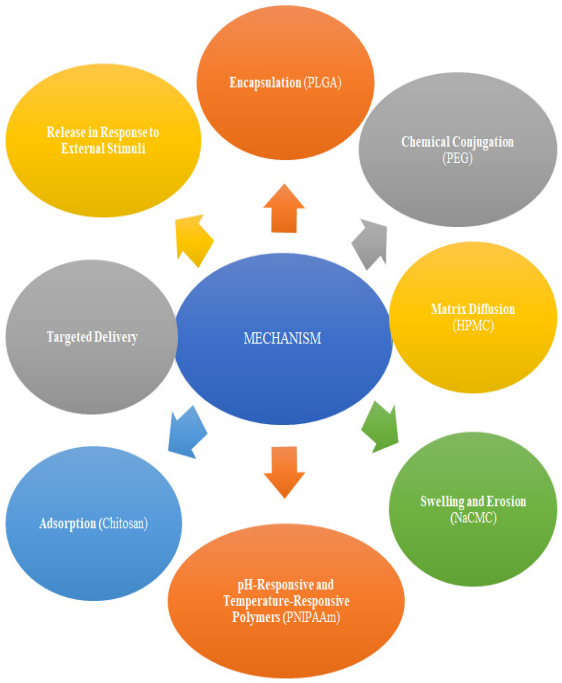

Figure 1: Choice of polymer based on the mechanism of polymer

Significance of Polymer in Different Routes of Administration

The concentration of polymers in pharmaceutical formulations can vary widely depending on the specific route of administration, the desired drug release profile, and other formulation requirements. Some examples of significant polymer concentrations in different routes of administration:

Oral Route:

Tablets and capsules

In oral solid dosage forms, the concentration of binders and disintegrants is typically in the range of 2-10% w/w. Hydrophilic polymers like hydroxypropyl methylcellulose (HPMC) and microcrystalline cellulose (MCC) are commonly used.[57]

Oral solutions and suspensions

Polymers are used as suspending agents, viscosity enhancers, and stabilizers. The concentration of polymers like xanthan gum, HPMC, or carboxymethyl cellulose (CMC) can vary from 0.5 to 5% w/v.

Injectable Route (Intravenous, Intramuscular, Subcutaneous)

Depot formulations

In long-acting injectable formulations, the concentration of polymers such as PLGA or PEG can range from 10 to 40% w/v. These polymers form a depot that releases the drug slowly over time.[58]

Transdermal Route

Transdermal patches

The concentration of adhesive polymers like acrylate-based adhesives in transdermal patches can range from 20 to 50% w/w, depending on the formulation.[59]

Ophthalmic Route

Ophthalmic solutions and gels

Polymers like HPMC or carbomer (Carbopol) are used at concentrations ranging from 0.2 to 1% w/v as viscosity-enhancing agents and mucoadhesives.[60]

Intranasal Route

Intranasal sprays and gels

Polymers such as chitosan or HPMC can be used at concentrations of 0.5 to 1% w/v to enhance drug adhesion to the nasal mucosa and control release.[61]

Pulmonary Route (Inhalation)

Dry Powder Inhalers (DPIs)

In DPIs, the concentration of polymers in carrier particles can vary from 1 to 10% w/w. Lactose or mannitol may be used as carriers, along with a small percentage of fine polymers like HPMC.[62]

Intravaginal Route

Vaginal gels

The concentration of polymers like HPMC can range from 0.5 to 2% w/v in vaginal gels, depending on the desired viscosity and drug release characteristics.[63]

Rectal Route

Suppositories and enemas

Polymers such as polyethylene glycol (PEG) can be used at concentrations ranging from 10 to 70% w/w, depending on the formulation and drug solubility.[64]

Formulation scientists often conduct extensive studies and tests to optimize the polymer concentration for each pharmaceutical product based on the mechanism of drug release, as mentioned in Table 2.

Bioavailability Enhancing Polymers

Several natural polymers have been explored for their potential to increase the bioavailability of drugs and bioactive compounds (Figure 2). These polymers can be used in various pharmaceutical and nutraceutical formulations to improve the absorption and effectiveness of the active ingredients. Some natural polymers known to enhance bioavailability include:

Curcumin with piperine

Curcumin is a bioactive compound found in turmeric that has numerous health benefits, but it has low bioavailability. Piperine, a natural compound found in black pepper, can significantly increase the bioavailability of curcumin by inhibiting its rapid metabolism in the liver and intestines.[75]

Quercetin

Quercetin, a flavonoid found in various fruits and vegetables, enhances the absorption of certain drugs and nutrients, like resveratrol and catechins. It inhibits efflux transporters, which typically reduce the absorption of these compounds.[76]

Rutin

Rutin, another flavonoid, has been found to enhance the bioavailability of certain drugs, particularly those with low water solubility. It can increase the solubility of these drugs and improve their absorption.[77]

Chitosan

Chitosan, a biopolymer derived from chitin in crustacean shells, has mucoadhesive properties that improve drug absorption by extending their contact time with mucous membranes in the gastrointestinal tract.[78]

Hyaluronic acid

Hyaluronic acid, a natural component of connective tissues, is used in drug delivery systems to boost the bioavailability of specific drugs. It protects drugs from enzymatic degradation and enhances their release at the target site.[79]

Lecithin

Lecithin, a natural lipid typically derived from soybeans, is used in lipid-based drug delivery systems to improve the

Table 2: Mechanism of drug release for polymer-based drug delivery system

Drug delivery system	*Mechanism of drug release*
Diffusion-controlled release	Drug molecules diffuse through the polymer matrix, with the release rate influenced by factors such as drug solubility in the polymer, the matrix thickness, and the concentration gradient[65].
Erosion-controlled release	Some polymers are designed to erode gradually when exposed to bodily fluids or external factors, and it release the encapsulated drug. Example: poly(lactic-co-glycolic acid) (PLGA) [66].
Swelling-controlled release	Certain polymers, particularly hydrogels, can swell when in contact with water or bodily fluids. It creates pores and channels, allowing for the drug to diffuse out[67]
Chemically-responsive release	Polymers can be designed to release drugs in response to changes in pH, temperature, or other environmental factors[68].
Stimuli-responsive release	Polymers can be designed to respond to external stimuli like light, ultrasound, or magnetic fields, causing structural changes that trigger drug release[69].
Biodegradation-triggered release	Biodegradable polymers, like PLGA, gradually degrade in the body, releasing the encapsulated drug over time[70].
Polymeric micelles	In this mechanism, amphiphilic polymers self-assemble into micelles, with the hydrophobic core encapsulating hydrophobic drugs. The drugs are released as the micelles disassemble[71].
Surface erosion	Some drug delivery systems consist of a polymer coating that erodes over time, exposing the drug core. This mechanism is often used in oral controlled-release tablets[72].
Hydrolysis of bonds	The drug release is controlled by the hydrolysis of covalent bonds within the polymer backbone. As the polymer degrades through bond cleavage, it releases the drug[73].
Complexation and ion exchange	Some polymers, like ion-exchange resins, can bind to ionic drugs and release them when exposed to competing ions in the surrounding environment[74].

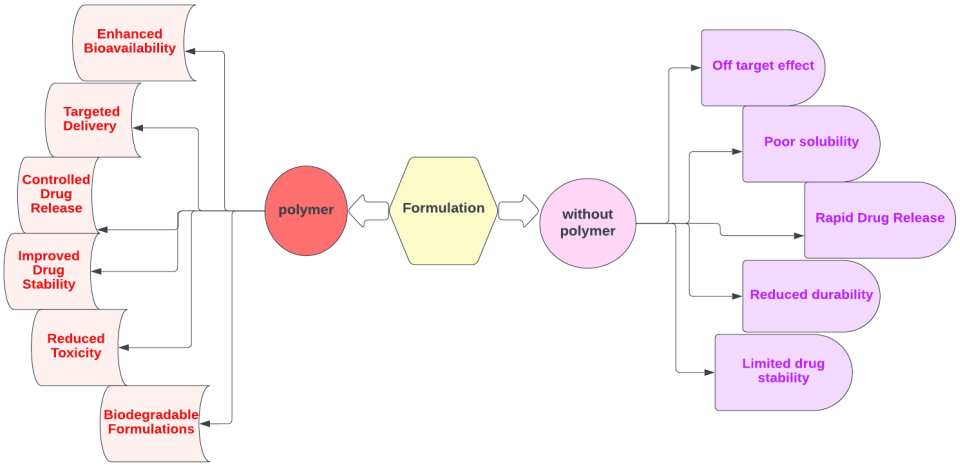

Figure 2: Significance of polymer in pharmaceuticals

solubility of poorly water-soluble drugs and enhance their bioavailability.[80]

Ginsenosides with piperine

Ginsenosides are bioactive compounds found in ginseng. When combined with piperine, their bioavailability can be increased, similar to the enhancement observed with curcumin. Piperine inhibits the enzymes responsible for metabolizing ginsenosides.[81]

Saponins

Saponins, found in various plant sources like ginseng, gynostemma, and soybeans, have been shown to enhance the bioavailability of certain drugs and nutrients. They can increase the permeability of cell membranes in the gastrointestinal tract.[82]

Proanthocyanidins

Proanthocyanidins are natural polyphenolic compounds found in foods like grape seeds and pine bark. They can enhance the bioavailability of certain nutrients by protecting them from degradation and improving their absorption.[83]

Oligosaccharides

Some oligosaccharides, like inulin and fructose oligosaccharides (FOS), can improve the bioavailability of minerals such as calcium and magnesium by enhancing their absorption in the intestines.[84]

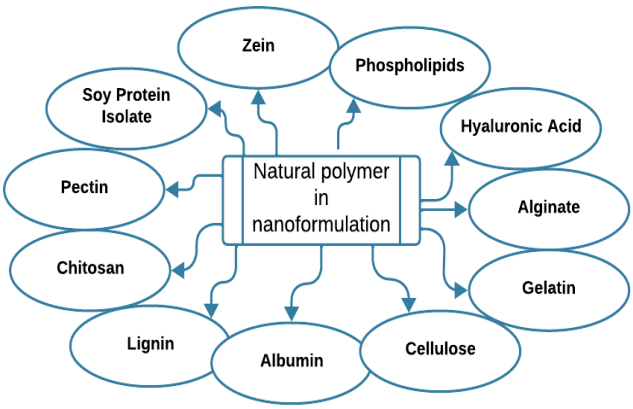

Figure 3: Naturally derived polymer widely used in nanoformulation

Polymer In Nano-World

Polymers play a significant role in nanoformulations, which involve the design and development of nanoparticles at the nanoscale (typically ranging from 1 to 1000 nm) for various applications. Polymers are a crucial component of nanoformulations, enhancing their safety, efficacy, and specificity (Figure 3). The choice of polymer and the design of the nanoparticle system depends on the specific therapeutic or diagnostic goals, as well as the nature of the payload (drug or imaging agent). This makes polymer-based nanoformulations a versatile and essential technology in modern pharmaceutical and medical research.

Key roles and significance of polymers in nanoformulations:

Controlled release

Polymers can be used to create nanoparticles that encapsulate drugs, allowing for controlled and sustained release over time. This approach improves therapeutic efficacy and reduces side effects.[85]

Solubility enhancement

Hydrophobic drugs can be rendered water-soluble and more bioavailable when encapsulated in polymeric nanoparticles. This enhances drug delivery and increases drug absorption.[86]

Targeted delivery

Functionalized polymer nanoparticles can be engineered to target specific tissues, cells, or receptors. Surface modifications enhance drug accumulation at the target site while reducing off-target effects.[87,88]

Contrast agents

Polymers can be used as carriers for imaging agents, such as fluorescent dyes and magnetic nanoparticles, or contrast agents for MRI and CT scans. These polymer-based nanoparticles improve the visibility and accuracy of imaging techniques.[89,90]

Stability and protection

Polymers can provide a protective shell around active compounds, preventing degradation due to environmental factors such as oxygen, light, or enzymes. This enhances the stability of sensitive drugs or imaging agents.[91]

Biocompatibility

Biocompatible polymers are commonly used in nanoformulations to ensure that nanoparticles are well-tolerated by the body, minimizing adverse immune responses and toxicity.[92]

Intracellular delivery

Polymers can aid in the internalization of nanoparticles into cells, which is valuable for drug delivery, gene therapy, and diagnostics. This enables the targeted delivery of therapeutic agents to specific intracellular compartments.[93]

Reduced toxicity

Polymers can reduce the toxicity of certain drugs by encapsulating them within polymer nanoparticles, minimizing the drug's interaction with healthy tissues and thereby improving the therapeutic index.[94]

Extended circulation time

Polymeric nanoparticles can extend drug circulation time in the bloodstream. Surface modifications with polymers such as PEG (polyethylene glycol) reduce recognition and clearance by the immune system, leading to prolonged systemic circulation.[95]

Tissue penetration

Polymers can improve the penetration of nanoparticles into tissues, including solid tumors. This can increase the accumulation of drugs or imaging agents within the target tissue.[96]

Ease of formulation

Polymers provide a versatile platform for the formulation of nanoparticles. Their physicochemical properties can be tailored to suit the specific needs of the application, making them valuable tools for pharmaceutical and biomedical researchers.

Tailored drug release profiles

Polymers allow for the fine-tuning of drug release profiles. By selecting the appropriate polymer and controlling its properties, one can achieve the desired drug release kinetics for a particular application.[97,98]

Limitations of polymer availability in research

Despite these limitations, natural polymers offer significant advantages, including biocompatibility, biodegradability, and reduced toxicity (Table 3). Researchers are continually working to address these challenges through advanced processing techniques, purification methods, and the development of innovative natural polymers that can meet the requirements of pharmaceutical research and drug delivery systems.[99]

The availability of polymers for research faces significant limitations, including restricted chemical diversity, scalability issues, and challenges related to biocompatibility and toxicity. Current polymers often lack the necessary functional groups for specialized applications, while novel polymers may be difficult or expensive to produce on a large scale. Furthermore, many polymers do not meet the stringent safety standards required for biomedical applications, and regulatory hurdles further complicate their use in pharmaceutical research.[100] Additionally, concerns about environmental impact and

Table 3: Preference over selection of natural polymer over synthetic polymer

Natural polymer	*Synthetic polymer*
Batch-to-batch variability	Biocompatibility and toxicity
Limited mechanical strength	Biodegradability
Biodegradability and stability	Inflammatory response
Allergenic potential	Limited drug loading
Limited drug loading capacity	Burst release
Potential for microbial contamination	Complex formulation
Immunogenicity	Regulatory challenges
Lack of standardization	Limited targeting precision
Complex processing	Stability and degradation
Regulatory challenges	Allergic reactions
	Cost and scalability
	Interference with drug activity
	Lack of standardization

intellectual property rights contribute to the challenges surrounding polymer availability. To address these limitations, new polymers that can revolutionize drug delivery systems and enhance therapeutic outcomes are desperately needed by the pharmaceutical industry. These new polymers must offer targeted drug delivery capabilities, controlled release mechanisms, and improved solubility to increase drug efficacy and patient compliance.[101] Furthermore, the development of biodegradable carriers and smart polymers that respond to environmental triggers presents exciting opportunities for innovation in pharmaceutical research. By overcoming the limitations of current polymers and introducing versatile and biocompatible alternatives, researchers can advance drug delivery technologies and pave the way for more effective and safer pharmaceutical treatments.

Future Prospects in Polymer-Mediated Drug Delivery Systems

Polymer-based drug delivery systems are reshaping pharmaceutical practices by enabling precise, controlled, and extended drug release. Advances in biodegradable polymers like PLA and PGA improve the delivery of chemotherapeutics, reducing systemic side effects and enhancing effectiveness. Polymers that respond to specific physiological stimuli, such as pH, temperature, or enzymes, offer targeted treatment for conditions like cancer and diabetes. Nanopolymers are advancing the delivery of biologics, such as proteins and nucleic acids, by boosting stability and cellular uptake. Moreover, innovations in 3D printing allow for the customization of drug delivery devices, facilitating personalized treatment plans. These advancements have the potential to revolutionize the management of chronic diseases and improve patient outcomes.

CONCLUSION

Pharmaceutical polymers are fundamental to both traditional and innovative drug delivery systems. They are commonly employed as drug carriers to enhance drug delivery, improve bioavailability, and enable controlled release. These polymers are utilized in various applications, including cancer therapy, as well as in cosmetic and dermatological fields. This paper aims to explore the classification, properties, drug release mechanisms, applications, and limitations of polymers in drug delivery systems.

In summary, polymers are large molecules made up of repeating monomer units and have diverse applications across multiple fields. Natural polymers are valued for their biocompatibility, renewability, biodegradability, and minimal environmental impact, increasing their significance. Pharmaceutical polymers are vital in drug formulation and delivery, offering controlled release, enhanced solubility, and improved drug properties. The choice of polymers is influenced by factors such as chemical compatibility, physical properties, stability, safety, cost, processing ease, performance requirements, user experience, environmental impact, and manufacturing compatibility. Polymers are essential in drug formulations to enhance delivery, bioavailability, and controlled release.

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AUTHORS' CONTRIBUTIONS

PB: conceptualization, collection of information, data curation, drafting the manuscript. PVT: conceptualization, drafted the work and revised it critically for important intellectual content.

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