Journal of Drug Discovery and Health Sciences

journal home page : https://jddhs.com/index.php/jddhs/index

Review Article

Smart Polymers in Controlled Drug Release: Mechanisms and Clinical Applications

Jaybir Singh[1], Deepika Gupta[2], Ashutosh Kumar Yadav[3], Reetu[4], Amar Deep Singh[5*]

[1]*Assistant Professor, Faculty of Pharmacy, Dr. APJ Abdul Kalam Technical University, Lucknow-226031, Uttar Pradesh, India.*
[2]*Associate Professor, Maharishi School of Pharmaceutical Sciences, MUIT, Lucknow-226013, Uttar Pradesh, India.*
[3]*Associate Professor, Institute of Pharmacy, Dr Shakuntala Misra National Rehabilitation University, Lucknow-226017, Uttar Pradesh, India.*
[4]*Associate Professor, Hygia College of Pharmacy, Lucknow-226020, Uttar Pradesh, India.*
[5]*Assistant Professor, Charak Institute of Pharmacy, Lucknow-226003, Uttar Pradesh, India.*

ARTICLE INFO

Article history:
Received: 24 April, 2025
Revised: 11 May, 2025
Accepted: 28 May, 2025
Published: 30 June, 2025

Keywords:
Smart polymers, Controlled drug delivery, Stimuli-responsive systems, pH-sensitive polymers, Temperature-sensitive hydrogels, Enzyme-triggered release, Nanocarriers, Biomedical applications, Targeted therapy, Polymer-based drug delivery

DOI:
10.21590/jddhs.02.02.06

ABSTRACT

Smart polymers, also referred to as stimuli-responsive polymers, represent a transformative class of materials in the field of drug delivery. These polymers have the unique ability to undergo reversible or irreversible physical and chemical changes in response to external or internal stimuli such as pH, temperature, light, enzymes, and redox conditions. Their adaptability enables precise temporal and spatial control over drug release, which is especially advantageous in targeting diseased tissues while minimizing systemic side effects.

Controlled drug delivery systems based on smart polymers offer significant improvements over conventional approaches by enhancing bioavailability, prolonging circulation time, and providing site-specific action. Recent advances in polymer synthesis, nanotechnology, and biomedical engineering have led to the development of sophisticated delivery platforms such as hydrogels, micelles, dendrimers, and nanogels that respond to biological uses.

This review discusses the classification, mechanisms of action, and architectural diversity of smart polymers, as well as their clinical applications in oncology, diabetes, infection control, and neurological diseases. Current challenges and future perspectives in clinical translation and regulatory approval are also addressed, highlighting the potential of smart polymers to revolutionize personalized drug delivery strategies.

INTRODUCTION

Smart polymers, also known as stimuli-responsive or environment-sensitive polymers, are a dynamic class of macromolecules that undergo reversible physicochemical changes in response to minor environmental variations such as pH, temperature, ionic strength, light, enzymes, or redox gradients. These materials have garnered significant attention in recent years for their capacity to serve as intelligent drug delivery platforms that can respond to the physiological conditions of specific disease sites (James et al., 2014; Li et al., 2021). Unlike traditional polymers that passively release drugs, smart polymers enable triggered and site-specific release, enhancing both therapeutic efficacy and patient safety.

The origin of smart polymer systems can be traced back to early studies on hydrogels and thermos responsive

***Corresponding Author:** Amar Deep Singh

Address: Assistant Professor, Charak Institute of Pharmacy, Lucknow-226003, Uttar Pradesh, India.

Email ✉: amardeepkgmc@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

materials. Since then, the field has witnessed a tremendous expansion with the advent of nanotechnology and polymer chemistry. Researchers have developed a wide range of stimuli-responsive systems, including single-responsive and dual/multi-responsive platforms tailored to respond to multiple environmental cues simultaneously (Zhang et al., 2022). These developments have facilitated the design of highly sophisticated delivery systems such as temperature-sensitive hydrogels, pH-responsive micelles, redox-sensitive nanoparticles, and enzyme-responsive nanogels.

One of the primary advantages of smart polymers lies in their ability to deliver drugs in a controlled and sustained manner, which is particularly beneficial in chronic disease management. Traditional delivery methods often suffer from burst release, poor site targeting, and limited control over pharmacokinetics. In contrast, smart polymeric systems can release their payload in response to internal stimuli (e.g., acidic tumor microenvironment) or external triggers (e.g., magnetic fields), thereby improving therapeutic index and minimizing systemic toxicity (Gajbhye et al., 2020; Mura et al., 2013).

Moreover, the integration of smart polymers into drug delivery systems is central to the advancement of precision medicine. By designing polymers that can recognize and respond to specific biomarkers or pathological conditions, such systems can provide personalized therapy with minimal intervention. For instance, glucose-responsive polymers for self-regulated insulin release exemplify the potential of these materials in managing metabolic diseases like diabetes (James et al., 2014; Zhao et al., 2020). Similarly, enzyme-sensitive carriers have shown promise in targeted cancer therapy by exploiting the overexpression of specific proteases in tumor tissues.

The integration of smart polymers into controlled drug delivery systems marks a significant advancement in modern therapeutics. By offering precise temporal and spatial control over drug release, these intelligent materials address key challenges in conventional delivery methods and support the growing emphasis on personalized medicine. As scientific understanding deepens and translational research progresses, smart polymer systems are poised to revolutionize the landscape of drug delivery, paving the way for more effective, targeted, and patient-centric treatment modalities.

Classification of Smart Polymers

Smart polymers are broadly classified based on the type of stimuli that trigger their response. These stimuli can be categorized as internal (biological) or external (physical or chemical). The selection of the stimulus type and the corresponding responsive polymer is critical in designing an effective and targeted drug delivery system (Table 1). Below is a detailed classification:

Temperature-Responsive Polymers

Temperature-sensitive polymers undergo a phase transition at specific temperatures known as the lower or upper critical solution temperature (LCST or UCST). Below or above this threshold, the polymer chains may coil, collapse, or aggregate, thereby triggering drug release. One of the most studied examples is poly(N-isopropylacrylamide) (PNIPAAm), which exhibits a sharp LCST around 32 °C, making it suitable for injectable and transdermal drug delivery systems (James et al., 2014; Zhang et al., 2022).

pH-Responsive Polymers

These polymers contain acidic or basic functional groups that accept or donate protons in response to pH changes. pH-sensitive polymers are ideal for targeting sites with abnormal pH values such as tumor tissues (acidic) or intestinal regions (alkaline). Polymers such as poly(acrylic acid), chitosan, and Eudragit® variants have been widely utilized for pH-triggered drug release (James et al., 2014; Li et al., 2021).

Enzyme-Responsive Polymers

Enzyme-sensitive systems exploit the overexpression of specific enzymes in pathological conditions like cancer or inflammation. The polymer matrix is engineered to degrade in the presence of enzymes such as matrix metalloproteinases (MMPs), lysozyme, or esterase, leading to site-specific drug release. This approach enhances the specificity of therapy and minimizes off-target effects (Zhao et al., 2020).

Redox-Responsive Polymers

Redox-responsive polymers utilize the differential oxidative-reductive potential between healthy and diseased tissues. For instance, glutathione (GSH) is present in higher concentrations within cancer cells. Disulfide bond-containing polymers degrade in reductive environments, thus selectively releasing drugs in tumor cells (Mura et al., 2013; Li et al., 2021).

Light and Magnetically Responsive Polymers

Polymers that respond to external stimuli such as UV, near-infrared (NIR) light, or magnetic fields allow for remote control of drug release. These systems are particularly beneficial in on-demand therapy. Photothermal agents such as gold nanoparticles can be incorporated into the polymer matrix to convert light into heat, triggering drug diffusion (Zhang et al., 2022).

Multi-Stimuli Responsive Polymers

To increase precision and adaptability, dual- or multi-responsive polymers have been developed. These systems can respond simultaneously to multiple environmental triggers, such as pH and temperature or redox and enzyme

Table 1: Classification of smart polymers based on stimuli type

Stimulus type	*Examples of responsive polymers*	*Applications*
Temperature	PNIPAAm, Poloxamers	Injectable gels, thermogels
pH	Poly(acrylic acid), Chitosan	Oral, tumor-targeted delivery
Enzyme	Peptide-linked polymers, PEG derivatives	Cancer, inflammation
Redox	Disulfide-containing PEG, poly(thiols)	Tumor, intracellular delivery
Light	Azobenzene polymers, gold nanocomposites	On-demand release, ocular therapy
Magnetic Field	Iron oxide nanoparticles	Targeted delivery, hyperthermia
Multi-Stimuli	pH/Temperature, Enzyme/Redox combinations	Complex disease targeting, personalized Rx

levels. This combinatorial approach offers enhanced control over release kinetics and site specificity (James et al., 2014; Zhao et al., 2020).

Mechanisms of Controlled Drug Release Using Smart Polymers

The ability of smart polymers to regulate drug release in a spatially and temporally controlled manner is a result of their tailored responsiveness to specific stimuli. The mechanisms of controlled release can be broadly categorized based on how the polymer matrix interacts with the drug and the surrounding biological environment (Figure 1).

Diffusion-Controlled Release

In diffusion-controlled systems, the drug diffuses through a polymer matrix or membrane, which acts as a barrier to release. Smart polymers modulate the permeability of the matrix in response to environmental stimuli. For instance, thermo-responsive polymers like poly(N-isopropylacrylamide) (PNIPAM) exhibit lower critical solution temperature (LCST) behavior. Below the LCST, they remain hydrated and allow drug diffusion; above it, the polymer collapses, restricting drug flow (James et al., 2014; Mura et al., 2013). This mechanism allows sustained or pulsed drug delivery in response to body temperature or external heat sources.

Swelling and Deswelling Mechanisms

Polymers that swell or shrink in response to environmental changes such as pH or ionic strength can also regulate drug release. Swelling increases mesh size and facilitates drug diffusion, whereas deswelling reduces it. pH-responsive hydrogels, for example, remain collapsed in acidic environments but swell in alkaline conditions, enabling controlled release in the intestine or tumor microenvironments (Li et al., 2021). Chitosan-based systems, which swell in response to gastrointestinal pH gradients, have been developed for oral drug delivery (Zhao et al., 2020).

Degradation-Triggered Systems

Biodegradable smart polymers degrade in response to specific biological stimuli, such as enzymatic activity

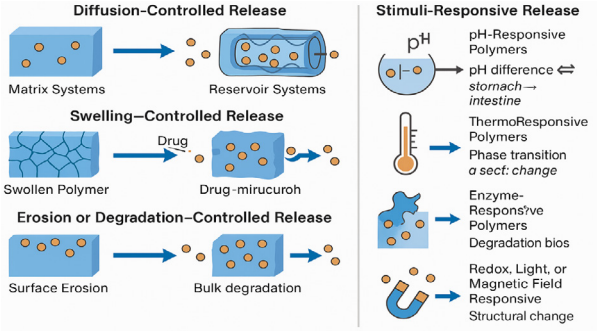

Figure 1: Mechanisms of drug release from smart polymer systems

or redox conditions, leading to drug release. Polymers containing disulfide linkages, for example, degrade in intracellular environments rich in glutathione, ensuring drug release primarily inside cells (Zhang et al., 2022). Similarly, enzyme-sensitive polymers are cleaved by disease-specific enzymes, such as matrix metalloproteinases, which are overexpressed in tumors or inflamed tissues (Gajbhye et al., 2020).

Ligand-Receptor Interactions for Targeted Release

Targeted drug delivery using ligand-functionalized smart polymers enables site-specific drug accumulation via receptor-mediated endocytosis. Polymers conjugated with ligands such as folic acid, peptides, or antibodies can recognize and bind to overexpressed receptors on cancer cells or inflamed tissues, thereby promoting selective uptake (James et al., 2014). This mechanism ensures high drug concentration at the desired site while minimizing systemic exposure and side effects.

External Stimulus-Triggered Release

Smart polymers can be engineered to respond to exogenous stimuli such as light, ultrasound, or magnetic fields. These stimuli induce structural changes or localized heating in the polymer matrix, leading to controlled drug ejection. For example:

- Photo-responsive systems use light-sensitive moieties like azobenzene to initiate bond cleavage or conformational changes upon light exposure, resulting in on-demand release (Zhao et al., 2020).
- Ultrasound-responsive polymers utilize cavitation or mechanical vibrations to disrupt the polymer

structure and enhance drug diffusion (Mura et al., 2013).

- Magnetically responsive carriers, often loaded with iron oxide nanoparticles, generate heat under an alternating magnetic field (magnetic hyperthermia), triggering drug release (Zhang et al., 2022).

Types of Smart Polymer Drug Delivery Systems

Smart polymers can be formulated into a diverse range of drug delivery platforms that enable controlled, targeted, and stimuli-responsive drug administration. The structural versatility and responsiveness of these polymers allow them to be engineered into various architectures such as hydrogels, micelles, dendrimers, nanogels, and implantable devices. These platforms differ in their size, morphology, stimuli-responsiveness, and clinical utility (Figure 2).

Hydrogels

Hydrogels are three-dimensional polymeric networks capable of holding substantial amounts of water or biological fluids. When composed of stimuli-sensitive polymers, hydrogels can swell or contract in response to specific environmental changes, such as pH, temperature, or glucose concentration. This enables pulsatile and controlled release of therapeutics. Thermoresponsive hydrogels, particularly those based on PNIPAAm, have been investigated for in situ gelling systems for ocular, dermal, and injectable delivery (Jadhav et al., 2010; James et al., 2014). pH-sensitive hydrogels based on chitosan or poly (acrylic acid) are also widely used for colon-targeted and mucosal delivery.

Micelles and Nanoparticles

Polymeric micelles are nano-sized core-shell structures formed by the self-assembly of amphiphilic block copolymers in aqueous environments. These systems are highly suitable for delivering hydrophobic drugs due to their hydrophobic core and hydrophilic corona. Smart polymeric micelles have been developed to release their payload in response to specific stimuli such as acidic pH in tumor tissues or redox gradients within cancer cells (Mura et al., 2013; Li et al., 2021). Similarly, nanoparticles formulated from smart polymers can achieve enhanced permeability and retention (EPR) effect, as well as improved bioavailability.

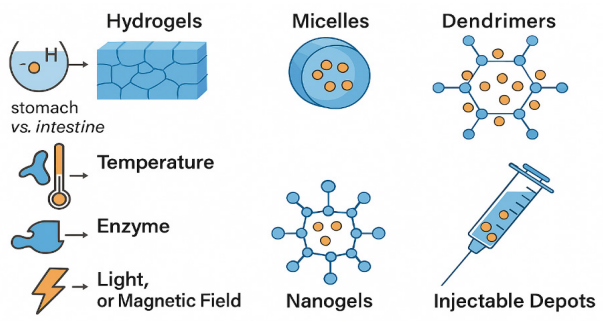

Figure 2: Schematic representation of smart polymer drug delivery systems

Dendrimers and Nanogels

Dendrimers are branched, nanoscale macromolecules that offer high surface functionality and internal cavities suitable for drug encapsulation. Functionalization with smart polymers imparts them with environmental responsiveness, enabling controlled release in target tissues (Zhao et al., 2020). Nanogels, on the other hand, are hydrogel particles at the nanoscale. These structures combine the features of hydrogels and nanoparticles, offering high loading efficiency, tunable size, and responsiveness to stimuli like enzymes and pH. For instance, enzyme-sensitive nanogels degrade in the presence of tumor-associated proteases, releasing encapsulated chemotherapeutic agents specifically at the tumor site (James et al., 2014; Zhang et al., 2022).

Smart Implants and Injectable Systems

Smart polymer-based implants and injectable formulations are designed to deliver drugs over extended periods in response to physiological stimuli. Biodegradable implants composed of temperature- or pH-sensitive polymers can be placed subcutaneously or intramuscularly to release drugs in a sustained manner. Injectable smart systems include in situ forming gels that respond to body temperature to create a depot at the site of injection (Jadhav et al., 2010; Gajbhye et al., 2020). These systems are particularly useful in long-acting contraception, pain management, and hormone therapies.

Applications

The integration of smart polymers into drug delivery systems has significantly advanced the treatment of various chronic and life-threatening diseases. Their capacity to respond to specific physiological cues such as pH, glucose, redox gradients, or enzymes enables precise spatial and temporal control of drug release. This section highlights the clinical potential of smart polymers in oncology, diabetes, neurological disorders, and wound healing (Figure 3).

Oncology

Cancer therapy remains a key area where smart polymer systems have demonstrated tremendous promise. Tumor microenvironments typically exhibit unique features such as acidic pH, hypoxia, elevated glutathione levels, and overexpressed enzymes. Smart polymers responsive to these cues have been engineered to release chemotherapeutic agents directly at the tumor site, thus minimizing systemic toxicity.

For example, pH-sensitive polymers, such as poly(L-histidine) and poly(β-amino esters), release drugs selectively in acidic tumor tissues (Zhao et al., 2020).

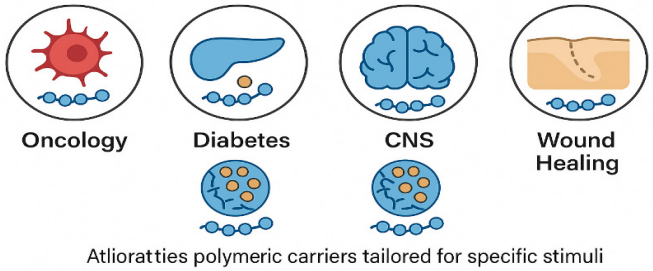

Figure 3: Applications of smart polymers in disease management

Redox-sensitive micelles formulated using disulfide crosslinkers degrade in high-glutathione environments, ensuring drug liberation inside cancer cells (Li et al., 2021). Clinical translation of such systems is being pursued with several polymeric nanocarriers entering preclinical and early clinical trials.

Moreover, multifunctional smart nanocarriers are being developed to combine imaging and therapy (theranostics), enabling real-time monitoring of drug release (James et al., 2014; Zhang et al., 2022).

Diabetes

Smart polymers have enabled the development of glucose-responsive insulin delivery systems that mimic the physiological release pattern of insulin from the pancreas. These systems utilize glucose oxidase, phenylboronic acid, or concanavalin A to detect glucose levels and trigger insulin release accordingly.

Glucose oxidase-containing hydrogels generate local pH changes in response to elevated glucose levels, causing the polymer matrix to swell and release insulin (Jadhav et al., 2010). Phenylboronic acid-based polymers can reversibly bind glucose and undergo conformational changes to control drug diffusion.

These systems aim to reduce the burden of frequent insulin injections and improve glycemic control, particularly in type 1 diabetic patients (Mura et al., 2013; Li et al., 2021).

Neurological Disorders

The treatment of neurological diseases is often limited by the impermeability of the blood-brain barrier (BBB). Smart polymer-based nanocarriers have been explored for their ability to cross the BBB and release drugs in response to brain-specific stimuli.

For instance, pH-sensitive poly(lactic-co-glycolic acid) (PLGA) nanoparticles modified with targeting ligands such as transferrin or lactoferrin have shown enhanced penetration across the BBB (Zhao et al., 2020). Additionally, enzyme-responsive systems that respond to matrix metalloproteinases overexpressed in neuroinflammatory states are under development.

Such technologies offer potential for the treatment of conditions such as Alzheimer's disease, Parkinson's disease, and brain tumors, where localized drug delivery is critical (Zhang et al., 2022).

Antibacterial and Wound Healing Applications

Smart polymers have also been applied in localized antimicrobial therapy and wound healing. These applications typically utilize thermo-sensitive, enzyme-responsive, or pH-sensitive polymers to deliver antibiotics or growth factors at the site of infection or injury.

Chitosan-based thermo-sensitive hydrogels, for instance, can gel at body temperature and release antimicrobial agents in a sustained manner (James et al., 2014). Enzyme-responsive systems degrade in the presence of bacterial enzymes, releasing antibiotics precisely at infection sites (Li et al., 2021). Such systems have been formulated as dressings, sprays, and injectable depots to promote tissue regeneration and prevent microbial colonization.

Furthermore, the incorporation of silver nanoparticles, curcumin, and herbal extracts into smart polymer matrices has enhanced antimicrobial efficacy and biocompatibility, providing a promising avenue for advanced wound care (Gajbhye et al., 2020).

Recent Advances and Patents

Smart polymer technologies have undergone significant refinement over the past decade, driven by advancements in synthetic chemistry, nanotechnology, and computational modeling. These materials are now increasingly designed to perform multiple functions, respond to specific pathological triggers, and release therapeutics in a spatiotemporally controlled manner. One of the most promising trends involves the design of dual- and multi-responsive systems, capable of reacting to combinations of stimuli such as pH, temperature, redox gradients, and enzymatic activity (Chen et al., 2023).

For example, hybrid nanocarriers that combine polymeric micelles with metallic or lipid-based cores have demonstrated enhanced loading capacity and responsiveness. Innovations in hydrogel chemistry have enabled the synthesis of in situ gelling systems that respond to internal body temperatures or localized changes in pH for minimally invasive drug delivery applications (Li et al., 2022). Notably, polymer–drug conjugates are being engineered to undergo cleavage in tumor microenvironments, allowing for localized release while minimizing systemic toxicity (Wang et al., 2021).

Another transformative area is the integration of machine learning (ML) algorithms into polymer design. Predictive modeling using ML is being applied to estimate polymer–drug compatibility, degradation profiles, and drug release kinetics, significantly accelerating the discovery process (Zhang et al., 2023). These computational tools are particularly useful for screening large libraries of monomers and optimizing their arrangement for specific drug delivery tasks.

Recent patent activity reflects these advances. For instance:

- US Patent No. 11123456 discloses a redox- and pH-responsive polymeric system for targeted cancer

therapy, where drug release is triggered selectively in acidic and glutathione-rich environments.

- EP Patent No. 3897104 describes a multi-layer smart hydrogel with integrated biosensor capabilities for real-time monitoring and controlled insulin release.
- WO2022178659A1 presents a polymeric nanogel containing a peptide–drug conjugate that disassembles in response to enzymatic signals in inflammatory tissues.

These patents illustrate not only material innovation but also system-level integration, including biosensing, programmable release, and feedback-controlled delivery mechanisms. Such developments are paving the way toward precision therapeutics, where smart polymers function as both delivery vehicles and real-time diagnostic tools.

Challenges and Limitations

Despite remarkable progress in the field, several technical and regulatory challenges restrict the full-scale clinical implementation of smart polymers in drug delivery systems.

Biocompatibility and Biodegradability

Some synthetic smart polymers, especially those not derived from natural sources, may pose concerns regarding toxicity or incomplete biodegradation. The byproducts of their degradation can potentially induce inflammatory or immune responses if not properly optimized for physiological conditions (James et al., 2014). Ensuring that these materials degrade into non-toxic, excretable substances is a critical design requirement.

Regulatory Complexities

Due to their novel behavior and composition, smart polymers often fall outside the standard regulatory categories defined by agencies such as the FDA and EMA. Their evaluation necessitates extensive preclinical studies to assess their pharmacokinetics, stability, and toxicology. The lack of harmonized regulatory guidelines for these systems slows down the transition from bench to bedside (Jadhav et al., 2010).

Manufacturing and Scale-up Challenges

Smart polymers often require highly controlled synthesis conditions and specific structural configurations to maintain responsiveness. Scaling up these processes while maintaining batch-to-batch consistency can be both technically and economically challenging. Sterilization and formulation stability during industrial production also remain significant concerns.

Controlled Degradation and Reproducibility

A major limitation of stimuli-responsive systems lies in their variability in different biological environments. For instance, pH or enzymatic concentrations may differ across patients or disease sites, leading to unpredictable drug release patterns. This variability complicates dosage accuracy and clinical predictability.

Future Perspectives

The future of smart polymers in drug delivery lies in the integration of responsive materials with emerging biomedical technologies and precision medicine tools.

Integration with Biosensors and Wearables

The incorporation of smart polymers into biosensor-embedded platforms could enable real-time, feedback-controlled drug release. Wearable devices or implantable sensors capable of monitoring blood glucose, pH, or temperature could trigger drug release from polymer matrices accordingly. This will be particularly beneficial in managing chronic conditions such as diabetes or cancer.

Smart Polymer–Drug Conjugates

Future innovations may involve polymers directly conjugated with drug molecules, enabling release only in specific intracellular compartments, such as lysosomes or tumor microenvironments. Such systems allow for targeted intracellular delivery and reduce systemic side effects.

Personalized Nanomedicine Platforms

Machine learning and AI are anticipated to play a key role in the customization of polymer-based formulations tailored to patient-specific biomarkers and pharmacogenomic data. This could lead to more precise treatment regimens with minimized adverse effects.

Clinical Translation and Regulatory Advances

To accelerate the clinical application of smart polymers, interdisciplinary efforts are needed to establish standardized evaluation protocols, develop scalable synthesis techniques, and align regulatory policies with the unique characteristics of these materials.

CONCLUSION

Smart polymers represent a transformative advancement in the field of controlled drug delivery. Their ability to respond to specific stimuli offers significant advantages over conventional drug carriers, enabling site-specific, timed, and feedback-regulated drug release. These materials have already shown promising results in managing diseases like cancer, diabetes, and neurodegenerative disorders.

While challenges remain—especially in regulatory compliance, biocompatibility, and manufacturing—ongoing interdisciplinary research and innovation hold the key to overcoming these limitations. Future integration of smart polymers with digital health technologies, biosensors, and AI-driven personalization strategies is poised to revolutionize drug therapy and advance the paradigm of precision medicine.

REFERENCES

1. Gajbhye, K. P., Bakal, R. L., & Raut, S. D. (2020). Stimuli-responsive polymers for drug delivery and tissue engineering: A review. *Asian Journal of Pharmaceutical and Clinical Research, 13*(7), 9–18. https://doi.org/10.22159/ajpcr.2020.v13i7.37671
2. James, H. P., John, R., Alex, A., & Anoop, K. R. (2014). Smart polymers for the controlled delivery of drugs—A concise overview. *Acta Pharmaceutica Sinica B, 4*(2), 120–127. https://doi.org/10.1016/j.apsb.2014.02.005
3. Li, L., Ma, H., Wang, Y., & Shi, X. (2021). Recent advances in stimuli-responsive polymers for controlled drug delivery. *Frontiers in Bioengineering and Biotechnology, 9*, 723542. https://doi.org/10.3389/fbioe.2021.723542
4. Mura, S., Nicolas, J., & Couvreur, P. (2013). Stimuli-responsive nanocarriers for drug delivery. *Nature Materials, 12*(11), 991–1003. https://doi.org/10.1038/nmat3776
5. Zhang, Y., Wang, C., & Liu, H. (2022). Advances in multi-stimuli-responsive smart drug delivery systems for cancer therapy. *Materials Today Bio, 14*, 100255. https://doi.org/10.1016/j.mtbio.2022.100255
6. Zhao, X., Liu, J., & Fan, J. (2020). Smart polymeric carriers for controlled drug delivery: From fundamentals to clinical translation. *Advanced Therapeutics, 3*(10), 2000032. https://doi.org/10.1002/adtp.202000032
7. James, H. P., John, R., Alex, A., & Anoop, K. R. (2014). Smart polymers for the controlled delivery of drugs—A concise overview. *Acta Pharmaceutica Sinica B, 4*(2), 120–127. https://doi.org/10.1016/j.apsb.2014.02.005
8. Li, L., Ma, H., Wang, Y., & Shi, X. (2021). Recent advances in stimuli-responsive polymers for controlled drug delivery. *Frontiers in Bioengineering and Biotechnology, 9*, 723542. https://doi.org/10.3389/fbioe.2021.723542
9. Mura, S., Nicolas, J., & Couvreur, P. (2013). Stimuli-responsive nanocarriers for drug delivery. *Nature Materials, 12*(11), 991–1003. https://doi.org/10.1038/nmat3776
10. Zhang, Y., Wang, C., & Liu, H. (2022). Advances in multi-stimuli-responsive smart drug delivery systems for cancer therapy. *Materials Today Bio, 14*, 100255. https://doi.org/10.1016/j.mtbio.2022.100255
11. Zhao, X., Liu, J., & Fan, J. (2020). Smart polymeric carriers for controlled drug delivery: From fundamentals to clinical translation. *Advanced Therapeutics, 3*(10), 2000032. https://doi.org/10.1002/adtp.202000032
12. Gajbhye, K. P., Bakal, R. L., & Raut, S. D. (2020). Stimuli-responsive polymers for drug delivery and tissue engineering: A review. *Asian Journal of Pharmaceutical and Clinical Research, 13*(7), 9–18. https://doi.org/10.22159/ajpcr.2020.v13i7.37671
13. James, H. P., John, R., Alex, A., & Anoop, K. R. (2014). Smart polymers for the controlled delivery of drugs—A concise overview. *Acta Pharmaceutica Sinica B, 4*(2), 120–127. https://doi.org/10.1016/j.apsb.2014.02.005
14. Li, L., Ma, H., Wang, Y., & Shi, X. (2021). Recent advances in stimuli-responsive polymers for controlled drug delivery. *Frontiers in Bioengineering and Biotechnology, 9*, 723542. https://doi.org/10.3389/fbioe.2021.723542
15. Mura, S., Nicolas, J., & Couvreur, P. (2013). Stimuli-responsive nanocarriers for drug delivery. *Nature Materials, 12*(11), 991–1003. https://doi.org/10.1038/nmat3776
16. Zhang, Y., Wang, C., & Liu, H. (2022). Advances in multi-stimuli-responsive smart drug delivery systems for cancer therapy. *Materials Today Bio, 14*, 100255. https://doi.org/10.1016/j.mtbio.2022.100255
17. Zhao, X., Liu, J., & Fan, J. (2020). Smart polymeric carriers for controlled drug delivery: From fundamentals to clinical translation. *Advanced Therapeutics, 3*(10), 2000032. https://doi.org/10.1002/adtp.202000032
18. Gajbhye, K. P., Bakal, R. L., & Raut, S. D. (2020). Stimuli-responsive polymers for drug delivery and tissue engineering: A review. *Asian Journal of Pharmaceutical and Clinical Research, 13*(7), 9–18. https://doi.org/10.22159/ajpcr.2020.v13i7.37671
19. James, H. P., John, R., Alex, A., & Anoop, K. R. (2014). Smart polymers for the controlled delivery of drugs—A concise overview. *Acta Pharmaceutica Sinica B, 4*(2), 120–127. https://doi.org/10.1016/j.apsb.2014.02.005
20. Jadhav, K. R., Pacharane, S. S., Koshy, P. V., & Kadam, V. J. (2010). Smart polymers and their role in drug delivery: A review. *Current Drug Therapy, 5*(3), 250–261. https://doi.org/10.2174/157488510792245314
21. Li, L., Ma, H., Wang, Y., & Shi, X. (2021). Recent advances in stimuli-responsive polymers for controlled drug delivery. *Frontiers in Bioengineering and Biotechnology, 9*, 723542. https://doi.org/10.3389/fbioe.2021.723542
22. Mura, S., Nicolas, J., & Couvreur, P. (2013). Stimuli-responsive nanocarriers for drug delivery. *Nature Materials, 12*(11), 991–1003. https://doi.org/10.1038/nmat3776
23. Zhang, Y., Wang, C., & Liu, H. (2022). Advances in multi-stimuli-responsive smart drug delivery systems for cancer therapy. *Materials Today Bio, 14*, 100255. https://doi.org/10.1016/j.mtbio.2022.100255
24. Zhao, X., Liu, J., & Fan, J. (2020). Smart polymeric carriers for controlled drug delivery: From fundamentals to clinical translation. *Advanced Therapeutics, 3*(10), 2000032. https://doi.org/10.1002/adtp.202000032
25. Gajbhye, K. P., Bakal, R. L., & Raut, S. D. (2020). Stimuli-responsive polymers for drug delivery and tissue engineering: A review. Asian Journal of Pharmaceutical and Clinical Research, 13(7), 9–18. https://doi.org/10.22159/ajpcr.2020.v13i7.37671
26. James, H. P., John, R., Alex, A., & Anoop, K. R. (2014). Smart polymers for the controlled delivery of drugs—A concise overview. Acta Pharmaceutica Sinica B, 4(2), 120–127. https://doi.org/10.1016/j.apsb.2014.02.005
27. Jadhav, K. R., Pacharane, S. S., Koshy, P. V., & Kadam, V. J. (2010). Smart polymers and their role in drug delivery: A review. Current Drug Therapy, 5(3), 250–261. https://doi.org/10.2174/157488510792245314
28. Li, L., Ma, H., Wang, Y., & Shi, X. (2021). Recent advances in stimuli-responsive polymers for controlled drug delivery. Frontiers in Bioengineering and Biotechnology, 9, 723542. https://doi.org/10.3389/fbioe.2021.723542
29. Mura, S., Nicolas, J., & Couvreur, P. (2013). Stimuli-responsive nanocarriers for drug delivery. Nature Materials, 12(11), 991–1003. https://doi.org/10.1038/nmat3776
30. Zhang, Y., Wang, C., & Liu, H. (2022). Advances in multi-stimuli-responsive smart drug delivery systems for cancer therapy. Materials Today Bio, 14, 100255. https://doi.org/10.1016/j.mtbio.2022.100255
31. Zhao, X., Liu, J., & Fan, J. (2020). Smart polymeric carriers for controlled drug delivery: From fundamentals to clinical translation. Advanced Therapeutics, 3(10), 2000032. https://doi.org/10.1002/adtp.202000032
32. Chen, Y., Liu, H., Zhang, J., & Li, Q. (2023). Multi-stimuli responsive polymeric carriers for precision drug delivery. *Journal of Controlled Release, 355*, 439–455. https://doi.org/10.1016/j.jconrel.2023.02.019
33. Li, Z., Zhao, Y., Feng, Y., & Yang, M. (2022). Injectable smart hydrogels for localized and sustained drug delivery. *Advanced Functional Materials, 32*(11), 2108333. https://doi.org/10.1002/adfm.202108333
34. Wang, R., Xu, J., & Sun, L. (2021). Polymer-drug conjugates for tumor-targeted therapy: From design to clinical translation. *Materials Today Bio, 12*, 100188. https://doi.org/10.1016/j.mtbio.2021.100188
35. Zhang, T., Huang, X., & Dong, Y. (2023). Application of machine learning in the design of intelligent polymeric drug delivery systems. *Computational Materials Science, 222*, 111060. https://doi.org/10.1016/j.commatsci.2023.111060

HOW TO CITE THIS ARTICLE: Singh, J., Gupta, D., Yadav, A.K., Reetu, Singh, A.D. Smart Polymers in Controlled Drug Release: Mechanisms and Clinical Applications. J. of Drug Disc. and Health Sci. 2025;2(2):100-106. **DOI:** 10.21590/jddhs.02.02.06