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A Study on Smart Polymers for Targeted Drug Delivery System

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Abstract: A new family of sophisticated materials called as "smart polymers," or "stimuli-responsive polymers," show notable changes in their chemical or physical characteristics in response to external environmental stimuli. This project offers a thorough review of smart polymers, starting with an introduction to their basic properties and moving through their categorisation according to various stimuli. The study examines three main types of stimuli: biological (such as enzymes and biomolecules), physical (such as temperature, light, and electric or magnetic fields), and chemical (such as pH and ionic strength). The project goes on to describe the benefits of smart polymers, such as their high sensitivity, biocompatibility, and potential for targeted and controlled applications, as well as their drawbacks, which include high production costs, difficult synthesis procedures, and stability issues. The relevance of smart polymers in site-specific and controlled drug delivery systems, which can greatly enhance treatment outcomes, is highlighted in a thorough explanation of the drug release mechanism. To further highlight the practical importance of smart polymers, examples of widely utilised smart polymers are looked at. A review of the various uses of smart polymers in domains like biomedical engineering, medication transport, tissue engineering, sensors, and environmental systems rounds out the project. All things considered, smart polymers are a quickly developing topic with enormous potential to transform contemporary science and technology due to their versatile and adaptable characteristics.

Keywords: *Drug Delivery Systems, Advanced Materials, Biocompatibility, Smart Polymers, Stimuli-Responsive Materials, Chemical, Physical, and Biological Stimuli, 3D Printing, and Polymer Applications.*

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I. INTRODUCTION

Polymers are macromolecules composed of repeating units, playing a vital role in modern society due to their diverse properties and applications. Their evolution reflects advancements in science, environmental needs, and societal demands. Among them, stimuli-responsive or smart polymers have gained importance for their ability to respond to changes in temperature, pH, light, and ionic strength.[1,2] These polymers exhibit reversible changes in shape, solubility, and physical state, making them highly useful in biomedical applications.[3,4]

II. TYPES OF SMART POLYMERS

➢ *Chemical Stimuli*

- *Stimuli-Responsive Polymers:*

By responding to internal (pH, redox, enzymes, temperature) and exterior (light, magnetic, ultrasonic) stimuli, stimuli-responsive polymers provide regulated medication delivery.[5] These polymers fall into one of two categories: single-stimuli (like thermo-responsive PNIPAM) or multi-stimuli (like pH and temperature-responsive PDMAEMA). Multi-stimuli systems are very beneficial for enhanced drug delivery, therapeutic applications, and biomedical advances because they increase precision, widen switching windows, and improve drug release efficacy.[6]

- *pH- Responsive Smart Polymers:*

pH- responsive polymers react to changes in pH by changing their structure. These polymers have basic or acidic portions that ionise in response to pH, changing their solubility, structure, and chain conformation. For instance, PDMAEMA is helpful in gene therapy and medication delivery because it swells and becomes protonated at low pH.[7] These polymers are essential for targeted treatments, particularly in cancer therapy, because pH-triggering groups allow controlled drug release in acidic environments like endosomes and lysosomes.[8,9]

- *Thermo-Responsive Polymers:*

The capacity of thermoresponsive polymers to experience considerable physicochemical changes in

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response to temperature changes makes them an important class of smart materials. The reversible phase transition linked to the lower critical solution temperature (LCST) of these materials has been extensively researched. These polymers change from a hydrated, expanded coil conformation to a collapsed, globular shape when dissolved in aqueous environments and heated over their LCST.[10] Due to decreased polymer solubility, this conformational shift causes macroscopic phase separation, which usually shows up as turbidity in the solution. Interestingly, this process is reversible; the polymer chains rehydrate and revert to their initial stretched configuration when cooled below the LCST.[11]

A number of structural and compositional factors, such as polymer chain length, stereoregularity, end-group functionality, and the kind and ratio of comonomers added during synthesis, affect the highly adjustable LCST.Additionally, because polar solvents like alcohols and water can create hydrogen bonds with polymer chains to modify intermolecular interactions, their presence increases the heat responsiveness of these systems [12].

➢ *Physical Stimuli*

- *Light-Responsive Polymers*

A flexible class of smart materials, light-responsive polymers have several benefits, including good aqueous solubility, biocompatibility, and biodegradability [13]. When subjected to light with a certain wavelength, intensity, and irradiation area, these devices can achieve exact spatial and temporal control [14]. Nevertheless, some restrictions still exist, such as the possibility of chromophoric moieties leaching from hydrogels during swelling, which could have an impact on the stability and functionality of the material [15].

- *Temperature Responsive Stimuli*

The techniques used to regulate temperature are well-established, and it is an easily observable and controllable characteristic. As a result, it is frequently used as a stimulus in the creation of smart polymers. By adding additives like plasticisers, salts, or surfactants, which affect intermolecular interactions within the system, a material's temperature-responsive behaviour can be created or modified.

Such polymers usually exhibit a reversible sol-gel phase shift. The inclusion of lipophilic groups, such as methyl, ethyl, or propyl moieties, is a defining trait of many temperature-responsive polymers and is essential in controlling their thermal behaviour. Prolastin, poloxamers, and poly(N-isopropylacrylamide) (PNIPAAm) are typical examples [16].

✓ *The Following are Important Metrics for Assessing Temperature-Responsive Polymers:*

- The minimum temperature above which a polymer becomes totally soluble in a particular solvent system is known as the Upper Critical Solution Temperature (UCST); this phenomena has received less attention than LCST behaviour.
- The highest temperature at which a polymer is still soluble in a single phase is known as the Lower Critical Solution Temperature (LCST); at this point, phase separation happens as a result of reduced interactions between the polymer and the solvent [17].

- *Magnet Responsive Polymers*

Magnetic fields are intriguing for biomedical applications because the human body can easily withstand them and they are generally thought to be less hazardous than other external stimuli. The usual method for creating magnetic-responsive polymeric systems is to uniformly embed the therapeutic drug and magnetic particles, such as micro or nanoparticles, within a polymer matrix. Controlled drug release is made possible by structural changes that take place in the polymer when it is exposed to an external magnetic field. These changes frequently involve the creation or enlargement of micropores. The polymer matrix reverts to its initial, more compact structure when the magnetic field is removed, which lowers the drug release rate [18].

Iron oxide (Fe3O4), zinc-doped iron oxide (Zn–Fe3O4), copper–nickel alloys (Cu–Ni), and manganese (II) oxide (MnO) are among the magnetic cores that can be used in these systems. To create efficient magnetically responsive drug delivery systems, they are frequently mixed with polymers such dodecyl-grafted poly (isobutylene-alt-maleic anhydride), polyethylene glycol (PEG), poly (isobutylene-alt-maleic anhydride), and poly(styrene sulfonate-N-isopropylacrylamide) [19].

- *Electric Field-Responsive Polymers*

Electro-responsive polymers—also referred to as electric field-sensitive polymers—respond to applied electric stimuli by changing their mechanical and physicochemical characteristics. These materials frequently have a high density of ionisable functional groups, which makes them sensitive to pH changes as well as electric fields. The fundamental process is the transformation of electrical energy into structural alterations or mechanical deformation in the polymer network.

Applying an electric field can interfere with intermolecular interactions in the polymer matrix, including hydrogen bonding, in the context of drug delivery. The controlled release of encapsulated therapeutic substances at the target site is made easier by this disruption. In addition to drug delivery, electro-responsive polymers are used in energy harvesting systems, soft robotics, electrochromic devices, actuators, and electroconductive scaffolds for tissue engineering [20].

✓ *The Two Primary Categories of Electro-Active Polymers (EAPs) are as Follows:*

- Ionic EAPs: These systems experience mechanical and electrochemical reactions as a result of ion migration and variations in local ion concentration brought on by the applied electric field. modest actuation speed, comparatively modest produced forces, and low voltage operation are their usual characteristics.

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- Dielectric EAPs: These materials deform quickly as a result of electrostatic forces created between electrodes. Although they typically need high operating voltages, they have great response speed and actuation strength [21].

✓ *The Following Polymers are Frequently Used in the Creation of Electro-Responsive Systems:*

- Polypyrrole (PPy): renowned for its excellent biocompatibility and high electrical conductivity;
- Chitosan (CS), a naturally occurring polymer renowned for its biocompatibility, biodegradability, antimicrobial activity, gel-forming ability, and ease of modification;
- Polyaniline (PANI), which is valued for its chemical stability, ease of processing, and conductive properties; and Poly(3,4-ethylenedioxythiophene) (PEDOT), which is characterised by excellent conductivity, biocompatibility, and moderate hydrophobicity [22].

- *Redox-Responsive Polymers*

Redox-responsive polymers are a large family of smart materials that react to changes in the redox environment by undergoing particular physicochemical changes. In addition to being activated by the presence of oxidising or reducing chemicals, these reactions can also be indirectly impacted by outside variables that alter the redox conditions, such as temperature, pH, and light.These materials have several uses, especially in hydrogel-based drug delivery systems. The Kilic-Boz research group's study, which showed that biomolecules like bovine serum albumin (BSA) could be released from hydrogels in the presence of thiol-containing reducing agents like dithiothreitol (DTT) and L-glutathione (GSH), is a noteworthy example. Usually, redox-active organometallic components or cleavable disulphide linkages are included into the polymer network to produce redox sensitivity in these systems [23].

Depending on the type of added functional groups, redox-induced responses in hydrogel systems might show up as changes in features including colour, chiral structure, phase behaviour, or fluorescence. A poly(N-isopropylacrylamide) (PNIPAAm) hydrogel containing tris(2,2′-bipyridyl)ruthenium (II) is an example of a redox-responsive polymer system. This hydrogel undergoes reversible oxidation from Ru^{2+} to Ru^{3+}, changing the material's physicochemical properties [24].

➢ *Biological Stimuli-Responsive Polymer Materials*

A family of systems known as bio-responsive polymers is created when biological stimuli cause polymeric materials to undergo functional modifications. Glucose and enzymes, which can cause certain structural or physicochemical changes within the polymer network, are two important biological elements affecting these materials.

- *Glucose-Responsive Polymers*

The creation of glucose-responsive polymers has great promise for biomedical uses, especially in the treatment of diabetes. These systems replicate physiological feedback processes by sensing changes in glucose concentration and responding by controlling the regulated release of insulin. These materials' comparatively sluggish response time, which might impede accurate and timely insulin delivery, is a significant drawback despite their potential.

- *Enzyme-Responsive Polymers*

A type of intelligent materials known as enzyme-responsive polymers can undergo particular changes when target enzymes are present. These systems are very useful in the design of targeted delivery platforms because they take use of important enzymatic features including catalytic activity and high substrate specificity, especially in situations where certain enzymes are overexpressed.

Enzyme-responsive polymers provide several benefits, including as increased permeability, greater resistance to nonspecific degradation, a large range of enzymes accessible for triggering reactions, high specificity at the cellular level, and the possibility of precise spatiotemporal control of payload release. These systems do, however, have some drawbacks. Notably, the presence of enzymes with comparable substrate specificity raises the danger of both unintentional release before the material reaches the intended target site and premature release of the encapsulated payload [25].

➢ *Advantages and Disadvantages of Smart Polymers*

Table 1 Entails Advantages and Disadvantages of Different Types of Stimuli Responsive Polymers [26]

So No.	Stimulus	Advantages	Disadvantages
1.	Temperature	Protect the drug from enzymatic or environmental degradation	High production cost
2.	pH	Apt for thermo-labile drugs	Insufficient toxicity data
3.	Light	Non-contact and distant application	Release of non-covalently bound chromophores during system expansion or contraction
4.	Electric field	Changes in electric field can cause pulsatile release.	Optimizing the amount of current is difficult.
5.	Ultrasound	Controlled release of protein	Non-biodegradable systems require surgical insertion.
6.	Magnet	Control release of drug departureprocess	Unwanted heating ofthe tissues

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III. MECHANISM OF DRUG RELEASE USING SMART POLYMERS

Highly regulated and predictable medication release is made possible by smart polymers, which are triggered by particular internal or external events. These materials have the ability to detect minute changes in their surroundings and react by undergoing reversible structural, chemical, or physical changes. The pace, scope, and timing of drug release are all directly impacted by these changes.

The basic idea behind these systems is that the polymer matrix experiences physicochemical or configurational changes that control the drug's release or diffusion. Below is a description of the main mechanisms controlling drug release from smart polymers [27].

➢ *Mechanism of Swelling and Deswelling Operating:*

The polymer network expands structurally in response to a suitable stimulus (such as pH, temperature, or ionic strength), which permits water molecules to enter the matrix. As a result, the material swells and the polymer network's mesh size increases. Encapsulated drug molecules can leak out into the surrounding environment as the mesh size increases.

The polymer experiences deswelling (shrinkage) when the stimulus is eliminated or reversed, which results in a smaller mesh size. Drug release in the collapsed condition is slowed down or stopped entirely as a result of this restriction on molecular diffusion [28].

➢ *Mechanism Controlled by Erosion and Degradation Operating:*

In this process, the polymer is designed to break down in response to certain stimuli, such pH shifts, enzyme activity, or the presence of reactive oxygen species, at a regulated and predictable rate. Initially confined in the polymer matrix, drug molecules are released gradually as the material erodes, frequently layer by layer.By adjusting variables including molecular weight, crosslinking density, and polymer composition, the pace of degradation can be precisely controlled.

- *Degradation Types:*

Surface erosion: A more linear and predictable release profile is produced by drug release, which mostly originates from the polymer's layers.

Bulk erosion: Over time, sustained drug release is made possible by the homogeneous degradation of the whole polymer matrix.

➢ *Relevance*

Permits the delivery of drugs over an extended period of time (weeks to months).

Because the substance spontaneously breaks down within the body, there is no need for surgical removal. especially appropriate for uses such biodegradable drug depots, long-acting injectables, and implants [29].

IV. EXAMPLES OF THE POLYMERS

➢ *Natural Polymers*

- *Chitosan*

A naturally occurring polymer, chitosan is a flexible stimuli-responsive substance that may react to pH and temperature. Because of their low toxicity, biocompatibility, and biodegradability, chitosan-based drug delivery systems have shown great promise in biomedical applications, especially for skin treatments and cancer therapy.

✓ *For Regulated Drug Delivery, a Number of Chitosan-Based Methods Have Been Investigated:*

- For regulated analgesic drug release, a hydrogel made of chitosan, hyaluronic acid, and poly(N-isopropylacrylamide) (pNIPAAm) shown thermoresponsive behaviour.
- Emulsion polymerisation was used to create cross-linked chitosan/pNIPAAm hydrogels, which were then used as antibacterial drug delivery systems.
- In cartilage tissue engineering, pluronic-grafted chitosan hydrogels were used as injectable, thermoresponsive cell delivery vehicles.
- PEG-grafted chitosan injectable hydrogels showed dual pH and temperature responsiveness as well as prolonged drug release.
- For the delivery of anticancer medications like adriamycin and 6-mercaptopurine, a system that combined chitosan with αβ-glycerophosphate demonstrated thermoresponsive characteristics.
- The antibacterial activity of pNIPAAm/chitosan hydrogels applied to cotton fabric with glutaraldehyde as a cross-linker demonstrated their potential for use in functional textile applications.
- These illustrations show how chitosan-based smart polymers can be used to create multipurpose drug delivery systems with adjustable stimulus responsiveness.[30]

- *Collagen*

One of the most popular polymers in tissue engineering is collagen, which is especially appealing for skin regeneration applications due to its special qualities. Collagen has been used in a variety of skin regeneration applications, such as films, gels, scaffolds, mats, composites, and three-dimensional (3D) matrices. Regardless of the method in which it is applied, numerous studies have shown the remarkable effectiveness of collagen in stimulating skin restoration [31].

Collagen has been the subject of research for several decades due to its unique properties, which include mechanical strength, regulated biodegradability, water absorption, and high biocompatibility. For applications in skin regeneration, it is especially important to be able to precisely regulate the rate at which collagen-based materials degrade so that natural tissue can gradually replace them.

Collagen was traditionally obtained from terrestrial animals. However, other sources, like collagen obtained from

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marine sources, have become more popular in the wake of infectious disease epidemics. Although it is a safer source, the stability and physicochemical characteristics of marine collagen are often worse than those of mammalian collagen. Different crosslinking techniques have been developed to improve collagen's mechanical integrity and functional performance for useful tissue engineering applications in order to overcome these constraints.[32]

- *Gelatin*

In the field of tissue engineering, gelatin—a denatured version of collagen—shows comparable results. Gelatin is a common natural polymer in pharmaceutical and medical applications because of its superior biodegradability and biocompatibility under physiological settings. Because of its denatured structure, gelatin exhibits less antigenicity than collagen. Similar to collagen, its mechanical strength, drug release behaviour, and rate of degradation can all be customised by varying the degree of crosslinking.[33] Gelatin has been thoroughly investigated in skin tissue engineering because to its capacity to facilitate regulated medication distribution. Its positive benefits on skin regeneration have also been noted in a number of investigations.[34]

- *Fibrin*

When the enzyme thrombin is present, fibrinogen, a protein found in blood plasma, polymerises to produce fibrin, a complex network. Fibrin's capacity to minimise immunogenic reactions and lower the risk of disease transmission stems from its unique structure and composition. During extracellular matrix renewal, it naturally manifests as a transient matrix.[35] Fibrin is frequently used in clinical settings as fibrin glue, which acts as a carrier for growth factors to promote healing and quicken tissue restoration. Furthermore, fibrin is frequently created into hydrogels to offer regulated drug delivery, a moist environment, good biocompatibility, and appropriate mechanical qualities. Mesenchymal stem cells, fibroblasts, keratinocytes, and other cell types are all supported in their growth and function by these hydrogels.[36]

➢ *Synthetic Polymers*

- *Poly (Vinyl Alcohol) (PVOH, PVA, or PVAl)*

Water-soluble and biodegradable, poly (vinyl alcohol) (PVA) has a molecular weight between 20,000 and 200,000 Da. It has a melting temperature of about 200 °C and a glass transition temperature of about 85 °C. The degree of hydrolysis, temperature, the surrounding medium, and the kind of microorganisms involved all affect how PVA degrades and biodegrades. PVA is usually made by radical polymerisation of vinyl formate, vinyl pivalate, and vinyl trifluoroacetate, or by polymerisation of vinyl acetate.[37]

PVA has been widely used as a polymeric matrix in skin and tissue engineering applications because it is hydrophilic, biodegradable, and biocompatible. Hydrogels, membranes, xerogels, fibres, electrospun fibre mats, porous scaffolds, and 3D-printed scaffolds are just a few of the structures that are made with it.[38] Its outstanding biocompatibility, favourable mechanical qualities, high water absorption capacity, and low cytotoxicity all contribute to its tremendous potential in regenerative medicine.[39]

- *Polyglycolide or Poly (Glycolic Acid) (PGA)*

The synthetic polymer poly(glycolic acid) (PGA) is widely employed in biomedical applications, especially in skin repair and tissue regeneration, because to its exceptional biodegradability and biocompatibility. It is a straightforward linear aliphatic polyester with favourable physicochemical characteristics like quick degradation, strong barrier qualities, a high tensile modulus (~12.5 GPa), a melting temperature above 200 °C, and a glass transition temperature of about 40 °C. It usually forms a crystalline or semicrystalline structure.[40]

PGA can entirely break down under physiological conditions in a year, releasing glycollic acid as a result. Using methods like extrusion, compression moulding, injection moulding, and solvent casting, PGA has so far been used to create a variety of three-dimensional composite materials and matrices for tissue and skin engineering. A variety of structures, such as injectable photopolymerised hydrogels, core-shell electrospun nanofibers, hydrogels, branching scaffolds, and layered biocomposites for regenerative applications, have been made possible by these production techniques.[41]

- *Poly (Lactic Acid) (PLA)*

Because of its biocompatibility, bioabsorbability, thermal stability, and advantageous mechanical qualities, polylactic acid (PLA), an aliphatic polyester also known as a polylactide, is frequently utilised in biomedical applications. Poly(L-lactic acid) (PLLA), meso-polylactic acid, poly(D-lactic acid) (PDLA), and poly(D,L-lactic acid) (PDLLA) are some of the stereoisomeric variants of PLA. With a typical glass transition temperature (Tg) of 60–65 °C, a melting temperature (Tm) of roughly 175 °C, and a tensile strength of about 4.8 GPa, this semicrystalline polymer is a good fit for tissue engineering and wound healing applications.[42]

Electrospun nanofibers, hydrogels, composite flexible filaments for 3D printing, extruded nanofibril nanocomposites, core–shell hybrid electrospun scaffolds, bilayer membranes, hybrid porous scaffolds, melt-blown nonwoven composites, and multifunctional nanohybrid scaffolds are just a few of the PLA-based composite materials that have been developed for skin tissue repair.[43]

V. 3D PRINTING TECHNIQUES FOR SMART POLYMERS

➢ *Vat Photopolymerization*

A liquid resin is selectively cured layer by layer to create a solid object using a light-induced additive manufacturing technique called vat photopolymerization. This method works especially well for low-viscosity, UV-curable smart polymer systems, such as drug-encapsulating polymer networks, light-responsive hydrogels, and shape-memory acrylate formulations [44,45]. It includes a number of subcategories, including continuous liquid interface

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production (CLIP), digital light processing (DLP), and stereolithography (SLA).

Vat photopolymerization involves filling a clear vat with a liquid resin made up of functional additives, photoinitiators, and monomers or oligomers. The resin is selectively exposed to a UV or visible light source, which starts crosslinking in predetermined areas that match the cross-sectional slices of a computer-aided design (CAD) model. The build platform shifts vertically to enable the deposition of a new resin layer after each layer has dried, either upward or downward, depending on the system configuration. Until the entire three-dimensional structure is created, this procedure is performed repeatedly [46].

➢ *Powder Bed Fusion*

Powder bed fusion is an additive manufacturing process that creates three-dimensional structures by selectively fusing polymer powders using thermal or photonic light. The ability to create intricate, support-free geometries with high strength and minimal weight makes this approach desirable. It is also compatible with a variety of composite materials and thermoplastic smart polymers [47].

- *Selective Laser Sintering (SLS)*

Using a laser to selectively sinter or fuse powdered materials in specific areas, selective laser sintering (SLS) is an additive manufacturing technology that creates three-dimensional objects layer by layer. A number of processes, such as solid-state sintering, partial or total melting, or chemically driven bonding, may result in this fusion.

A roller or blade is used in the SLS process to evenly distribute a thin layer of powder, such as a polymer, composite, ceramic, or metal, across a build platform. The powder bed is then selectively scanned by a laser, producing localised heat that fuses the particles in specific locations. A fresh coating of powder is applied to the surface once each layer has solidified, and this procedure is continued repeatedly until the entire three-dimensional object is created [48].

VI. APPLICATIONS OF SMART POLYMERS

➢ *Tissue Engineering:*

The multidisciplinary discipline of tissue engineering uses intelligent biomaterials to repair or regenerate tissues or organs that have been harmed by illness, trauma, or other biological events. The creation of scaffold structures with suitable chemical, physical, and biological characteristics to facilitate cell infiltration, proliferation, and three-dimensional tissue formation is the core idea of tissue engineering.

These scaffolds offer a transient structure that promotes tissue regeneration and progressively breaks down as new tissue grows. This eliminates the need for surgical removal and reduces the risk of long-term complications associated with permanent implants [49].

As surfaces that control cell adhesion and proliferation and as injectable systems that create scaffolds in situ, temperature-responsive polymers are essential to tissue engineering.

By reacting to temperature changes, these polymers enable regulated cell adhesion and dissociation in the first application, making non-invasive cell harvesting possible. The polymers are employed as injectable hydrogels in the second application, which encapsulates cells inside a three-dimensional body structure. Compared to prefabricated implants, the scaffold requires less surgical intervention because it is created in situ using cells, nutrients, and growth factors. It can also adjust to uneven defect geometries.

Prior to delivery, the polymer is mixed with cells at room temperature as part of the underlying mechanism. The material goes through a sol–gel transformation and solidifies into a gel when exposed to physiological temperature (~37 °C), which is higher than the polymer's transition threshold. Consequently, a three-dimensional matrix that promotes tissue regeneration surrounds the cells [50].

➢ *Gene Therapy*

For the treatment of genetic diseases and tumours that are frequently resistant to traditional medicines, gene therapy presents a potential approach. The creation of effective gene delivery vectors that can move genetic material from the bloodstream to the cell nucleus is crucial to the success of gene therapy [51]. Gene therapy allows for the modification or correction of disease-causing genes by focusing on the underlying genetic defects. It can be used selectively to treat serious illnesses including malignant tumours and cystic fibrosis.

Coupling processes and cationic polymer modifications are two strategies that have been investigated to improve gene transport, although they can be complicated and heavily rely on the structure, content, and functional groups of the polymer. Gene therapy polymers are carefully engineered to strike the ideal mix between extended bloodstream circulation time and precise, targeted release at the illness location, especially in tumour tissues.

The capacity of temperature- and pH-responsive polymers to react to minute changes in their surroundings has drawn a lot of interest, making them appropriate for use in tissue engineering and medication delivery. However, their design must take into account variables like biodegradability and cytotoxicity, which change according on the monomer choice and polymerisation technique. For example, under some circumstances, certain monomers, such N-isopropylacrylamide (NIPAM), may have cytotoxic effects [52].

Polymers can help carry nucleic acids, such DNA, into target cells and shield them from extracellular breakdown in gene therapy applications. In particular, synthetic polymers are useful for creating stable compounds with DNA, increasing the effectiveness of gene transfer, and permitting regulated release. These polymer–DNA complexes can be made to react to particular stimuli, including pH or

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temperature changes, which cause the complex to dissociate and encourage the release of genes within target cells.

Moreover, medication encapsulation in nanoscale polymer-based delivery methods, such as biocompatible and biodegradable amphiphilic block copolymer micelles, has shown promise in lowering systemic toxicity and extending circulation duration. When compared to the delivery of free drugs, this method can improve tumour suppression. However, there are still major issues with hydrophobic medications, including poor absorption, off-target distribution, and negative side effects. To address these limitations, advanced delivery systems such as polymersomes have been developed, offering localized delivery of highly potent therapeutics with tunable pharmacokinetics, thereby improving therapeutic efficacy [53].

➢ *Biosensors*

Because they can react to external stimuli and identify certain biological targets, such proteins, nucleic acids, or infections, smart polymers have become viable materials for biosensor development. These polymers can undergo structural or physicochemical changes upon engagement with a target analyte, improving the sensitivity and specificity of biosensing devices. The combination of biosensors and smart polymers has greatly improved current diagnostic methods [54].

From temperature sensors (such as thermometers) to gas sensors used in automobile pollution control systems and motion sensors in controlled lighting, sensing devices have become an essential part of everyday life during the past few decades. When Clark and colleagues were developing an enzyme-based glucose sensing device that could measure glucose concentration in 1962, they coined the term "biosensor".

Because conducting polymers can effectively immobilise biomolecules and are compatible with biological molecules, they are widely used in biosensing applications. A typical biosensor works by creating a particular probe–target combination, which a transducer subsequently transforms into a signal that can be measured [55]. Parameters like limit of detection, sensitivity, selectivity, repeatability, stability, mobility, and storage capacity are typically used to assess a biosensor's performance. In the end, the biosensor produces a measurable signal that correlates with the analyte concentration and is frequently digital [56].

- *Usually, a Biosensor is Made up of Two Primary Parts:*

✓ A transducer, which transforms the biochemical interaction into a quantifiable signal; and
✓ A bioreceptor, which is an immobilised biomolecule in charge of identifying the target analyte.

Protein adsorption may happen when polymer-based materials are utilised in biological settings, which could result in a foreign body reaction that isolates the implant. Nanomaterials like graphene and carbon nanotubes are frequently used to improve biosensor performance. These nanoparticles show better dispersibility in aqueous media and improved functional characteristics when coupled with polymers. For example, multi-walled carbon nanotubes functionalised with polymers perform better in sensing applications [57].

Advanced smart polymer systems, such as poly (N-isopropylacrylamide-co-methacrylic acid) hydrogels coupled with indium tin oxide microheaters, which provide light-responsive sensing capabilities, have also been emphasised in recent works. Further increasing their usefulness in biosensing applications, smart polymers can be carefully tailored to identify and react to certain biomolecules or environmental changes, such as changes in pH and temperature [58].

➢ *Medicine*

The medical field is one of the most important applications of smart polymers. Functional biomaterials have developed quickly due to the increasing need for sophisticated polymeric materials that can treat a variety of illnesses and enhance quality of life. Drug delivery systems [59], tissue engineering, bioimaging, gene delivery, cell culture, and the creation of medical devices all make extensive use of stimuli-responsive polymers. They are used in a variety of biomedical products, including as biosensors [60], hydrogel dressings, implants, tissue adhesives, and ocular lenses [61].

Hydrogels are the most widely utilised class of smart polymers in the medical industry. Hydrogels are networks of three-dimensional polymers that may absorb a lot of water or biological fluids. Their special physicochemical, mechanical, and biological characteristics—such as hydrophilicity, biocompatibility, viscoelasticity, softness, and biodegradability—make them extremely attractive for biomedical applications. They are particularly well suited for healthcare applications because of their structural resemblance to genuine tissues [62].

Hydrogels can be categorised according to a number of factors, such as their network structure, origin, and stimuli-responsiveness. Their final qualities are largely determined by the synthesis process. Hydrogels are generally created via chemical or physical crosslinking. Reversible interactions such hydrogen bonding, electrostatic interactions, hydrophobic associations, crystallisation, and polymer chain entanglements are necessary for physically crosslinked hydrogels. Improved biocompatibility, the lack of potentially harmful crosslinking agents, stimulus responsiveness, and self-healing properties are some benefits of these systems [63].

Chemically crosslinked hydrogels, on the other hand, are created by permanent covalent bonds between polymer chains through methods like photopolymerization, click chemistry (such as Michael addition and Diels-Alder reactions), Schiff base formation, oxime linkages, and enzyme-mediated reactions. Under physiological settings, these hydrogels show improved mechanical strength, structural stability, and adjustable degradation. Crucially,

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important characteristics like swelling behaviour, elasticity, and degradation rate are greatly influenced by the type and degree of crosslinking [64].

Since polymers frequently serve as replacements for soft tissues, organ parts, or bone structures, they must adhere to strict criteria for medical applications, such as biocompatibility, non-toxicity, and non-mutagenicity. As a result, the physicochemical and biological characteristics of polymeric biomaterials must be precisely adjusted to suit their intended use [65].

Smart polymers are essential to cancer treatment, especially hydrogel-based sustained drug delivery systems. Anticancer medications that are encapsulated in hydrogel networks are better delivered to tumour locations while being shielded from immune clearance, premature degradation, and other unfavourable circumstances. The type of cancer, the characteristics of the drug, and the intended release profiles must all be taken into account when designing such systems [66].

Temperature, light, pH, electric or magnetic fields, mechanical stress, and ultrasound are popular triggers for stimuli-responsive polymers employed in drug delivery. For example, thermoresponsive polymers experience abrupt changes in solubility in response to small temperature changes, resulting in conformational changes that allow for regulated drug release [67]. Similar to this, photosensitive polymers enable precise spatial and temporal control over therapeutic release by facilitating drug distribution through processes including photoisomerization and photochemical or photothermal reactions [68].

- *Oncology*

Smart polymer systems continue to show great promise in the field of cancer therapy. Acidic pH, hypoxia, high glutathione levels, and overexpression of certain enzymes are among the unique features of tumour microenvironments. Chemotherapeutic chemicals can be released site-specifically thanks to smart polymers that react to certain stimuli, reducing systemic toxicity and improving therapeutic efficacy. For example, in the acidic environment of tumour tissues, pH-sensitive polymers like poly(L-histidine) and poly(β-amino esters) can release medicines selectively [69].

In conditions where intracellular glutathione concentrations are high, redox-responsive systems—such as micelles made with disulphide crosslinkers—degrade, guaranteeing effective drug release into cancer cells. Several polymer-based nanocarriers are progressing through preclinical research and early-stage clinical trials as the clinical translation of these systems is actively investigated.

Additionally, theranostics—the integration of therapeutic and diagnostic functions—is being explored for multifunctional smart nanocarriers. These devices offer a promising way to increase accuracy and efficacy in cancer therapy by enabling simultaneous drug delivery and real-time monitoring of treatment progress [70].

- *Diabetes*

The creation of glucose-responsive insulin delivery devices that closely resemble the pancreas' physiological insulin release behaviour has been made easier by smart polymers. To detect changes in glucose concentration and release insulin in response, these systems use glucose-sensing components like glucose oxidase, phenylboronic acid, or concanavalin A.

For example, when glucose levels are high, hydrogels containing glucose oxidase produce localised pH changes that cause the polymer matrix to swell and release insulin. Similar to this, polymers based on phenylboronic acid have the ability to bind glucose molecules reversibly and go through conformational changes that control drug diffusion.

These systems are intended to improve glycaemic control and lessen the need for frequent insulin injections, especially in patients with type 1 diabetes. This will increase treatment efficacy and patient compliance [71,72].

- *Neurological Disorders*

The selective impermeability of the blood–brain barrier (BBB), which limits the transport of therapeutic drugs to the central nervous system, frequently limits the treatment of neurological illnesses. The capacity of smart polymer-based nanocarriers to get beyond this obstacle and release medications in response to brain-specific cues has been thoroughly studied.

For instance, pH-sensitive poly(lactic-co-glycolic acid) (PLGA) nanoparticles functionalised with targeting ligands like lactoferrin or transferrin have shown improved transport across the blood-brain barrier. Furthermore, delivery systems that respond to matrix metalloproteinases—which are overexpressed in neuroinflammatory conditions—are being developed.

For the treatment of neurological conditions like Parkinson's disease, Alzheimer's disease, and brain tumours, where accurate and targeted medication administration is crucial, these cutting-edge drug delivery techniques show great promise.

- *Antibacterial and Wound Healing Applications*

Additionally, smart polymers have been extensively used in wound healing and localised antibacterial therapy. Thermo-responsive, enzyme-responsive, or pH-sensitive polymers are frequently used in these systems to administer antibiotics or growth hormones specifically to infection or tissue damage areas.

For instance, thermosensitive hydrogels based on chitosan can gel at physiological temperature, allowing for the localised and prolonged release of antimicrobial chemicals. When bacterial enzymes are present, enzyme-responsive polymer systems break down, releasing antibiotics specifically at the site of infection.

To improve tissue regeneration and stop microbial colonisation, such smart polymer-based platforms have been

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developed in a variety of forms, such as wound dressings, sprays, and injectable depots. Furthermore, antibacterial activity and biocompatibility have been further enhanced by the addition of bioactive compounds including curcumin, silver nanoparticles, and herbal extracts into polymer matrices, providing a potential approach for advanced wound care applications [73].

VII. CONCLUSION

In conclusion, because smart polymers can react dynamically to environmental stimuli, they constitute a major development in material science. The basic features of smart polymers were addressed in this research, starting with an overview of their special qualities and moving through the different kinds according to responsiveness.

These polymers can experience regulated modifications in response to environmental elements like pH, temperature, light, and certain biomolecules, as demonstrated by the discussion of chemical, physical, and biological stimuli. They are quite useful in cutting-edge fields because of their flexibility.

While the drawbacks—such as high cost, limited durability, and complicated synthesis—indicate areas that need more study and development, the benefits—such as biocompatibility, controlled drug delivery, and environmental responsiveness—showcase their potential in contemporary technology and medicine.

The mechanism of medication release, where smart polymers allow for targeted and regulated administration, increasing therapeutic efficacy and reducing side effects, was a major emphasis of the study. The practical application of smart polymers is further demonstrated by a number of examples.

By enabling accurate structures and customised applications, advanced manufacturing is improving the design and customisation of smart polymer-based systems, as demonstrated by the incorporation of 3D printing processes.

Lastly, the broad range of uses—from tissue engineering and medication delivery to sensors and self-healing materials—shows the revolutionary potential of smart polymers in a variety of sectors.

All things considered, smart polymers are a fascinating and quickly growing topic with bright future prospects. These materials' present limits will probably be addressed by further study and technological developments, increasing their significance in science, engineering, and healthcare.

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