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Review Article

Smart Polymers: Next-Generation Platforms for Advanced Drug Delivery

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ABSTRACT

Smart polymers possess significant potential for various applications. Smart polymeric drug delivery systems have been examined as "intelligent" mechanisms capable of releasing encapsulated medications in response to specific physiological signals at the appropriate time and location of action. A slight stimulus induces these polymers to behave nonlinearly, altering their structure and properties on a macroscopic scale. Smart polymers, or stimulus-responsive materials, are a category of substances that can react to particular stimuli by enduring reversible alterations in their properties. Smart polymers possess remarkable characteristics derived from their adaptability and reactivity. Researchers must determine the optimal applications of smart polymers across several domains, as these materials respond to diverse stimuli, including temperature, pH, electric and magnetic fields, light intensity, and biological molecules. Smart polymers have potential applications in gene therapy, protein folding, actuator stimulation, tailored medication administration, and enhanced drug transport.

1. INTRODUCTION

Clinical efficacy of pharmaceutical and biological therapies is frequently constrained by issues like short half-lives, low bioavailability, and vulnerability to physical and chemical instability. Denaturation, aggregation, and precipitation are some of the unpleasant outcomes that can occur when highly organized biomolecules, like proteins, undergo structural changes, leading to physical instability and, in the long run, a decrease in therapeutic efficacy (Khan et al., 2022; Hunter & Moghimi, 2017). In response to these difficulties, polymers, which are big molecules made up of repeating subunits, have developed into useful drug delivery methods. Polymers are very versatile for many biomedical uses because their physical, chemical, and biological characteristics can be exhibited by varying the chemical composition, sequence, and structural arrangement of these subunits (Aundhia et al., 2024; Bharti et al., 2023; Sajjad et al., 2024).

Every living thing relies on polymers. Important cellular processes are carried out by polymeric macromolecules like proteins, nucleic acids, and polysaccharides inside biological systems. They are involved in intricate biochemical signalling networks,

aid in the storage of genetic information, permit catalysis, and give structural support. To improve the stability, solubility, and targeted distribution of drugs, synthetic and semi-synthetic polymers have been developed to mimic or enhance these biological properties. The term "smart polymer" has been more popular in engineering and science journals as of late, indicating a rise in curiosity about polymers with the ability to react to their surroundings (Handa et al., 2022; Krug et al., 2017).

An example of an external stimulus is changes in temperature, pH, light, or electric and magnetic fields. Materials with this capability are called smart polymers, stimulus-responsive polymers, or intelligent polymers. Because of their reactivity, their structural and functional characteristics may be precisely controlled, making them perfect for high-tech drug delivery systems. With their ability to control the release kinetics and target therapeutics to specific tissues or cellular microenvironments, smart polymers show great promise in providing controlled, site-specific, and responsive treatment options, surpassing the current limitations of pharmaceuticals and biological therapies (Xia et al., 2024; Rahim et al., 2021).

2. SMART POLYMERS

Smart or stimuli-responsive polymers undergo rapid, non-linear changes in their physical properties when exposed to minor environmental cues. These reversible transitions may involve alterations in swelling or shrinking behavior, conductivity, physical state, structural conformation, or solubility. Injectable delivery systems based on smart polymers offer major advantages, including simple preparation, ease of administration, and prolonged drug release, with their applications continuing to expand into more advanced therapeutic areas (Givarian et al., 2024; Jamirad et al., 2025).

Stimuli that activate smart polymers generally fall into three categories: (a) physical, (b) chemical, and (c) biological. Physical triggers include temperature, electric or magnetic fields, electromagnetic radiation, mechanical stress, and ultrasound. Chemical triggers involve changes in pH or the presence of specific ions or molecules, while biological triggers include enzymes or other biomolecules (Ziegler et al., 2024).

A small external stimulus can induce a sudden shift in a smart polymer's properties. These materials, often referred to as intelligent polymers, can undergo reversible structural changes once the trigger is removed, returning to their initial state. Their hallmark non-linear response allows minimal stimuli to produce distinct macroscopic effects (Mann et al., 2024). Figure 1 illustrates the concept of smart polymer-based drug delivery. The left side represents a smart polymer carrier containing different drug molecules, shown as colored shapes. The capsule in the center depicts the dosage form releasing these drug-loaded polymers into the body. The human figure on the right represents targeted delivery, where the smart polymer system transports the drug to the intended site and releases it in a controlled manner. Each component demonstrates a step in the drug delivery pathway - from encapsulation to administration to targeted release.

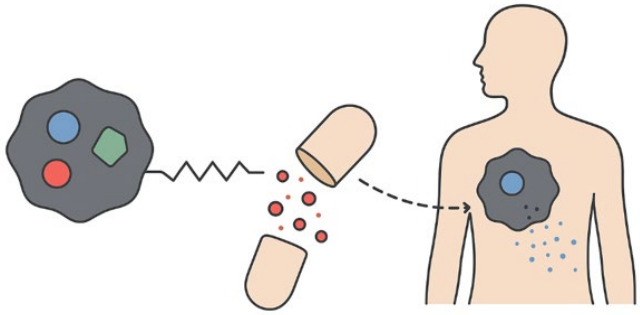

Figure 1: Smart polymers in drug delivery (the figure summarizes the key stages of smart polymer-mediated drug delivery, such as encapsulation of therapeutic agents within a stimuli-responsive polymeric carrier, administration through an appropriate dosage form, transport and distribution within the body, and targeted, stimulus-triggered release at the desired site).

2.1. Polymers that react to temperature

A slight change in temperature can cause thermosensitive polymers to suddenly change solubility. In addition to preserving physicochemical stability and biological activity, an aqueous thermosensitive polymeric solution exhibits temperature-dependent, reversible sol-gel transitions near body temperature that regulate the release rate of the integrated medication (Zhou et al., 2025; Fattah-alhosseini et al., 2024).

2.2 Polymers responsive to electric fields

A tiny change in the electric current alters the physicochemical characteristics of electric-field-sensitive polymers. These polymers are pH-responsive and have a comparatively high concentration of ionisable groups along the backbone chain. Electro-responsive polymers are widely used in energy transduction, controlled medication delivery, artificial muscle actuation, and sound absorption because they convert electrical energy into mechanical energy (Balcerak-Woźniak et al., 2024).

3 DRUG DELIVERY MECHANISMS

A variety of drug delivery techniques can utilize smart polymers, including hydrogels, implants, and nanoparticles. The release mechanisms can be broadly categorized as follows. The release of drug molecules is regulated by diffusion as they move through the polymer matrix. One way to adjust the rate is to change the polymer's properties. The polymer undergoes swelling-controlled release when exposed to certain stimuli, allowing the drug to be released over time. This is a typical behavior of hydrogels that respond to changes in pH or temperature. The drug, which is chemically attached to the polymer, is released when specific stimuli trigger a chemical reaction.

Smart polymers used as parenteral delivery platforms for peptide and protein therapeutics are ideal since they are biocompatible and biodegradable. Smart polymers used as parenteral delivery platforms for peptide and protein therapeutics are generally designed to be biocompatible and biodegradable, with minimized risks of carcinogenicity, immunogenicity, and genotoxicity. However, their safety profile ultimately depends on polymer composition, degradation products, and formulation strategy, which must be carefully evaluated in preclinical and clinical studies (Singh et al., 2025; Singh & Nayak, 2023). Table 1 comprises the classification and applications of smart polymers in drug delivery.

3.1 Diffusion-Controlled Drug Release

In diffusion-controlled drug delivery systems, the therapeutic agent is released as drug molecules migrate from the polymer matrix into the surrounding medium along a natural concentration gradient. The rate at which diffusion takes place is strongly influenced by factors such as the polymer's porosity, crosslink density, molecular weight, degradability, and external environmental conditions, including pH and temperature. Diffusion may occur through two major structural arrangements within the polymer. In matrix-type systems, the drug is uniformly dispersed throughout the polymer network, and release proceeds gradually as the drug slowly diffuses outward while the polymer structure remains largely intact. In contrast, reservoir-type systems consist of a drug-filled core enclosed by a polymeric membrane, and release is governed by the selective permeability of this outer shell. Conceptually, this can be visualized as either drug molecules moving outward from a dispersed matrix or permeating through a surrounding membrane in a reservoir configuration. Diffusion-controlled mechanisms are widely employed in sustained-release formulations because they enable predictable, consistent, and prolonged drug release profiles, which are essential for maintaining therapeutic levels over extended periods (Khalil et al., 2025).

3.2 Swelling-Controlled Drug Release

Swelling-controlled drug delivery systems function through the polymer's ability to expand when exposed to specific physiological stimuli such as pH, ionic strength, or temperature. Upon contact with biological fluids, the polymer absorbs water, causing its three-dimensional network to loosen and increasing the free volume within the matrix. This expansion enlarges the mesh size of the polymer structure, enabling drug molecules to diffuse outward more readily. Hydrogels are the most common examples of such systems, as they undergo substantial swelling in aqueous environments, while stimuli-responsive variants-for instance, temperature-sensitive or pH-responsive polymers-swell only under defined conditions. Conceptually, this process can be visualized as a transition from a dense, dry polymer to a swollen, hydrated network through which the drug diffuses via newly created channels. Swelling-controlled mechanisms are particularly advantageous for on-demand release, as they allow the polymer to respond selectively to localize physiological cues, ensuring controlled and site-specific drug delivery (Bikram & West, 2008).

3.3 Chemically Controlled Drug Release

Chemically controlled drug delivery involves the release of therapeutic agents through polymer degradation, cleavage of chemical bonds, or reactions triggered by specific internal or external stimuli. In many such systems, the drug may be covalently attached to the polymer backbone or embedded within a biodegradable matrix, from which release occurs only when the polymer undergoes chemical transformation. Hydrolytic degradation, such as the cleavage of ester or amide linkages, is a common pathway, while enzyme-mediated degradation provides selective release within biological environments rich in specific catalytic proteins. Redox-sensitive systems, often incorporating disulfide linkages, respond to the highly reducing intracellular milieu to trigger drug liberation. Additionally, photo-cleavable or pH-sensitive linkers enable external control through light exposure or localized acidity changes. This mechanism can be visualized as a polymer-drug conjugate that releases its payload only when exposed to the appropriate biochemical or environmental trigger. By ensuring that

Table 1: Classification and Applications of Smart Polymers in Drug Delivery

Type of Smart Polymer	Stimulus Trigger	Mechanism of Action	Example Polymers	Applications in Drug Delivery
pH-responsive polymers	Changes in pH (acidic or basic environment)	Ionization or deionization of functional groups leading to swelling or collapse	Poly(acrylic acid), Chitosan derivatives	Oral delivery targeting the stomach or intestine, tumor-targeted delivery
Temperature-responsive polymers	Changes in temperature	Phase transition at Lower Critical Solution Temperature (LCST) or Upper Critical Solution Temperature (UCST)	Poly(N-isopropylacrylamide) (PNIPAAm)	Injectable depot systems, hyperthermia-triggered release
Enzyme-responsive polymers	Presence of specific enzymes	Enzyme-mediated cleavage or degradation of the polymer backbone	Peptide-based polymers, Dextran derivatives	Cancer therapy, site-specific delivery in inflammatory tissues
Light-responsive polymers	Exposure to UV, visible, or NIR light	Photoisomerization, photocleavage, or photothermal effects	Azobenzene-containing polymers, Gold nanoparticle hybrids	On-demand drug release, ocular delivery
Redox-responsive polymers	Changes in cellular redox potential	Cleavage of disulfide linkages in reducing environments	Poly(disulfide)s, PEG-SS-PLA copolymers	Intracellular drug delivery, gene delivery
Magnetic-responsive polymers	External magnetic field	Heat generation or mechanical movement of magnetic nanoparticles	Magnetic nanoparticle-polymer composites	Targeted delivery to deep tissues, hyperthermia therapy

drug release occurs exclusively in targeted microenvironments, chemically controlled systems offer high specificity and precision, making them especially valuable for therapies requiring strict spatial or temporal control (Xu et al., 2021).

4. SMART POLYMERS' BENEFITS FOR MEDICATION DISTRIBUTION

Smart polymers can be engineered to target drug delivery to specific body regions, thereby enhancing therapy efficacy and minimizing systemic adverse effects. These polymers enable precise regulation of medication release rates and timing, facilitating enduring and effective treatment. Smart polymers facilitate personalized therapy by customizing their properties to meet the specific needs of each patient, hence ensuring effective treatment for particular diseases. Minimized toxicity and adverse effects can be attained through targeted and controlled release, hence reducing the duration of drug exposure to healthy tissues. Notwithstanding their potential, numerous problems persist in the advancement and execution of smart polymers for drug delivery (Sobczak, 2022).

Ensuring that smart polymers do not cause adverse immune responses is essential for their application in clinical environments. Producing these materials in a cost-efficient and scalable fashion continues to pose a difficulty. Smart polymer systems are intricate and necessitate comprehensive testing and approval procedures, potentially delaying their market launch. The integration of several stimuli-responsive processes is expected to be the primary focus of forthcoming research to enhance the functioning and adaptability of individual polymer systems. Moreover, improvements in nanotechnology may enable the development of more efficient and accurate delivery methods (Gupta et al., 2002).

5. EXPANDED APPLICATIONS OF SMART POLYMERS

Smart polymers have shown their revolutionary potential in several areas of medicine by being used in more ways. These polymers enable localized release of anticancer drugs within the tumor microenvironment, enhancing treatment efficacy while reducing systemic toxicity. Drug release can be triggered by an acidic pH, high enzyme activity, and localized hyperthermia. Researchers are working on making glucose-responsive polymers that can distribute insulin on their own. This is a big topic of study in diabetes care. These polymers would allow insulin to be given in amounts that match the levels of glucose in the blood, which would mean fewer doses. Smart polymer platforms have revolutionized gene therapy by making it easier to transfer genes and nucleic acids (Gupta et al., 2002).

They do this by stopping DNA and RNA molecules from being broken down by enzymes and letting them be released in cells in response to signals from inside the cell. Smart polymers have been used in ocular delivery systems to make the release of medicine in the eye more controlled and longer-lasting. This is especially useful for people with long-term conditions like glaucoma, and to keep infections from occurring after surgery. Thermosensitive hydrogels made of smart polymers can help with tissue regeneration and infection prevention at the site of injury by delivering growth factors and antimicrobials in a targeted way. These hydrogels are used to help wounds heal. One area that shows promise for treating neurological diseases is the use of stimuli-sensitive nanoparticles that can cross the blood-brain barrier and release therapeutic medications in a controlled way. This is a crucial application for delivering drugs to the brain (Gupta et al., 2002; Noro et al., 2023).

6. ADVANCED TYPES OF SMART POLYMERS

Advanced smart polymers have made drug delivery systems more flexible and accurate than ever before. Researchers have created multi-stimuli sensitive polymers that can respond to changes in pH, temperature, and other environmental parameters at the same time. This makes it possible to deliver medications exactly where they are needed in complex physiological situations. Shape-memory polymers can go back to their original shape when they are exposed to things like heat, light, or magnetic fields. Because of this, they are perfect for usage as biomedical implants, scaffolds, and adaptive devices that don't need to be obtrusive. Self-healing polymers can also fix structural damage that happens while they are being used. This means that drug delivery systems are stronger and can work for longer without breaking down. Biodegradable smart polymers break down into safe, biocompatible chemicals after they release their medicine, so you don't have to worry about long-term safety or having to have surgery to remove them. 4D-printed smart polymers are a newer type of technology that combines materials that respond to stimuli with additive manufacturing processes. This makes it possible to make personalized drug carriers and implants that can respond to changes in the body's physiology and administer drugs with incredible accuracy (Shi et al., 2020).

7. DRUG DELIVERY STRATEGIES ENHANCED BY SMART POLYMERS

Drug delivery systems enhanced by smart polymers offer innovative solutions to enhance therapeutic outcomes and patient adherence. With on-demand release systems, clinicians and patients have more control over treatment programs since drugs can be begun or managed to release at certain times and places using outside stimuli like light, ultrasound, or magnetic fields. Sustained and pulsatile release devices can lower the number of doses needed while keeping therapeutic medicine levels in the body for longer by imitating physiological rhythms such as the pulsatile secretion of insulin. Redox-sensitive polymers have made it possible to focus on certain organelles inside cells. These polymers react with reducing agents in cells, which lets medications get straight into the cytoplasm or mitochondria. This has many uses, such as delivering genes and treating cancer. Combination therapy is another significant advance. It uses smart polymers to administer and release multiple medications at different rates. This makes it easier to treat complicated diseases like cancer, diabetes, and infections, and it can also make treatments work better together (Shi et al., 2020; Bejarano et al., 2018).

8. CURRENT LIMITATIONS AND CHALLENGES

The widespread clinical application of smart polymers for drug delivery is currently obstructed by existing limitations and challenges. Even little changes in temperature, pH, or metabolic signals might make drug release less reliable and reproducible. This makes it very hard to get a precise response to certain physiological conditions. Making stimuli-responsive polymers usually involves complicated chemical reactions that are hard to scale up and keep consistent and cost-effective, which makes the scaling up and manufacturing processes even harder. It is essential to evaluate the long-term safety of these compounds, considering the risks of immunogenic reactions, systemic accumulation, or toxic degradation products, prior to their appropriate administration to humans. Moreover, smart polymers require extensive preclinical and clinical research to demonstrate biocompatibility, efficacy, and safety; this may prolong the duration of regulatory approval, thereby delaying their market entry. Lastly, cost-effectiveness is still something to consider because smart polymers are more expensive to develop and design than regular excipients. This could mean that they aren't employed as often in healthcare (Hosseini et al., 2016; Hoare & Kohane, 2008).

A deeper comparison of different stimulus-responsive systems further highlights how the choice of stimulus is dictated by therapeutic needs and physiological constraints. For instance, temperature-

responsive polymers are often preferred over pH-responsive systems when localized, externally controlled activation is required. Temperature-sensitive carriers, particularly those exhibiting an LCST near physiological temperature, enable minimally invasive in situ gelation and sustained release upon slight thermal variation, making them suitable for injectable depots and thermally triggered tumor therapies. In contrast, pH-responsive systems rely primarily on inherent physiological gradients, such as gastric acidity or tumor acidosis, which may vary significantly between patients and disease states. Consequently, temperature-responsive systems offer better reproducibility and spatiotemporal control in situations where endogenous pH changes are insufficient or unpredictable.

An analysis of previously reported approaches reveals both the advantages and limitations of existing smart polymer platforms. Thermoresponsive systems have demonstrated high drug-loading capacity, good biocompatibility, and effective depot formation; however, issues such as slow biodegradation, incomplete drug release, and temperature heterogeneity within tissues remain challenges. Similarly, pH-responsive polymers show promising results in targeting acidic tumor microenvironments and gastrointestinal drug delivery. Yet, their performance is often hindered by premature swelling, sensitivity to minor pH fluctuations, and potential instability during storage. Studies utilizing enzyme-, light-, or redox-responsive systems have shown improved specificity and on-demand release. However, many still face limitations related to synthesis complexity, inconsistent trigger penetration, or scalability for clinical translation. By evaluating these successes and limitations collectively, it becomes evident that while smart polymer technologies hold strong therapeutic potential, careful optimization of sensitivity, stability, and manufacturing feasibility is essential for improving their clinical applicability (Hamzy et al., 2024).

9. FUTURE PERSPECTIVES

Smart polymers have the potential to dramatically change the healthcare and medication delivery industries in the future. When nanotechnology is added to hybrid nanosystems, they are expected to be multifunctional carriers that can do targeted distribution, controlled release, and therapeutic activity at the same time. Polymers mixed with lipids, metals, or biomolecules will make up these systems. Machine learning models may help with release kinetics, predict how polymers will respond, and speed up the search for new materials that are more suited for certain biological uses. These are all good things for AI to do in polymer design (Tran et al., 2024; Ferji, 2025). Smart polymers will also help personalized medicine because they can be made to fit each patient's unique physiology and sickness profile, which will make treatments more accurate and less likely to cause side effects. Theranostic polymers are a new way to combine therapy and diagnostics (Rajora et al., 2024). For example, MRI-visible nanogels can carry drugs and give imaging feedback to show how well the treatment is working in real time. Smart coatings on ecologically friendly packaging can keep medications from breaking down because of light, humidity, or oxygen. This makes the drugs more stable and gives them a longer shelf life. This is just one more way that smart polymers could be useful outside of delivering medications (Long et al., 2025; Gao et al., 2024).

10. CONCLUSION

Smart polymers represent a transformative class of materials that enable precise, stimulus-responsive, and patient-tailored drug delivery. The advancements discussed in this review demonstrate substantial progress in polymer design, responsiveness, and therapeutic applicability; however, challenges related to safety, scalability, regulatory acceptance, and reproducibility remain key barriers to clinical translation. Future efforts must focus on integrating multi-responsive behaviors, improving biodegradability and long-term biocompatibility, and harnessing emerging tools such as machine learning to accelerate material optimization. By aligning scientific innovation with practical clinical and manufacturing considerations, smart polymers have the potential to evolve from experimental platforms into robust, next-generation drug delivery technologies that meaningfully improve therapeutic outcomes.

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Conflict of interest

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