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A Concise Review on Stimuli-Responsive Smart Polymers: Revolutionizing Drug Delivery Systems

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A B S T R A C T

Stimuli-responsive polymers, often referred to as smart polymers, are micromolecules that demonstrate significant physicochemical changes when exposed to minor environmental variations, such as temperature, pH, light, magnetic fields, and ionic factors. The hallmark of smart polymers is their ability to exhibit non-linear responses to small stimuli. These materials can detect slight changes (stimuli) and revert to their innovative state once the stimulus is no longer present. This review article explores smart polymers that respond to temperature, pH, and enzymes as stimuli-responsive materials. Additionally, it highlights recent advancements in the use of smart polymers for drug delivery and the challenges that lie ahead for drug delivery systems utilizing these stimuli-responsive polymers.

Keywords: Smart polymers, stimuli-responsive polymers, drug delivery, temperature, pH, enzymes.

1. Introduction

The distribution of drugs pertains to the targeted administration of pharmaceutical compounds to certain cells or tissues. It encompasses the processes of administering, distributing, absorbing, and eliminating drugs. For most conventional methods to work, the "drug" has to get into the body's processes. This isn't useful because the kidneys remove over 90% of the drug from the bloodstream [1]. Smart or carrier-mediated drug delivery methods are increasingly popular due to their ability to deliver medicine to the specific areas of the disease that require it, thereby creating targeted drug delivery systems (TDDS) [2-4]. Microspheres, hydrogels, and nanoparticles are just a few of the drug transport methods that have been made possible by recent progress [5, 6]. Nanoparticles are drug transport systems that are designed to absorb drugs slowly and over a long period of time, which increases the plasma half-life [7, 8].

Polymers are large macromolecules consisting of several repeating subunits, exhibiting various features based on their arrangement and connectivity. [1–5] Smart polymers, which are also called stimuli-responsive or intelligent polymers which are getting a lot of attention and study right now. These polymers may change their chemical or physical properties in response to things like pH [11,12], temperature [13,14], force [15], molecules [16], and magnetic or electric fields [17–19]. The reversibility and regulation of these modifications may be created by the strategic design of the polymer structure Smart polymers have the capability to intellect and respond to their surroundings [8, 20]. Looking at these polymers' special features and what they could become in the future shows that they have a lot of uses in biomaterials, such as being biologically compatible, biodegradable, and mechanically flexible. Furthermore, these advanced polymers respond to natural stimulation, which lets them do things like deliver drugs, move cells, or keep an eye on the environment [21–23]. These have been used in many areas of biology and medicine, such as controlled and generated drug delivery, devices and biosensors, chemo-mechanical actuators, cleaning up the environment, and more [24–27]. This area of study is always getting better, and we expect new smart polymers to appear and be used in many areas in the future. Recently, smart polymers have garnered increased interest and undergone further development. These adaptable polymers may alter their properties in response to diverse environmental stimuli. It depends on the pH and ionic strength of the solution whether this hydrogel grows or shrinks. The breakthrough initiated research into smart polymers, which has subsequently proliferated across other sectors.

On January 29, 1967, Scarpa et al. wrote about how poly (N-isopropyl acrylamide) (PNIPAM) reacts to heat [29]. Over the next few decades, more scientific discoveries were made, such as polymers that change how they look when the wavelength and energy of light change. Because of this progress, these polymers were labelled as photo-responsive in the 1970s [30]. In 1988, scientists at Michigan State University made a polymer that could change how thick it was based on electric currents [31]. Dagani came up with the term "smart polymers" in 1995 to describe materials that can change based on their surroundings, like biological polymers [32]

This review presents a comprehensive examination of smart polymers, which are components capable of altering their characteristics in reaction to external stimuli. We will explore different categories of smart polymers, their defining features, and their various applications. Furthermore, we will investigate the development and analysis of these materials, as well as the current challenges and future research objectives within this domain. The aim

of this study is to deliver an extensive and up-to-date assessment of the present landscape and future possibilities of smart polymers. It encompasses both physically responsive stimuli and biologically reactive responses, providing a thorough insight into this evolving field.

2. Types of smart polymer

Polymers with responsive systems can undergo significant alterations in their properties after exposed to external stimulus. These stimuli can affect polymer chains in various manners, leading to changes in hydrophilicity, morphology, solubility, degradation, and bond cleavage. Chemical stimuli, including pH, ionic strength, and redox conditions, can modify how polymers interact with solvents or other polymers. Additionally, physical stimuli such as temperature, light, and electro-responsiveness influence the movement of polymer chains. Biological stimuli, which encompass molecular activities like enzymatic reactions and receptor-mediated substance detection, also play a role, particularly in responses to enzymes and glucose. Furthermore, dual stimulus-responsive polymers have the ability to react to multiple stimuli at once.

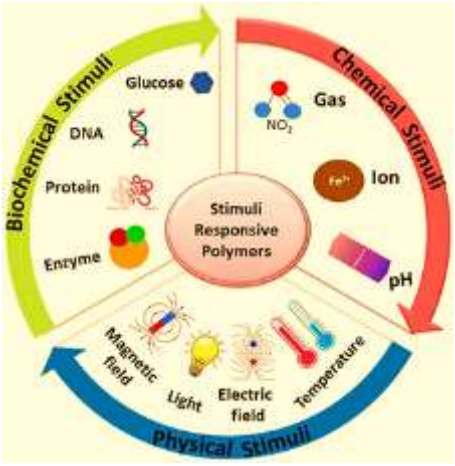

Figure 1: Schematic illustration of the different categories of smart polymers within the realm of stimuli-responsive polymers.

Table no. 1: Stimuli responsive polymers with their advantages and limitation

Stimulus	**Advantage**	**Limitation**	**Responsive material Examples**
Temperature	• Facilitation of integrating active components • Streamlined production and formulation • Decreased Systemic Adverse Effects	• Injectability issues under application conditions • Low mechanical strength, biocompatibility issues and instability of thermolabile drugs	• Poloxamers • Poly(N-alkylacrylamide)s • Poly(N-vinylcaprolactam)s • Cellulose, xyloglucan • Chitosan
pH	• Suitable for thermolabile drugs	• Lack of toxicity data • Low mechanical strength	• Poly(methacrylicacid)s • Poly(vinylpyridine)s • Poly(vinylimidazole)s
Light	• Ease of controlling the trigger mechanism • Accurate control over the stimulus	• The gel's low mechanical strength and the possibility of noncovalently bound chromophores leaking out.	• Azobenzene • spiropyean
Electric field	• Pulsative release with changes in electric current	• Surgical implantation is necessary Requirement for supplementary apparatus for the external application of stimuli Challenges in optimizing the intensity of electric current	• Ionic polymer-metal composites (IPMC) • Ferroelectric polymer • Polypyrrole (PPy) • Polyaniline (PANI)

Ultrasound	Controllable protein release	Equipment specifically designed to regulate the release Surgical implantation is necessary for a delivery method that is not biodegradable.	• Poly(lactic-co-glycolic acid) (PLGA) • Poly(methacrylic acid) (PMMA)

2.1 Physically dependent stimuli

A. Temperature responsive polymers

Thermosensitive polymeric systems present various advantages, such as the elimination of toxic organic solvents, the versatility in drug type distribution, reduced side effects, precise drug delivery mechanisms, and extended release profiles. However, they also face several challenges, including the swift release of pharmaceuticals, potential inadequacy in gel potency that could lead to overdose, uncertainties about the compatibility of the polymeric system with biological entities, and the system's progressive acidification resulting from acidic degradation(49). Frequently employed thermoresponsive polymers include poly(N-isopropylacrylamide) (poly(NIPAAm)) and poly(N,N-diethylacrylamide) (PDEAAm), as well as Pluronics®, Tetronics®, and PLGA–PEG–PLGA (ReGel®).

Thermosensitive polymers are classified as responsive materials that adjust their properties in relation to temperature changes. The straightforward measurement and control of temperature facilitate the expansion or contraction of polymer chains, which in turn affects their solution and phase states. [41, 42] This transition is contingent upon the balance between hydrophilic and hydrophobic regions and the energy of the system, with the lower critical solution temperature (LCST) and upper critical solution temperature (UCST) being essential elements [43–45].

The lower critical solution temperature (LCST) refers to the temperature at which a polymer remains soluble at lower temperatures but becomes insoluble as the temperature rises. Conversely, the upper critical solution temperature (UCST) represents the opposite behavior. [20]. At the LCST, water molecules form hydrogen bonds with the polymer, which are disrupted as the temperature increases, leading to the aggregation of insoluble and hydrophobic polymer chains. This transition at the LCST is reversible and is influenced by entropy[46]. Notable examples of LCST polymers include poly(vinyl amide), poly(N-substituted acrylamide), poly(N-vinylcaprolactam), cellulose, chitosan, xyloglucan, and PLGA–PEG–PLGA triblock copolymers.

When the temperature goes up, UCST polymers break apart because their chain links are weaker. This is because enthalpy plays a more significant role than entropy. The change is not definitive and is dependent on enthalpy. A lot fewer UCST polymers are found than LCST polymers, like polybetaines and poly(2-dimethyl)methacryloxyethyl-ammonium propane sulfonate.

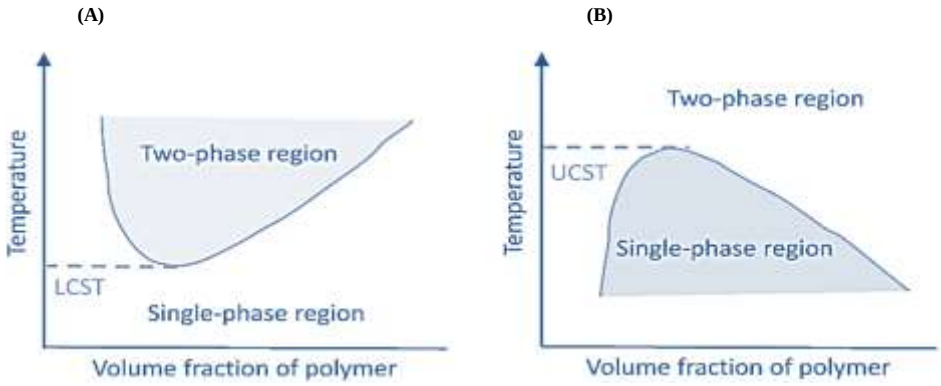

Figure 2: The graph shows how temperature changes with the polymer volume fraction. The phase diagrams for polymer solutions are presented, illustrating (a) the behavior at the lower critical solution temperature (LCST) and (b) the behavior at the upper critical solution temperature (UCST).

A. Properties of Temperature responsive polymers

a) PNIPAM

The process of grafting PNIPAM onto CNF results in an increase in the lower critical solution temperature (LCST) from 32 to 36 °C. This grafting establishes a covalent bond between PNIPAM and CNFs, which restricts the mobility of the PNIPAM chains within the network. Consequently, for the PNIPAM chains to cluster above the LCST, the CNFs must rearrange to form denser bundles and voids. The energetic cost associated with this reorganization likely accounts for the observed rise in LCST. Given that PNIPAM-g-CNFs exhibit an LCST that is close to human body temperature, their potential applications in the biomedical sector warrant investigation. Further research into the temperature-dependent conformational changes of PNIPAM chains grafted onto CNF under varying pH and salt concentrations could provide insights. This would enable the fine-tuning of the thermosensitive properties of PNIPAM-g-CNF hydrogels, influencing their gel structure, strength, and gelation temperature critical factors for biomedical applications such as organoid culture, drug delivery, smart sensing, and tissue engineering. [50]

The research focuses on creating a dual stimuli-responsive therapeutic delivery system for targeted drug delivery. The system, PNIPAM-co-PAAm, was created through free radical polymerization and a melamine-glutaraldehyde precursor. The system's phase transition properties were analyzed, and the pH-responsive release efficiency of curcumin was assessed. The PNIPAm-co-PAAm-Mela HG system showed a significant drug loading capacity of 74% when subjected to combined stimuli of pH 5.0 and 45 °C. The hydrogel was also tested on a human liver cancer cell line (HepG2), revealing its biocompatibility. The PNIPAm-co-PAAm-Mela HG system holds potential for use in pH and temperature-responsive drug delivery, encompassing stimuli responsive polymers [51].

b) Poloxamers and their derivatives

The A-B-A type triblock copolymer has two separate parts, A and B, which usually stand for segments that are hydrophilic and segments that are hydrophobic. 7 to 10. Copolymers with PEO-PPO sequences are a type of commercially available triblock copolymers. These include Pluronics®, Poloxamers®, and Tetronics®. Poloxamers® are non-ionic polymers made up of polyoxyethylene and polyoxypropylene (PEOn-PPOn-PEOn). They are used a lot in medicine. When they are present in fairly high concentrations, they go from a sol-gel phase transition at or near physiological temperature to a gel-sol phase transition at about 50°C. Pluronics® and Tetronics® are FDA-approved polymers that are used as food additives, pharmaceutical ingredients, and drug delivery systems in parenteral applications, among other things.

Poloxamer sol-gel reversible hydrogels have become a focal point of interest for their practical applications in the biomedical and pharmaceutical sectors, attributed to their solubility, compatibility with biological systems, and the ease with which pharmaceutical formulations can be administered. These hydrogels find utility in several areas, including the solubilization of hydrophobic drugs, controlled release, delivery of biomacromolecules such as proteins and genes, and tissue engineering. The predominant focus is on Poloxamer P407, which is widely used for the delivery of protein and peptide drugs [52], including insulin factor [53], interleukin-2 [54], epidermal growth factor[55], bone morphogenic protein [56], fibroblast growth factor, and endothelial cell growth factor [57]. Recently, these hydrogels have been explored as carriers for various routes of administration, with the most compelling applications.

2.2 Chemically-dependent stimuli

A. pH-responsive polymers

pH-responsive polymers, which feature acidic or basic functional groups, experience changes in their structure and physical properties when there are variations in environmental pH. These polymers can either absorb or release protons as a means of response. Polyelectrolytes, which are rich in ionizable groups, are particularly sensitive to pH changes, resulting in the contraction or expansion of their polymer chains in aqueous environments. This behavior is primarily attributed to the electrostatic repulsion generated by the charges formed. Common examples of pH-responsive materials include polyacids and polybases. [58, 59].

Polymers that exhibit responsiveness to pH variations contain functional groups such as carboxylic acids (COOH), sulfonic acids (SO_3H), and trivalent nitrogen, which are capable of donating or accepting protons. The ionization of these groups leads to alterations in their structure. The pKa value serves as an indicator of the pH at which significant changes in ionization occur, thereby affecting the apparent dissociation constantPolyelectrolytes are categorized into acidic or basic types and can originate from renewable resources or be produced through a range of industrial methods. Recently, there has been a significant rise in interest regarding natural polymers that demonstrate pH responsiveness and exhibit multiple forms of responsiveness. [60]

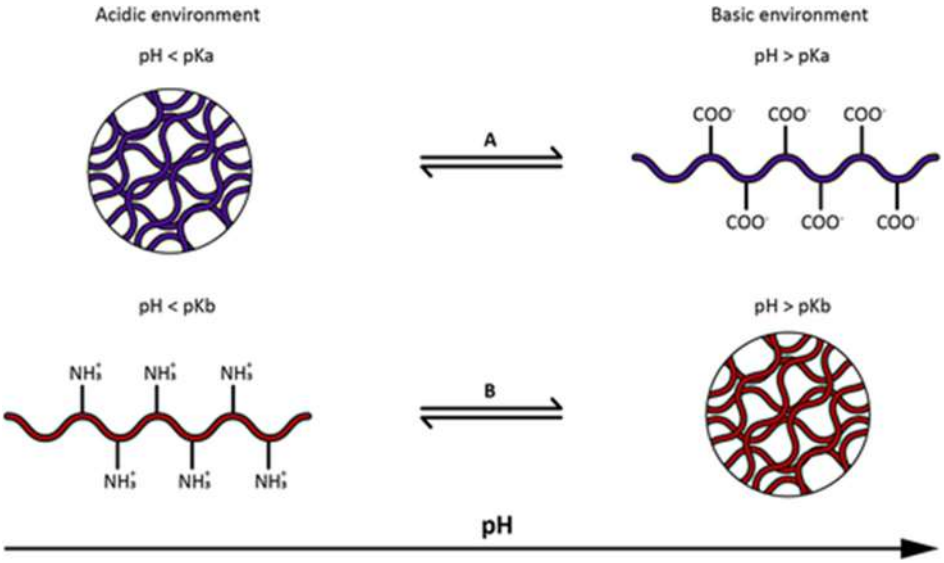

Figure 3: Polymer responsive to pH changes in acidic and basic environments

a) pH-responsive acidic polymer

Polymeric acids, commonly referred to as polyanions, are acidic polymers that exhibit sensitivity to pH fluctuations due to their inherent acidic functional groups. The quantity of negatively charged groups present in a polymer molecule is influenced by the pH of the surrounding water, which in turn impacts its hydrophilic characteristics. Among these polymers, poly(acrylic acid) (PAA) is frequently the subject of research [61]. The concentration of H+ ions (pH levels) determines the number of negatively charged groups in these polymers. Elevated pH levels lead to an increase in negatively charged groups, whereas lower pH levels decrease ionization. Poly acrylic acid has a well-established pKa value of 4.28. When the pH is below this threshold, the polymer is primarily uncharged; conversely, at or above pH 4.28, it gains an anionic charge [62]. The dissociation constant of the acid (Ka) plays a crucial role in determining the pH at which ionization occurs, a factor that differs between polymeric acids and monoacids sharing the same functional group. Additionally, the composition and molecular weight of the polymer also affect this ionization process [63]

b) pH-responsive basic polymers

Polymeric bases, or polycations, are pH-responsive basic polymers with elementary functional groups within the molecule. The number of positively charged groups in the polymer molecule can change with the external pH, accepting protons at pH levels lower than their pKa value[61]. The transition between ionization and deionization typically takes place throughout a pH range of 7 to 11[64]. Commonly utilized monomers in the creation of pH-responsive polymers encompass acrylamide, vinyl compounds, acrylates, methacrylamide, and methacrylates that incorporate tertiary amine groups [65]. Poly(N,N′-diethylaminoethyl methacrylate) (PDEAEMA) serves as an illustrative case of a pH-responsive polymer, exhibiting a pKa value nearing 7.3.

The biomedical sector has revealed significant interest in pH-responsive polymers due to the common occurrence of changes in pH in biological tissues and specific diseases. pH is a vital environmental parameter in biomedical applications, as it changes in various pathological or specific compartments. pH-responsive polymers can straight react to changes in pH in specific tissues or cellular units [66]. They possess weak basic or acidic groups capable of ionization, linked to a hydrophobic backbone, illustrated by polyelectrolytes. Upon ionization, these groups generate charges (anions or cations) that repel one another, resulting in the release of coiled chains. Several natural polymers, such as albumin, gelatin, and chitosan, show pH sensitivity.

A. Chitosan

This polymer is appropriate for oral or mucosal administration due to its mucoadhesive qualities. Its negative charge, which readily interacts with the positively charged amino groups of chitosan, is responsible for its capacity to carry DNA. Because of its porous character, which improves the release of macromolecules and poorly soluble medications, the chitosan/glycerophosphate pharmaceutical system is a beneficial substitute for conventional drug implants. When the hydrophobic anticancer medication paclitaxel is incorporated into the chitosan/glycerophosphate combination, it prolongs drug absorption and efficiently inhibits the growth of cancer cells. When injected, a chitosan and glycerol-2-phosphate solution may gel, passing through a sol-gel transition at room temperature and biological pH. The regulated release of insulin over a two-week period has been effectively enabled by this method.

B. Poly(acrylic acid) (PAA or Carbomer)

When water is neutral (pH 7), polyacrylic acid (PAA) acts as an ionized polymer. It ionizes parts of its side chains and gives them a negative charge. Comparable to polyethylene glycol, polyacrylic acid may absorb and hold onto water, which causes them to significantly expand often to many times their initial volume. The market sells dried PAAs as pale, white powders. Numerical identifiers such as 910, 934, 940, 941, and 934P designate carbomers. The data provides information about the molecular weight of the carbomers and the types of polymeric structures they produce. Polyacrylic acids, like sodium polyacrylate, are usually found as salts that come from ammonium or alkaline metals.. It is believed that mucoadhesive polymers improve carrier formulation retention on mucosal surfaces. Variations in pH and temperature can cause these polymers to physically form hydrogels. It is easier for drugs to get into the stomach and GI tract when they are taken by mouth, especially when smart polymers like Carbopol® are used that are pH-sensitive and stick to mucosa.

Properties of Carbomer

1. These substances might be made up of homopolymers that come from acrylic acid and are linked by pentaerythritol allyl ether, glucose allyl ether, ethylene allyl ether, and other chemicals.

2. At a neutral pH, PAA displays the properties of an ionized polymer.

2.3 Biologically dependent stimuli

a) Enzyme-responsive polymers

Smart polymers, also known as enzyme-responsive polymers, are a unique class of polymers that alter their functionality when they encounter specific enzymes, shifts in pH or temperature, or other environmental factors. In the area of stimuli-responsive materials, the current emphasis on enhancing these enzyme-responsive polymers has emerged as an interesting and promising research topic. When subjected to certain stimuli, these polymers are designed to alter irreversibly in terms of their chemical or physical properties. Numerous potential uses are presented by this property, including tissue engineering, biosensing, and medication delivery [67–69]. Solutions, gels, self-assembled clusters, multilayer coatings, and solid materials are some of the many forms of enzyme-responsive polymers.

The chemical and physical characteristics of polymers may change in ways that are either irreversible or retrievable. One may utilize polymers that are easily broken down by enzymes or add functional groups that interact with certain enzymes to develop polymeric systems that react to them. Enzyme-

responsive systems have been developed using both natural and synthetic polymers. Natural alternatives include dextran, polypeptides, and gelatin; synthetic ones include PNIPAAm, PEG, and PLL. A segment that replicates the enzyme's natural substrate or a component that modifies the polymer's interaction with other molecules, leading to changes in form or activity, are often found in polymers that can react with enzymes. Proteases, lipases, phosphatases, kinases, acyl transferases, glycosidases, and redox enzymes are among the many enzymes that interact with the most recent enzyme-responsive polymers, which often depend on supramolecular structures, chemical crosslinking, and nanoparticle coatings [70,71].

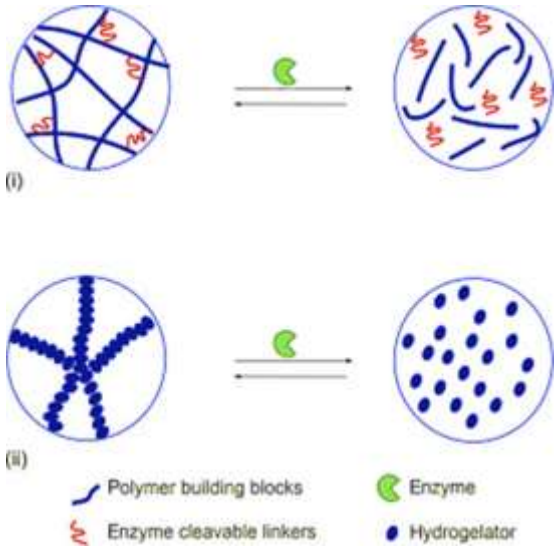

Figure 4: Enzyme-responsive polymers

3. Application of Smart Polymers in Drug delivery system

Drug delivery involves the administration of pharmaceutical drug for the treatment of diseases or conditions in humans or animals. The main objectives include targeting drugs to the significant site, making the correct dosage, and timing the delivery effectively [72–74].

a) Smart Polymers Used in Drug Delivery

- Targeted Drug Delivery: Advanced smart polymers can be tailored to deliver drugs selectively to specific locations within the body, such as tumor regions or inflamed tissues, thereby decreasing systemic side effects and enhancing the efficacy of the treatment.
- Controlled Release: These polymers are capable of controlling both the rate and timing of drug release, allowing for extended and effective therapeutic outcomes.
- Stimuli-Responsive Release: The release of pharmaceuticals can be activated by certain stimuli, such as shifts in pH (acidic or alkaline), changes in temperature, or the detection of specific biomolecules.

Smart polymeric carriers facilitate the administration of drugs according to specific stimuli. The goal of smart polymers, which were created by polymer scientists, is to allow controlled and embattled drug release in response to certain stimuli. Polymers that change their behavior in response to different conditions can be used in many ways in treatment, especially to deliver drugs in a controlled or targeted manner. In the late 1970s, researchers first used lipid-based carriers that made it easier for drugs to be released when they were heated. This phase was the start of using condition-responsive polymers in drug delivery. Since then, a lot of work has been done on materials that can respond to different conditions in order to deliver drugs. This work has mostly been on making and using responsive polymers. Smart polymers that work well are biocompatible, biodegradable, have controlled drug release, can hold a lot of drugs, and don't have any harmful effects like immunogenicity, toxicity, carcinogenicity, or reproductive toxicity. They are also stable overall. These polymers demonstrate considerable structural alterations when subjected to minimal stimuli.

Numerous polymer-based materials that respond to stimuli have been applied in drug delivery contexts. They can change their shape, solubility, physical state, hydrophilic and lipophilic properties, conductivity, and how they interact with solvents. These changes can be undone. These changes happen when polymers with different charges are added, when the temperature changes and hydrogen bonds or the balance of lipophilic and hydrophilic components is upset, or when the pH changes and charged groups are neutralized. [70,74].

Benefits of Using Smart Polymers in Drug Delivery:

- Higher Therapeutic Effectiveness: Targeted and regulated drug delivery systems can get higher drug levels to the right place, which improves therapeutic outcomes.
- Decreased Adverse Effects: Smart polymers can limit systemic drug exposure, which helps in diminishing side effects.

- Improved Patient Adherence: Controlled release formulations can reduce the frequency of drug administration, leading to an increase in patient adherence.
- Improved Drug Integrity: Smart polymers can safeguard drugs from degradation within the challenging conditions of the body.

4. Application of Stimuli Responsive Polymers in drug delivery

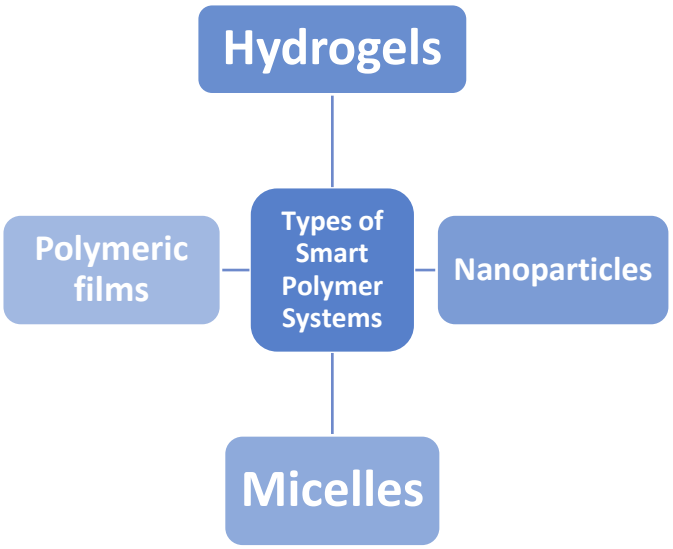

Figure 5 : Types of Smart Polymer Systems

A. Thermosensitive Polymers in drug delivery

1. Surface design for on-off switchable traps using self-heating smart polymers We developed an innovative self-heating, temperature-responsive chromatographic technology to efficiently separate biomolecules. We covalently grafted temperature-responsive poly(NIPAAm-co-HMAAm) onto the surface of magnetite/silica composites to serve as switchable surface traps. The lower critical solution temperature (LCST) of the poly(NIPAAm-coHMAAm)s was regulated from 35 to 55°C by increasing the HMAAm content. The heat generated by magnetic particles in an alternating magnet field was used to separate the hydrophilic and hydrophobic phases of the grafted temperature-responsive polymers.
2. Temperature-responsive gels and thermogelling polymer matrices for the delivery of proteins and peptides The progress in protein and peptide therapeutics has made it very important to find effective ways to deliver these drugs. A lot of research on how proteins are distributed in polymeric systems has shown how useful gels that respond to environmental cues like temperature can be. We can design protein and peptide release to occur in a pulsatile manner. Polymer design significantly alters the mechanism of its release. A new trend in the delivery of proteins and peptides is the use of thermodynamically stable self-assembled lyophilic colloids. These are called smart amphiphilic copolymers.

B. pH sensitive polymers in drug delivery

1. Polymeric anti-cancer agents that respond to pH . Another effective way to treat cancer is to use macromolecular carriers that dissolve in water to deliver anticancer drugs. The medicines must be freed from the carrier system for these macromolecular anticancer conjugates to work as medicine. Adding acid-sensitive linkers between the drug and the carrier makes it easier for the active drug to get into tumor tissues, both in the slightly acidic space around cells and inside the endosomes or lysosomes of cancer cells after they have been taken in.
2. pH-Sensitive Muffled Polymer Microspheres for Drug Delivery. In scientific and technological fields, it would be very helpful to be able to make empty polymer particles that react to stimuli and have a narrow size distribution. Regulating the kinetics of medication release may provide a more advanced and intelligent drug delivery system

C. Enzyme-sensitive polymers in drug delivery

Enzyme-responsive nanoparticles for therapeutic delivery and diagnostic purposes. Putting enzymes together with the unique physical properties of nanomaterials makes it possible to make enzyme-responsive nanoparticles that quickly and effectively do their jobs when activated. The advancement of drug delivery devices has successfully used this strong principle to precisely target particular tissues via enzyme-triggered medicine release.

5. Future challenges for drug delivery systems encompassing stimuli-responsive polymers

Patients have not yet received the majority of current smart polymeric drug delivery devices. Several crucial aspects need consideration in this situation. The main worry is that smart polymers might hurt cells when biomolecular medicines like peptides, proteins, and nucleic acid medicines are given to them. Another factor is the polymer's reaction time; in most instances, it is fragile, requiring the use of rapid-acting polymer systems. Thermoresponsive polymeric drug delivery systems are well-studied and have proven beneficial in several applications. Most commonly used acrylamide or acrylic acid-based polymers, on the other hand, can't be broken down by water and are often linked to neurotoxicity. These undesirable consequences limit the domain of smart polymeric drug delivery.

Higher molecular weight Smart polymers are better at targeting cells, but they don't break down and can't be flushed out of the body, so they build up inside it. This may explain why clinical studies have not evaluated them. Research primarily focuses on intelligent drug delivery systems to identify more effective methods for cancer treatment. Some of the good things about these systems are that they can physically or actively target cancer cells and encapsulate drugs in polymers so that they are released slowly into the bloodstream. Clinical success is attained only when the medication delivery method can eradicate every individual cancer cell. Certain cancer cells experience metastasis and are very difficult to eradicate. The problematic behavior of cancer cells is a significant obstacle to the therapeutic use of smart polymers. There are many uses for smart polymeric drug delivery methods in oral drug administration for biological medicines that are easily broken down by stomach acid and enteric enzymes. Another use is in the realm of smart diagnostics, since their utilization often does not need direct contact with the body. We expect intelligent polymeric drug delivery devices to achieve significant success in this domain.

6. Conclusion

The elements that affect the recognition and interactions of macromolecules within biological and cellular environments are essential for progress in this area and demonstrate significant intricacy. The necessity for collaboration across disciplines and the integration of advanced technologies heightens the complexity. The temperature, pH, and enzyme-sensitive smart polymers are critical factors to consider. Optimal outcomes from the parenteral administration of smart polymers can only be realized through a comprehensive understanding of the movement and interactions of macromolecules. The growing interest in stimuli-responsive polymers is particularly notable in the areas of controlled and self-controlled drug delivery. Smart polymers are gaining significance in the delivery of proteins and peptides as experts seek improved methods to harness their distinctive characteristics. Every delivery system presents unique benefits, particularly in relation to prolonged protein delivery. The interplay between hydrophobic and hydrophilic groups, the length of polymer chains, molecular weight, and the overall structure and architecture of the polymer are critical properties influencing drug release and the robustness of delivery systems.

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