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Review Article

Recent developments in some types of smart stimuli-responsive polymers in advanced drug delivery systems and medicine, A mini review

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ABSTRACT

Smart polymers (also stimulus-responsive polymers) are an advanced class regarding materials which can undergo reversible chemical or physical transitions within broad spectrum of internal and external triggers, such as pH, temperature, light, magnetic or electric field, biologically derived cue. New innovations especially point at the integration of bio-responsive, photo-responsive and field-responsive polymers, which have distinctive operational benefits. Bio-responsive systems are highly physiologically specific and the light-activated polymers allow highly specific spatiotemporal control, and magnetic or electric field-responsive platforms enable non-invasive and remotely controlled drug delivery. The latest trends in research focus more on the development of multi-responsive systems, a combination of two or more stimuli, to improve the ability to be more adaptable and provide a further fine-tuning of the drug-release profiles. The merging hybrids have more selectivity, therapeutic precision, and responsiveness compared to the previous single-trigger methods. But they also bring about new problems with structural complexity, long-term biocompatibility, and scalable manufacturability, which distinguishes them as compared to their predecessors and will affect their clinical readiness. Comparatively, pH- and thermo-responsive polymers are relatively mature and closer to clinical translation, whereas photo-responsive and field-responsive systems are more versatile, but still have impediments linked to tissue penetration, stimulus delivery, and safety validation. The latest generation is multi-responsive and bio-integrated platforms that has the best potential.

Keywords: Smart polymers, drug delivery, stimuli-responsive polymers, Bioresponsive polymers.

INTRODUCTION

Smart polymers, also known as stimuli-responsive or environmentally sensitive polymers, undergo reversible physical and chemical changes in response to subtle environmental changes, such as pH, temperature, ionic strength, light, enzymes, or redox gradients. These materials have developed as smart drug delivery platforms that can respond to the physiological conditions of specific disease sites.The controlled and sustained delivery of drugs is one of the most significant benefits of smart polymers, and it is useful in the treatment of chronic diseases. The conventional modes of delivery mostly have a number of disadvantages, the main one included sudden release, poor targeting of sites and inadequate pharmacokinetics.

Conversely, smart polymer systems release their cargo because of internal (e.g. acidic tumor microenvironment) or external (e.g. magnetic fields) stimuli to enhance therapeutic efficacy and lower systemic toxicity (Balcerak *et al*., 2024) Smart polymers have been invested in incorporating into the drug delivery system to enhance precise medicine. The systems can be implemented to provide tailored treatment and minimum treatment by producing polymers that detect and respond to specific biomarkers or states of disease. The potential of such materials can be applied in the treatment of metabolic disorders like diabetes with the help of self-release of insulin- sensitive polymers (Zhao *et al*., 2023). The implementation of smart polymers in the regulated drug delivery systems may be regarded as the next step in the development of the contemporary therapeutics.

This property of these smart materials to deliver the drug in a high temporal and spatial precision can help overcome the challenges that pose the conventional delivery mechanism and provide the push to the trend towards the individual approach to medicine. As the field of science becomes more enlightened and the level of applied research continues to advance, the next step in the development of drug delivery technologies is represented by smart polymer systems, which will guarantee increased therapeutic effectiveness and a more accurate future in targeted medicine.

(Table 1) shows a comparison between the main stimuli-responsive polymers and their biomedical significance.

Table (1): Comparison of Major Stimuli-Responsive Polymers and Their Biomedical Importance

Stimulus Type	Response Mechanism	Representative Polymers	Key Biomedical Applications
pH-responsive	Ionization changes; swelling/deswelling	PAA, PAH, chitosan, PMAA	Tumor-targeted drug delivery, GI-tract delivery, smart vaccines, DNA/RNA carriers
Temperature-responsive	Phase transition (LCST/UCST); solubility change	PNIPAM, Pluronics, poly (OEGMA)	Heat-triggered drug release, tissue engineering, thermo-switchable nanocarriers
Light-responsive	Photocleavage, photo-isomerization, photothermal effects	Azobenzene-polymers, spiropyran-polymers, gold–polymer hybrids	Photothermal therapy, spatiotemporally controlled drug release, advanced imaging
Enzyme-responsive	Enzymatic cleavage of specific bonds	Peptide-based polymers, polysaccharides, enzyme-labile hydrogels	Targeted delivery to enzyme-rich tissues (e.g., tumors), tissue engineering, biosensors
Redox-responsive	Cleavage of disulfide bonds; redox-triggered structural changes	Disulfide-crosslinked polymers, polythiols, PEG–SS–polyesters	Intracellular drug/siRNA delivery, cancer therapy, cytosolic release systems
Magnetic field-responsive	Heat generation or guided movement	Fe_3O_4 polymer hybrids, magnetic nanocomposites	Magnetic hyperthermia, targeted nanocarriers, MRI-guided delivery
Electric field-responsive	Changes in conductivity, charge, or conformation	Conductive polymers (PANI, PEDOT: PSS)	Active drug release, implantable medical devices, neural interfaces
Mechanical-responsive	Shape changes under pressure/stretching	Mechano-responsive hydrogels, shape-memory polymers	Smart prosthetics, responsive stents, mechanically triggered drug release
Multi-stimuli responsive	Combined responses (pH + heat/light/redox)	Block copolymers, hybrid nanogels, smart micelles	Personalized therapy, precise tumor targeting, advanced multifunctional nanocarriers

MATERIALS AND METHODS

A transparent and structured review strategy was utilized to achieve methodological rigor and reliability. Three major databases of scientific journals, namely Scopus, PubMed and Web of Science, were searched through predefined keywords such as, smart polymers, stimuli-responsive polymers, drug delivery, bio-responsive polymers, photo-responsive polymers, field-responsive polymers and multi-responsive systems.

Inclusion criteria encompassed:

- Peer-reviewed research articles and review papers published between 2018 and 2025.
- Studies presenting clear mechanisms, fabrication strategies, or biomedical applications of smart polymers.
- Articles focused on drug delivery, targeted therapy, tissue engineering, or controlled-release systems.
- Full-text papers available in English.

Exclusion criteria included non-indexed papers, conference abstracts lacking methodological detail, and studies outside biomedical relevance.

Initial screening identified 106 papers, with duplicates removed before further sorting. After reviewing titles and abstracts, 89 articles remained for full evaluation. Ultimately, 50 studies met all eligibility criteria and were included in the final compilation. A chronological filtering process was applied to prioritize the most recent and innovative developments. The final dataset was categorized by catalyst type, polymer mechanism, and application area, enabling comparative and objective analysis.

Types of Smart Polymer

Smart polymers are classified based on the type of stimuli that trigger their response. These stimuli can be classified as (internal) biological or (external) physical or chemical. To design an effective and targeted drug, the type of stimuli and the corresponding responsive polymer must be carefully and effectively selected.

pH-Responsive Polymers

This is a pH-sensitive polymer, which is defined by the presence of an acidic or base functional group that receives or gives out protons according to pH changes. Ph-responsive polymers are a good option to be used in targeting those regions with abnormal pH conditions, like the acidic tumor tissue or the alkaline intestinal conditions. Some of the polymers employed in this area have included poly (acrylic acid), chitosan and Eudragit (ranges of Eudragit) given the fact that they are very responsive to changes in pH. Some of the most common pH-responsive materials include acidic and basic polymers (das *et al.,* 2020). These polymers are functionalized with functional groups that either can give up or receive protons like -COOH, -SO3H, and trivalent amino groups and these groups ionize as the pH varies resulting in alteration of the polymer structure. The pk a value is the value where the degree of ionization is significantly changed, causing an apparent dissociation constant (Ka) to differ with the dissociation constant of monobasic acids or bases of the same nature. These polymers are ionic polymers that are marked into two broad groups, acidic and basic polymers and may be derived naturally or made synthetically through many different ways. Natural multi- responsive polymers and pH-responsive polymers have gained growing popularity over the recent years.

pH-responsive acidic polymer

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pH-Responsive Basic Polymers

pH-responsive basic polymers are among the most important types of smart polymers, capable of altering their physical and chemical behavior in response to changes in the pH of the surrounding medium. Their action is based on the availability of free basic amino groups, including primary (-NH2), secondary (-NHR), or tertiary (-NR2), and can accept protons (H+) in acidic conditions, resulting in the change of the surface charge and the change of the solubility of the polymer. When pH is low ($pH < pKa$), the amino groups become ionized to the positive (-NH3+) form which repels the electrostatic force between the polymer chains, which ultimately results in the extension and high solubility in water. Conversely, at high PH (pH pKa), the groups de-ionize, to yield the non-ionized form (-NH2) resulting in the shortening of polymer chains and a corresponding drop in solubility. This can be reversed, which makes such materials useful in applications requiring accurate drug uptake and release regulation (Cherian *et al.*, 2024).

Prominent examples of these polymers include:

- Poly (2-dimethylaminoethyl methacrylate) (PDMAEMA), a polymer containing tertiary amino groups that give it high sensitivity to pH changes. It is utilized in systems of gene and drug delivery because of its capability for changing its charge depending on surrounding environment (Protsak *et al.*, 2025).
- Poly (ethylene imine) (PEI), containing primary, secondary and tertiary amines, is employed in delivering nucleic acids due to so-called proton sponge effect, in which, through ionizing amino groups in acidic cellular vesicles, osmotic pressure is enhanced and inner membrane is ruptured, releasing DNA into cytoplasm (Protsak *et al.*, 2025).
- Poly (L-histidine), a biopolymer containing imidazole groups with a pKa of approximately 6, making it sensitive to intracellular acidic conditions. It is utilized for delivering proteins and drugs to specific sites within the cell (Balcerak-Woźniak *et al.*, 2024.).
- Poly(2-vinylpyridine) (P2VP), containing pyridine groups ionizable at low pH, is utilized for releasing drugs in acidic environments like stomach or tumor environment.
- Features of these polymers include the capability of regulating release of drugs or genes based on variations in pH of biological medium, making these polymers very important in smart and targeted delivery systems.

The reversible nature of response to pH changes, in addition to the capability of adjusting surface charge, present extensive opportunities to utilizing these polymers in contemporary medical practices, especially in gene transfer and targeted therapy (Protsak *et al.*, 2025).

(Table 2) compares pH-responsive polymers based on their functional group type and response mechanism. The table highlights key differences between acidic and basic polymers in terms of charge nature in various environments, their behavior with pH changes, and the potential biopharmaceutical applications of each class in drug delivery. It also presents commonly used examples for each type, facilitating a better understanding of the properties and mechanisms of action of these polymers within intelligent, stimulus-responsive.

Table (2): Comparison of acidic pH-responsive with basic pH-responsive polymers.

Feature	Acidic-pH-Responsive Polymers	Basic-pH-Responsive Polymers
Functional Groups	$–COOH, –SO_3H, –PO_3H_2$	$–NH_2, –NHR, –NR_2$
Mechanism of Response	Protonation/deprotonation of acidic groups	Protonation/deprotonation of basic groups
Charge at Low pH (Acidic environment)	Mostly neutral ($–COOH$)	Positively charged ($–NH_3^+$)
Charge at High pH (Basic environment)	Negatively charged ($–COO^-$)	Mostly neutral ($–NH_2$)
Behavior in Low pH	Chains shrink due to reduced charge repulsion	Chains swell due to electrostatic repulsion
Behavior in High pH	Chains swell due to charge repulsion	Chains shrink due to loss of charge
Typical Applications	Drug release in intestines or neutral-basic microenvironments	Drug/gene delivery in acidic environments such as stomach or tumor microenvironment
Examples	Poly (acrylic acid), Poly (methacrylic acid), Poly (itaconic acid)	Poly (ethylene imine), Poly(L-histidine), Poly (2-dimethylaminoethyl methacrylate)

Temperature-responsive polymers

One of the most common stimuli-responsive polymer types are temperature-responsive polymers, capable of altering their physical or chemical characteristics with an ambient temperature change. They are reversible between a solution or a hydrogel state, meaning that these changes can be utilized easily in drug delivery area, biosensing, tissue engineering, or the creation of smart materials (Zhang *et al.,* 2023). Critical solution temperature (CST) principle forms the basis of thermoresponsive polymers that determine the thermal point at which a polymer behavior can be altered. These temperatures are divided into two main types:

1. Low critical solution temperature (LCST):

The polymer dissolves in water at lower temperature degrees than LCST, and shrinks or precipitates at higher temperature degrees than LCST. Poly (N-isopropyl acrylmolide, PNIPAM), is a typical example contracting at around 32deg C (Yoon *et al*., 2024).

2. Upper Critical Solution Temperature (UCST):

At temperature degrees above UCST, the polymer dissolves in water, while it precipitates at lower temperature degrees. This polymer type has limited use in medical and catalytic applications.

These transitions regulate the balance between the hydrophobic and hydrophilic forces of the polymer. The temperature degrees are high that results in the strengthening of hydrophobic interaction, which results in the shrinkage and loss of solubility in polymer.

Thermosensitive polymers have several important properties, including:

- Reversible shrinkage and swelling, allowing the return of polymer to its original state after temperature changes.
- Precise control of drug release: Drug delivery systems can be designed to release the drug at a specific temperature, such as in tumors or areas of inflammation.
- Ability to modify LCST and UCST by changing the chemical structure of the polymer or combining multiple polymers to achieve improved properties (copolymerization). As shown in Fig(1).

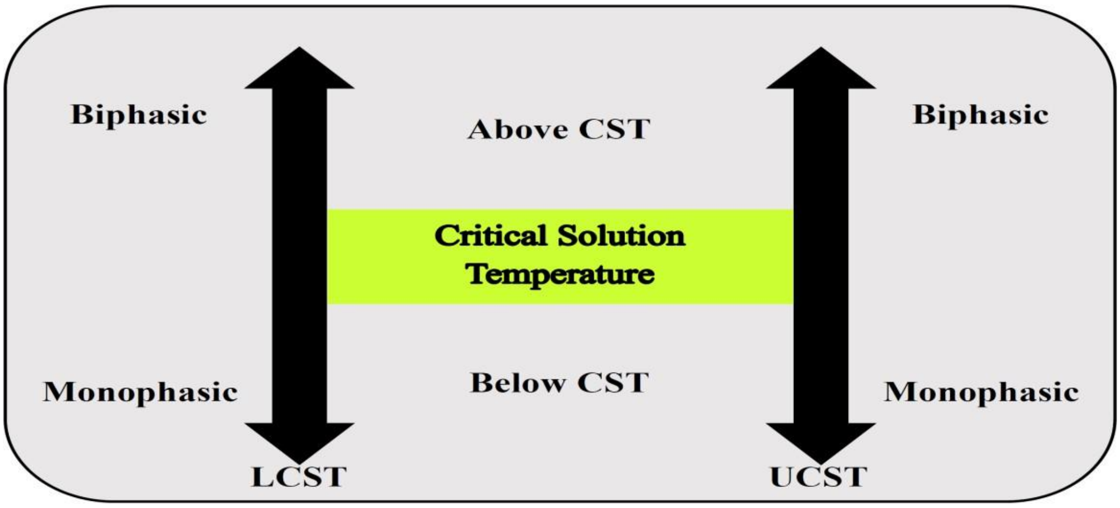

Fig. 1: The behavior of temperature-responsive polymer (Chen *et al*., 2014).

Bioresponsive Polymers

One of the most significant areas of smart polymers are bio responsible polymers, which have the capability to respond to biological stimuli in the body, like enzymes, proteins, glucose, or ions. It is based on this property that advanced applications in the delivery of drugs to specific targets, biodiagnostics, and tissue engineering are possible. They are highly valued in the field of modern medicine, as well as personalized medicine, because these polymers are based on specific molecular processes, which react to the biochemical changes of the surrounding environment (Zhang *et al.,* 2021).

Bioresponsive polymers function by changing their structure or physical properties in response to specific biological signals. These signals can be:

- Chemical signals: such as changes in pH or ionic concentration.
- Enzymatic signals: where specific enzymes catalyze the degradation or chemical modification of the polymer.
- Metabolic signals: like the presence of glucose or oxygen at specific levels in tissues.
- Redox signals: Changes in oxidative state within cells lead to polymer dissociation or drug release. For example, polymers containing enzyme-sensitive bonds can only be degraded in the presence of those enzymes, allowing drug release at a specific site, such as cancer cells that secrete specific enzymes (Spinelli *et al.,* 2025).

The main types of bioresponsive polymers are:

1. Enzyme-responsive polymers:

Contain chemical bonds that can be degraded by specific enzymes such as proteases or lipases. They are used to deliver anticancer or antibiotic drugs, where the drug is released only in the presence of the target enzyme.

2. Glucose-responsive polymers:

Used in insulin delivery systems, their response is adjusted based on blood glucose concentration. Some systems rely on the enzyme glucose oxidase, which catalyzes reactions that produce a change in pH, leading to the release of insulin.

3. Redox-responsive polymers:

Contain disulfide bonds (–S–S–) that break in the reducing environments within cancer cells, resulting in the release of the drug only within the cell.

4. Receptor-responsive polymers:

Interact with specific proteins or cell receptors and are used in targeted tumor therapy or gene delivery systems (Sobczak *et al*., 2022).

Medical Applications:

- **Targeted Drug Delivery Systems:**

  Bioresponsive polymers are used to deliver drugs to specific tissues or cells based on specific biological stimuli. For example, a protease-sensitive polymer can only be degraded in the tumor environment where protease activity is elevated, achieving selective drug delivery and reducing side effects (Li & Kataoka, 2021).

- **Smart Insulin Delivery Systems:**

  Glucose-sensitive polymers represent a revolutionary step in the treatment of diabetes, as they can release insulin in response to elevated blood glucose levels, reducing the need for repeated injections (Zhang *et al*., 2019).

- **Tissue Engineering:**

  Bioresponsive polymers are utilized for developing materials that can interact with cellular bio-signals to stimulate growth or tissue regeneration.

- **Biodiagnostic Systems:**

  These polymers are utilized for designing biosensors capable of intelligently and rapidly detecting biomarkers like glucose or pathological proteins.

Even though there was a lot of advancement in this area, there are still issues concerning stability of polymers in the body and the bioresponse rate which has to be accurately controlled. The development of these materials also requires ensuring that they're biosafe and non-toxic.

Recent studies are mainly concerned with creating multi-responsive polymeric systems that integrates bio-sensitivity, thermo-sensitivity or pH sensitivity to obtain more accuracy in delivery and controlled release. To create highly therapeutic and controlled-release targeted drug delivery systems, bioresponsive polymers are now being combined with nanocarriers (Li and Kataoka, 2021). Another progressive frontier of intelligent material used in precision medicine is bioresponsive polymers, which is a novel category of smart material integrating biochemistry and molecular engineering. They can respond to biological signals and hence serve as a good candidate in smart drug delivery and targeted therapies. As further design and molecular modification progress of these polymers are made, it is anticipated that these polymers in the near future will overhaul personalized medicine and targeted treatment of chronic diseases and cancers.

To clarify the key differences between the most important types of bioreactor-responsive polymers, (Table 3) provides a comprehensive comparison of these polymer types, their respective advantages, and their main disadvantages and associated biotechnological applications. This table highlights the unique properties of each class such as enzyme-responsive, glucose-responsive, and oxidative stress (Redox) polymers and demonstrates how these properties can be leveraged for targeted drug delivery, improved release efficiency, and reduced side effects. The table also provides a framework that facilitates the selection of the most suitable polymer for various therapeutic applications, depending on the disease environment and the desired response.

Table (3): **Comparison between the most important types of Bio Responsive Polymer in terms of advantage, disadvantage, and applications.**

Type of Bioresponsive Polymer	Advantages	Disadvantages	Drug Delivery Applications
Enzyme-responsive polymers	1-High biological specificity and selectivity.- Enable targeted and localized drug release at disease sites. 2-Adjustable degradation rate depending on enzyme type.	1- Variation of enzyme expression among patients. 2- 2-Risk of premature degradation in non-target tissues. 3-Limited control over timing and rate of release.	1- Cancer therapy (MMP-sensitive carriers). 2- Tissue engineering scaffolds. 3- Inflammatory disease targeting.
Glucose-responsive polymers	1-Self-regulated release based on glucose levels . 2-Mimics physiological insulin regulation. 3-Provides closed-loop drug delivery.	1-Reduced sensitivity in complex biological fluids 2.- Interference from pH or ionic strength. 3-Stability challenges during long-term use.	1- Smart insulin delivery systems for diabetes. 2- Continuous glucose monitoring devices.
Redox-responsive polymer	1- Respond to redox potential differences between normal and pathological tissues 2- Enable controlled release in oxidative or reductive environments. 3- Biodegradable and safe byproducts	1- Possible non-specific activation in fluctuating redox conditions. 2- Stability issues under physiological oxidative stress. 3- Complex synthesis of redox-sensitive linkers.	1- Tumor-targeted drug delivery (high intracellular GSH). 2- Intracellular delivery of nucleic acids or proteins 3- Controlled release under oxidative stress conditions.

Field-responsive polymers

One of the most developed and diverse forms of smart polymers that can be used today is field-responsive polymers (FRPs). These materials are defined by the behavior of the changing physical or chemical behavior on observation of the external field, i.e., an electric field, a magnetic field, or ultrasound. These polymers are designed with the principle of remote-controlled response, which makes them especially applicable to medical and precision engineering activities, as the response can be safely and accurately controlled without the necessity to make any changes to the environment in the body (Liu *et al.*, 2022). In terms of general response, such polymers have elements or functional groups that may respond to external fields via rearrangement of the charge, production of thermal power, or mechanical motion inside. Existing materials, when subjected to an electric or magnetic field, or an ultrasound wave, can: alter their shape, size, or surface charge; or depolarize stored pharmaceutical compounds by the disintegration or enlargement of the polymer net. This characteristic causes them to be the foundation of controlled release systems that can be remotely activated (Zhang *et al.*, 2019).

The most important types of electro-responsive polymers:

Electro-Responsive Polymers

These are some of the oldest and most researched types that depend on polymer behavior with an applied external electric field and the reaction leads to changes in charge, conductivity, or mechanical structure.

Such polymers normally include conducting or semiconducting polymeric material strings like polyaniline (PANI), polypyrrole (Ppy) and poly(3,4-ethylenedioxythiophene) (PEDOT).

In case of applying electrical voltage, these polymers can expand or contract, allowing for controlling fluid movement or releasing biomolecules that are stored within them.

These properties were used in:

- Artificial muscles mimicking biological movement.
- Biosensors detecting electrical changes in environment.
- Electro-controlled drug delivery systems (ECDR) (Shen *et al*., 2023).

One of the most important recent applied developments in this field is developing PPy/PVA hydrogel polymeric membrane that can release drug in response to low electrical voltage, allowing precise time-resolved control of dosage (Liu *et al.,* 2022).

Magneto-Responsive Polymers

These polymers are based on the idea of incorporating magnetic NPs like Fe3O4 or g-Fe2O3 into polymer structures, enabling them to respond to external magnetic field. Also, they can create local heat under magnetothermal effect influence when endured in AC magnetic field. This heat causes polymer network's local expansion or breakdown, in turn resulting in controlled drug release. In addition to that, they can be directed as well to the specific point of the body with the help of the magnetic field and find their applications in targeted cancer therapy (Zhou *et al*., 2023). Their most relevant uses are: 1- Magnetic hyperthermia (thermal therapy of tumors) 2- targeted drug delivery 3- smart materials in remotely controlled medical equipment. A hydrogel of poly(N-isopropylacrylamide)/Fe3O4 nanoparticles to release the drug on the exposure to a magnetic field is currently one of the most significant advances in this area, which led to the enhancement of the targeting efficiency and rate (Zhang *et al*., 2021).

Ultrasound-Responsive Polymers

These polymers respond to ultrasound stimulation via 2 main mechanisms:1. Localized heating resulting from the absorption of acoustic energy. 2. Cavitation, which induces mechanical stress that leads to the breakdown of polymer bonds or increased network permeability. This type of polymer is very useful in site-specific drug delivery systems, where ultrasound can be used to stimulate the release of the active ingredient at a specific site within the body without the need for surgical intervention. They are also used in ultrasound therapy, which combines physical stimulation with chemical release (Rezk *et al.,* 2022). Some of the most important recent applications in this field are: Release of sensitive genes or proteins via low-energy ultrasound stimulation, Disintegration of encapsulated polymer capsules in target tissues and treatment of deep tumors using focused ultrasound therapy. (Table 4) illustrates the advantages and limitations of three types of field-responsive polymer types.

Table (4): shows the advantages and limitations of field-responsive polymer types.

field-responsive polymer types	Advantage	disadvantage
Electro-responsive polymers	1- Fast, precisely controlled response across voltages. 2- Easy to integrate into electronic systems. 3- Suitable for precision instruments	1- Requires a constant power supply. 2- Susceptible to electrolysis in aqueous solutions. 3- Sensitivity is affected by temperature and humidity.
Magneto-responsive polymers	1- Can be controlled remotely without contact. 2-Fast and reversible response. 3-Relatively safe when using low-intensity fields.	1-Irregular particle distribution impairs response.- 2-High cost of nanomaterials. 3-Potential for excessive tissue heating.
Ultrasound-responsive polymers	1- Non-invasive and spatially precise control. 2- Can be used in deep tissues. 3- Does not require additional chemicals. 4- Relatively safe at low doses.	1- Difficulty in precisely controlling the intensity and duration of the waves. 2- Risk of local heating if the intensity is increased. 3- Some types may be mechanically damaged after repeated stimulation

Challenges and Future Perspectives

Despite the significant progress achieved in the design and application of smart stimuli-responsive polymers, several challenges continue to restrict their broader clinical translation. One major limitation lies in the scalability and manufacturing of complex multifunctional polymers. Many of these systems require sophisticated synthesis routes, stringent environmental controls, and high-purity reagents, making large-scale production costly and technically demanding. Ensuring batch-to-batch consistency also remains a critical barrier, particularly for polymers with integrated nanostructures or multiple responsive domains.

Another key issue is related to toxicity and biodegradation behavior. While smart polymers are engineered for biocompatibility, some may generate potentially harmful by-products upon degradation or accumulate in tissues due to incomplete breakdown. Long-term in vivo fate, immunogenicity, and interactions with biological fluids are not yet fully understood for many emerging polymeric systems. Addressing these concerns requires systematic toxicological evaluations and the development of materials with predictable and tunable degradation profiles (Protsak *et al.,* 2025).

Looking ahead, the integration of artificial intelligence (AI) and nanotechnology-based predictive modeling is expected to accelerate the design and optimization of next-generation smart polymers. Advanced computational tools can forecast polymer–drug interactions, responsiveness to stimuli, and in vivo performance with high accuracy, thereby reducing trial-and-error experimentation. Machine learning algorithms, when combined with high-throughput nanoparticle characterization, may enable the creation of tailor-made polymeric materials with optimized therapeutic efficacy and safety. These innovations are likely to play a pivotal role in overcoming current challenges and pushing stimuli- responsive polymer systems closer to widespread clinical adoption.

(Table 5) provides a summary comparison of the most important types of stimuli-responsive polymers, based on their Mechanism of Response, Representative Polymer, Biomedical Application.

Table (5): Comparative summary of the main catalyst-responsive polymers

Stimulus Type	**Mechanism of Response**	**Representative Polymer**	**Biomedical Application**
pH-responsive polymers	Swelling or dissolution behavior triggered by pH gradients	Chitosan, Polyacrylic acid	pH-dependent drug delivery systems
Thermo- responsive polymers	Ionization changes associated with LCST/UCST transitions	PNIPAM	Thermally regulated drug release
Redox-responsive polymers	Cleavage of redox-sensitive chemical bonds	Polyacrylic-based derivatives	Tumor-targeted and redox-triggered drug delivery
Glucose- responsive polymers	Enzymatic or affinity-based interactions with glucose	Polymeric glucose-sensitive systems	Smart insulin delivery platforms

CONCLUSIONS

The development of smart, stimuli-responsive polymers represents a paradigm shift in advanced drug delivery systems; however, their performance varies considerably across polymer categories. While temperature-, pH-, and redox-responsive polymers offer clear advantages—such as high on-site specificity, reduced systemic toxicity, and tunable drug-release kinetics—each class also presents inherent limitations. For instance, thermoresponsive systems often suffer from limited penetration depth and heat-induced tissue stress, whereas pH-responsive polymers may exhibit inconsistent behavior in heterogeneous tumor microenvironments, and redox-activated carriers can face challenges in maintaining stability during circulation. Moreover, their readiness for clinical translation remains uneven: pH- and redox-responsive platforms have progressed further into early clinical testing, while multi-stimuli and externally triggered systems remain largely at the preclinical stage due to complexities in design, manufacturing, and regulatory validation.

Importantly, recent studies highlight those multi-responsive polymers, which integrate two or more triggers (e.g., pH/redox or temperature/magnetic field), demonstrate synergistic interactions that enhance selectivity and therapeutic performance—an advancement now being explored in several ongoing Phase I/II trials for targeted tumor therapy and implantable biodevices. Despite persistent challenges related to large-scale production, long-term biocompatibility, and degradation control, the convergence of nanotechnology, molecular biology, and intelligent materials engineering continues to accelerate the evolution of clinically relevant smart systems capable of transforming modern pharmaceutical medicine.

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التطورات الحديثة في بعض أنواع البوليمرات الذكية المستجيبة للمحفزات في أنظمة توصيل الأدوية المتقدمة والطب، مراجعة قصيرة

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الملخص

البوليمرات الذكية - المعروفة أيضًا باسم البوليمرات المستجيبة للمحفزات - تُمثل فئة متقدمة من المواد القادرة على الخضوع لتحولات فيزيائية أو كيميائية عكسية تحت طيف واسع من المحفزات الداخلية والخارجية، بما في ذلك الرقم الهيدروجيني، ودرجة الحرارة، والضوء، والمجالات المغناطيسية أو الكهربائية، والإشارات المشتقة بيولوجيًا. تُبرز الابتكارات الحديثة بشكل خاص تكامل البوليمرات المستجيبة حيويًا، والمستجيبة للضوء، والمستجيبة للمجال، حيث يُقدم كل منها مزايا تشغيلية فريدة. تتميز الأنظمة المستجيبة حيويًا بخصوصية فسيولوجية عالية، بينما توفر البوليمرات المنشطة بالضوء تحكمًا دقيقًا في الزمان والمكان، وتُتيح المنصات المستجيبة للمجال المغناطيسي أو الكهربائي إطلاقًا غير جراحيًا للدواء يتم تنظيمه عن بُعد. تؤكد اتجاهات البحث الحالية بشكل متزايد على تطوير أنظمة متعددة الاستجابة، تجمع بين محفزين أو أكثر لتعزيز القدرة على التكيف وضبط أنماط إطلاق الدواء بدقة. وبالمقارنة مع مناهج المحفز الفردي السابقة، تُظهر هذه الهجائن الناشئة انتقائية فائقة، واستجابة، ودقة علاجية فائقة. ومع ذلك، فإنها تُطرح أيضًا تحديات جديدة تتعلق بالتعقيد الهيكلي، والتوافق الحيوي طويل الأمد، والتصنيع القابل للتطوير - وهي عوامل تُميزها عن سابقاتها وتؤثر على جاهزيتها السريرية. من منظور مقارن، تُعتبر البوليمرات التقليدية المستجيبة لدرجة الحموضة والحرارة ناضجة نسبيًا وأقرب إلى التطبيق السريري، بينما لا تزال الأنظمة المستجيبة للضوء والاستجابة للحقل، على الرغم من كونها أكثر تنوعًا، تواجه عقبات تتعلق باختراق الأنسجة، وتوصيل المحفزات، والتحقق من السلامة. يتمتع الجيل الأحدث - المنصات متعددة الاستجابة والمتكاملة بيولوجيًا - بأكبر إمكانات، ولكنه لا يزال إلى حد كبير في التقييم قبل السريري بسبب قيود التصميم والتنظيم. ومن المتوقع أن يُسرع دمج تصميم البوليمرات المُحرك بالذكاء الاصطناعي، والتصنيع النانوي المتقدم، والنمذجة الجزيئية التنبؤية، من إنشاء أنظمة ذكية من الجيل التالي. لن تُعزز هذه الابتكارات الأداء والاستقرار فحسب، بل ستُوسّع أيضًا من إمكانية التطبيق السريري لتقنيات توصيل الأدوية القائمة على البوليمرات الذكية، مما يجعلها أقرب إلى الاستخدام العلاجي الروتيني.

الكلمات الدالة: البوليمرات الذكية، توصيل الأدوية، البوليمرات الحساسة للمحفزات، البوليمرات الحيوية الحساسة.