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A Review on Smart Polymer in Novel Drug Delivery System

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ABSTRACT

Novel drug delivery system utilizing smart polymer to get significant and attracting changes in the targeting of drugs, increasing the bioavailability of drugs, enhancement patient compliance and gene therapy. The scientific community tries to mimic nature in the way that living organisms adopt their behavior as a function of environmental conditions to improve survival. In this sense, smart polymers offer materials that respond to numerous stimuli (temperature, pH, electric and magnetic fields, light intensity, biological molecules, etc.), and scientists must devise the best way to apply them in all research areas. Smart polymers are representing promising means for targeted drug delivery, enhanced drug delivery, gene therapy, actuator stimuli and protein folders. Smart polymers are very promising applicants in drug delivery, tissue engineering, cell culture, gene carriers, textile engineering, oil recovery, radioactive wastage and protein purification. The study is focused on the entire features of smart polymers and their most recent and relevant applications.

Keywords: Smart polymers, Drug delivery, Tissue engineering, Textile engineering, Gene carrier.

INTRODUCTION

Polymers, also known as macromolecules, are complex materials comprising repeating subunits of micro molecules. Derived from the Greek words "poly" (many) and "mere" (unit), polymers have been utilized since ancient times, leveraging their beneficial properties, such as mechanical strength and biocompatibility. The development of synthetic polymers revolutionized medicine, enabling tailored biomaterials for specific needs. Recent advancements in polymer science have unlocked innovative medical applications.

Key benefits of smart polymers include enhanced patient compliance, drug stability, and therapeutic window maintenance, as well as ease of manufacture. Additionally, smart polymers boast biocompatibility, strength, resilience, flexibility, and ease of shaping and colouring. They serve as effective nutrient carriers, can be easily charged and injected in- vitro, and form gels at body temperature.

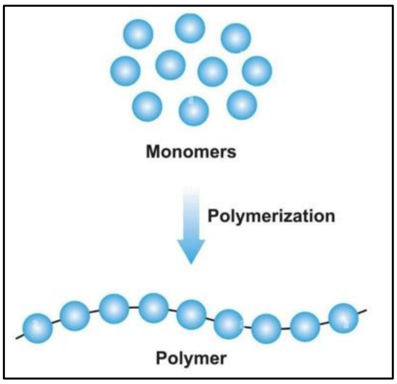

Fig-1 Polymer

Advantages of "smart" polymer

- Smart polymers are ideal because they are non-thrombogenic, biocompatible, robust, flexible, resilient, resistant, and easy to color and mold.
- Greater patient compliance.
- Maintain the consistency of medicine, and keep the dosage within the therapeutic window.
- It's simple to make, employed in a blood-contact application.
- Smart polymers efficiently carry nutrients to cells and produce.
- The main advantages of "smart polymer" based drug delivery systems include decreased dosing, easy handling, and maintenance of desired therapeutic concentration with a single dose.
- Extended-release of the incorporated drug, and lower side effects.

Disadvantages of "Smart" polymer

- They're usually mechanically weak.
- Drugs and cells often hard to load and crosslink in- vitro as a premade matrix,
- They can be difficult to sterilize.

CLASSIFICATION OF SMART POLYMER.

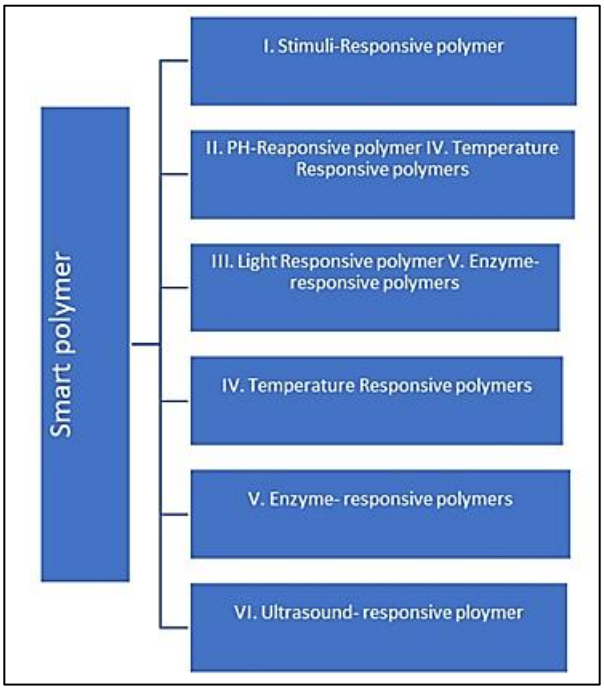

Fig-2 Smart Polymer

Stimuli-responsive polymers

A stimuli- sensitive or smart polymer undergoes an abrupt change in its physical properties in response to a small environmental stimulus. These polymers are also called as intelligent polymers because small changes occurs in response to an external trigger

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until acritical point is reached, and they have the ability to return to There original shape after trigger is removed. The exclusivity of these polymers lies in their non-linear response triggered by a very small stimulus and which produces a noticeable macroscopic alterations in their structure. depicts various stimuli responsible for controlling drug release from smart polymeric drug delivery systems. These transitions are reversible and include changes in physical state, shape and solubility, solvent interactions, hydrophilic and lipophilic balances and conductivity. The driving forces behind these transitions include neutralisation of charged groups by the addition of oppositely charged polymers or by pH shift, and change in the hydrophilic/lipophilic balance or changes in hydrogen bonding due to increase or decrease in temperature. The major benefits of smart polymer-based drug delivery systems Includes reduced dosing frequency, ease of preparation, maintenance of desired therapeutic concentration with single dose, prolonged release of incorporated drug, reduced side effects and improved stability.

e.g. Degradation of the polymeric structure due to irreversible bond breakage in response to an external stimulus.

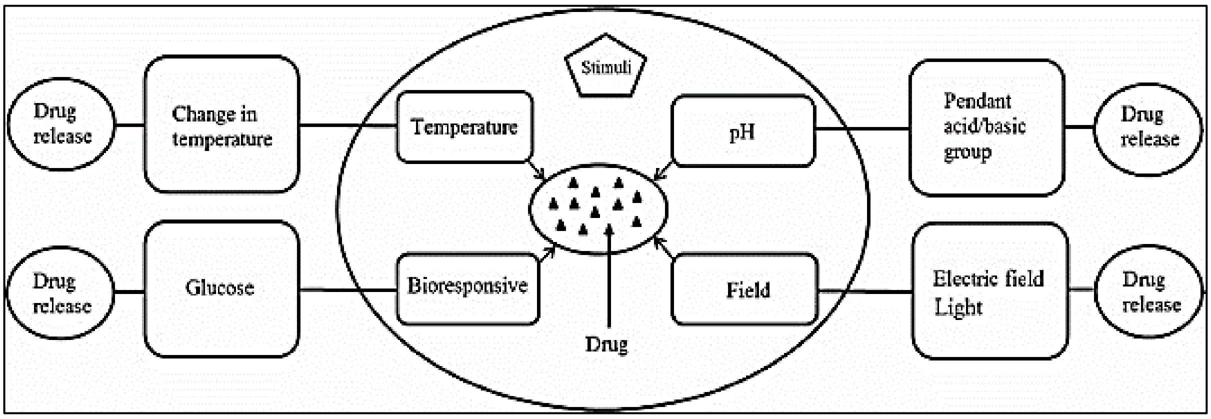

Fig-3 Stimuli Responsive Polymer

PH-RESPONSIVE POLYMER

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. Polymers that exhibit responsiveness to pH variations contain functional groups such as carboxylic acids sulfonic acids 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 constant Polyelectrolytes 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.

Mechanism: These polymers contain ionisable functional groups (e.g., carboxyl or amino groups) that undergo protonation or de protonation depending on the Ph . At lower pH (acidic conditions), the polymers become more hydrophilic, which can lead to swelling and drug release. At higher pH, the polymer becomes more hydrophobic and shrinks, retaining the drug.

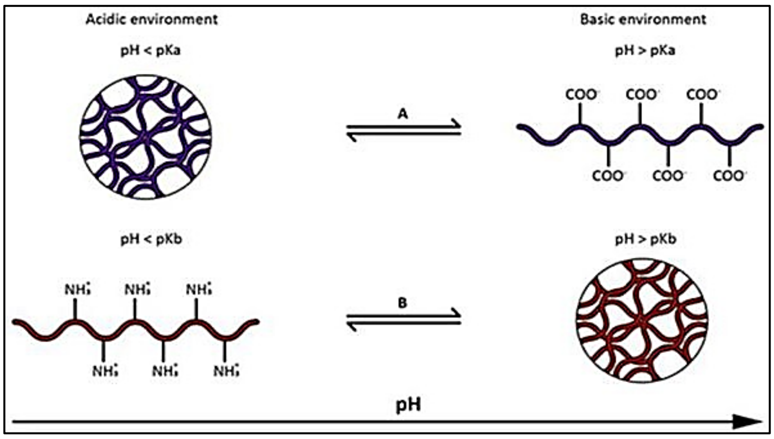

Fig – 4 PH–Responsive Polymer

Applications:

Oral drug delivery (e.g., enteric coatings), drug delivery to tum or sites (where the extracellular pH is lower), and controlled release in the stomach.

Table no 1:

Various applications of pH-responsive polymeric drug delivery system

Drug	**Polymer**	**Application**	**Study outcome**
Paclitaxand dauxorubicin	Poly(ethylene glycol)-block-poly(propylene glycol)- poly(ethylene glycol)	Prolongation of survival time in comparison with single drug therapy	The release rate can be accelerated by decreasing the environmental pH from acidic to alkaline
Fibroblast growth factor	Poly(*n*- isopropylacrylamide- *co*-propylacrylic acid-*co*- butylacrylate)	To improve angiogenesis in infracted myocardium	It provides the advantage of acidic microenvironment of ischaemic myocardium
Ketoprofen	Poly(acrylamide)-*g*- carrageenan and sodium alginate	For colon-targeted delivery	Ketoprofen release was significantly increased when pH of the medium was increased from acidic to alkaline
Dexamethasone	Poly(methoxyl ethylene glycol-caprolactone-*co*- methacrylic acid-*co*-poly(ethylene glycol) methylethylenemeth acrylate)	For oral drug delivery	The hydrogel demonstrated a sharp change at different pH values, with suitability for oral drug delivery
Protein drug	Alginate and chemically modified carboxymethyl chitosan	For oral delivery	Hydrogel protected the drug from the harsh acidity of stomach with potential release in the intestine

LIGHT RESPONSIVE POLYMER

Polymers are designed to change their properties when exposed to specific wavelengths of light (e.g., UV, visible, or near-infrared light). This allows for spatiotemporal control over drug release, making it an excellent strategy for precise delivery to specific sites. Light -responsive polymers are a class of stimuli-responsive polymers that undergo reversible changes in their physical or chemical properties upon exposure to specific wavelengths of light. The ability to control drug release via light offers significant advantages in terms of spatiotemporal control—meaning that drug delivery can be directed both in terms of location and timing. This property makes light-responsive polymers particularly promising in targeted therapy.

Non- invasive drug delivery, and personalised medicine isomerization: Some polymers contain light sensitive groups (like azobenzene, spiropyran, or diarylethene) that undergo reversible isomerization upon exposure to light. This can cause a change in solubility or hydrophilicity of the polymer, leading to drug release.

Examples: Azobenzene-based polymers.

Mechanism: Light induces reversible isomerization or cleavage of specific bonds in the polymer structure, altering its solubility, size, or charge. These changes can result in the polymer's ability to release encapsulated drugs upon light exposure.

TEMPERATURE RESPONSIVE POLYMER

These are the polymers which experience a volume phase transition at a certain temperature and thus a sudden change in solvation state. The unique characteristic of temperature responsive polymer is the critical solution temperature at which the polymer changes phase.

Therefore, it is defined as the temperature at which the polymer undergoes the phase transition according to its composition. If the polymer undergoes a phase transition from a soluble state (monophasic) to an insoluble state (biphasic) above the critical temperature, i.e., with increase of temperature, it is characterized as having a lower critical solution temperature (LCST); if transition of polymer occurs from an insoluble state to a soluble state with increasing temperature, it has an upper critical solution temperature (UCST) as depicted in Temperature is the most widely used stimulus in the synthetic and the bio-inspired stimulus-responsive system.

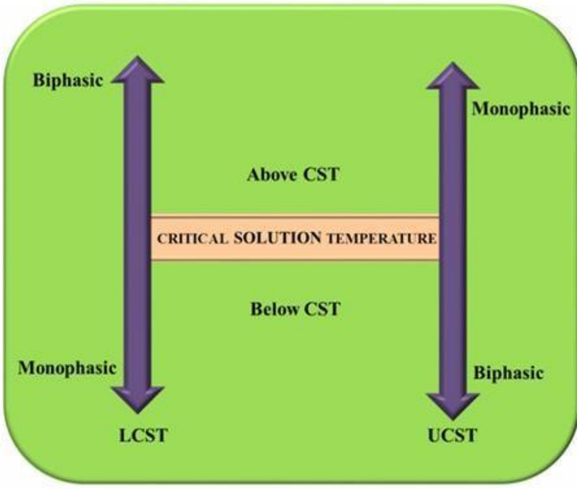

Fig – 5 Temperature Responsive Polymer

Enzyme-responsive polymers

Are designed to degrade or undergo conformational changes in the presence of specific enzymes. These polymers can be used for drug release in environments with high enzymatic activity, such as within the gastrointestinal tract or intracellular spaces. These polymers can be designed to degrade or undergo conformational changes upon exposure to particular enzymes, which are abundant in various physiological environments such as the gastrointestinal tract, tumour sites, or intracellular compartments. The specificity of the enzymatic response allows for controlled and localised drug release at disease sites, providing precision medicine while minimising side effects.

Mechanism: Enzyme-responsive polymers are engineered to contain specific enzyme- cleavable linkers or functional groups within their structures. When exposed to target enzymes, these polymers undergo biodegradation or structural transformation, releasing the encapsulated drug in a controlled manner.

Applications: Controlled drug release for cancer therapy (targeting enzymes over expressed in tumours), oral drug delivery (targeting enzymes in the stomach and intestines), and personalised medicine.

Table no 2:

Various applications of temperature-responsive polymeric drug delivery systems.

Drug	Polymer	Application	Study goal/outcome
Docetaxel	Conjugated linoleic acid coupled with pluronic F-127	Peritoneal dissemination of gastric cancer	Hydrogel produced controlled release and excellent antitumour activity
Exenatide	PLGA–PEG–PLGA	Treatment of type II diabetes	To produce a long- acting injectable formulation
Ethosuximide	Chitosan with glycerophosphate disodium salt and glycerol	Injectable gels for depot therapy	To produce a sustained-release injectable formulation
Human mesenchymal stem cells and desferroxamine	Chitosan-beta glycerophosphate	For the treatment of critical limbic ischaemia	To provide an *in situ* depot for the sustained release of drugs and provide protection and cohesion of stem cells
Leuprolide	Polybenzofulvene	For treatment of tumours	To protect the oligopeptide drug and regulate the release rate by external temperature

Ultrasound-responsive polymers

Considerable research has been done to exploit the use of ultrasound waves for controlled delivery of proteins using both bio-erodible and non-erodible polymer depots .Lavon and Kost have investigated a non-erodible ethylenevinylacetate (EVAc) copolymer matrix to regulate the protein release in response to ultrasound radiation .The mechanism of enhanced protein release includes convection generated by cavitation without alteration in the polymer structure and morphology, and is a useful stimulus for enhancing the drug delivery from diffusion-dependent non-bioerodable systems. The precise physical characteristics of polymers that respond to ultra sound is difficult to determine, but the factors that influence the drug release involve ultrasound frequency, structure and size of pores of polymer matrix, polymer degradation rate and the properties of drug incorporated. While these systems have potential of offering highly tuneable protein release, the lack of biocompatible and biodegradable ultrasound sensitive polymers can potentially hamper their widespread applications.

Why does polymer act as a drug carrier

Polymers are frequently used as drug carriers in pharmaceutical formulations to rally the delivery of drugs, enhance their bioavailability, and provide controlled release. Various types of polymer-based drug carriers are employed for different applications. Here are some common polymer drug carriers and their uses: Nanoparticles Polymer nanoparticles are used to encapsulate drugs, protecting them from degradation, improving solubility, and allowing for controlled release. They are suitable for oral, intravenous, and topical drug delivery. Poly (lactic-co- glycolic acid) (PLGA) nanoparticles, chitosan nanoparticles, and albumin nanoparticles.48 Liposomes Liposomes are lipid bilayer structures that can encapsulate both hydrophobic and hydrophilic drugs. They are used for drug delivery, particularly in cancer therapy, as well as for cosmetic and dermatological applications. Doxil (liposomal doxorubicin) for cancer treatment and various liposomal cosmetic products.49 Micelles Micelles, formed by self- assembling amphiphilic polymers, can solubilize hydrophobic drugs and enhance their delivery. They are used in cancer therapy and targeted drug delivery. Pluronics (poloxamers) and polymeric micelles are notable examples used for drug delivery.50 Hydrogels Hydrogels are three-dimensional networks of polymers that can absorb and retain a large amount of water. They are used for the controlled release of drugs, particularly in topical applications, wound care, and tissue engineering. PEG-based hydrogels, alginate hydrogels, and chitosan hydrogels.51 Polymeric microspheres Polymeric microspheres are often used for controlled drug release. They can be injected locally to release drugs over an extended period. They are commonly used in conditions like osteoarthritis and cancer. Injectable microspheres for long acting drug delivery.52 Dendrimers Dendrimers are highly branched polymers that improve their solubility, and provide controlled release. They are used in drug delivery, imaging, and diagnostics. Polyamidoamine (PAMAM) dendrimers for drug delivery and imaging.53 Polymeric prodrugs Polymeric prodrugs involve the covalent attachment of drug molecules to a polymer carrier. This strategy can enhance drug solubility, stability, and release. PEGylated prodrugs for improved.

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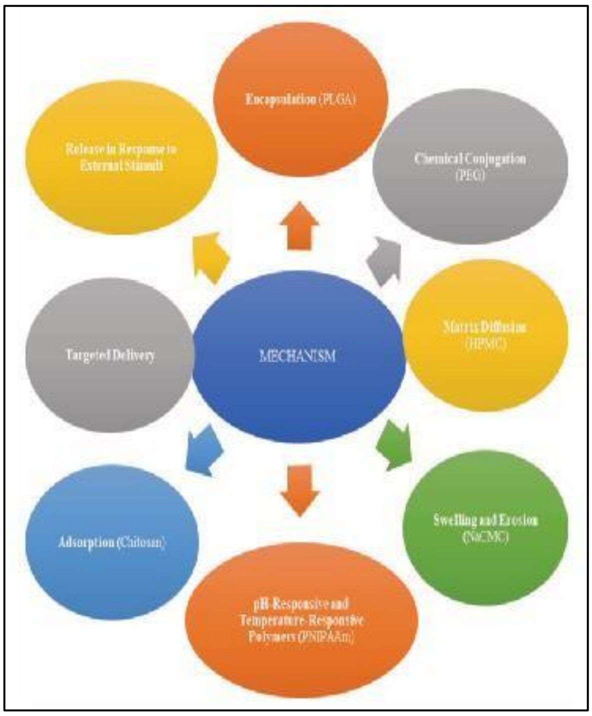

pharmacokinetics.54 Nanogels Nanogels are nanoscale hydrogels that can encapsulate drugs and bioactive compounds for drug delivery, particularly in cancer therapy and targeted delivery. Chitosan nanogels and PEG-based nanogels.55 Mucoadhesive polymers Mucoadhesive polymers can adhere to mucous membranes, prolonging drug contact and enhancing absorption. They are used in oral, nasal, and ocular drug delivery: carbopol-based formulations and chitosan-based mucoadhesive drug delivery systems.56 The choice of polymer- drug carrier depends on the specific drug, route of administration, and desired drug release profile. These polymer-based drug carriers have revolutionized drug delivery, offering improved therapeutic outcomes, reduced side effects, and better patient compliance in many medical treatments.

APPLICATION

There is various applications of smart polymer in various fields i.e.

1. Tissue engineering
2. Gene delivery
3. Micelles
4. Cross linked micelles
5. Films
6. Biosensing
7. Drug delivery

1] TISSUE ENGINEERING –

Tissue engineering is a part of science that works to make or repair human tissues and organs. It combines biology, engineering, and materials to create new tissues that can replace damaged ones. The process mainly uses three things — **cells**, **scaffolds**, and **growth factors**.

Cells are like building blocks of the body, scaffolds give them support to grow, and growth factors help them develop properly. Scientists can use a person's own cells or stem cells, which can turn into different types of tissues such as skin, bone, or muscle. The cells are placed on a scaffold and grown in a lab until they form a new tissue, which can then be put into the body to repair damage.

Tissue engineering has many uses, such as healing burns, repairing bones and cartilage, and replacing damaged organs. It also helps in testing new drugs safely without harming people. This field is a key part of **regenerative medicine**, which helps the body heal itself. With the help of new technologies like **3D bioprinting** and **biomaterials**, scientists are getting closer to growing complete organs for transplant in the future. Tissue engineering gives new hope for treating diseases and injuries that were once impossible to cure.

2] GENE DELIVERY –

Gene delivery is the process of introducing genetic material, such as DNA or RNA, into cells to treat diseases or improve cell functions. It is an important part of **gene therapy**, which aims to correct defective genes or provide new genes to help the body fight illnesses. The main goal of gene delivery is to make sure the desired gene safely reaches the target cells and works properly inside them. There are two main types of gene delivery methods — **viral** and **non-viral**.

In **viral gene delivery**, viruses are modified so they cannot cause disease but can carry the desired gene into the cells. These viruses act like natural carriers and are very efficient at delivering genes. Examples include adenoviruses, retroviruses, and lentiviruses. In **non-viral methods**, physical or chemical techniques are used instead, such as **liposomes** (fat-based carriers), **nanoparticles**, **electroporation** (using electric pulses), or **gene guns**. These methods are safer but sometimes less efficient.

Gene delivery can be used to treat many genetic disorders, cancers, and viral infections. It also helps in vaccine development and regenerative medicine. However, challenges remain, such as avoiding immune reactions and ensuring the gene reaches only the desired cells. With ongoing research, gene delivery continues to improve, offering great promise for the future of personalized and effective medical treatments.

3] MICELLES –

Micelles are tiny spherical structures formed when special molecules called **surfactants** are mixed with water. Surfactants have two parts — one part that likes water (**hydrophilic head**) and another part that dislikes water (**hydrophobic tail**). When these molecules are added to water, the hydrophobic tails come together in the center to avoid water, while the hydrophilic heads face outward toward the water. This arrangement creates a round shape called a **micelle**.

Micelles are very important in chemistry, biology, and medicine. In everyday life, they help in cleaning — for example, in soaps and detergents, micelles trap dirt and oil inside their center, allowing them to be washed away with water. In medicine, micelles are used as **drug delivery systems**, where they carry drugs that do not dissolve easily in water. The micelle protects the drug and releases it slowly at the target site, improving its effectiveness and reducing side effects.

Overall, micelles are simple but powerful structures that play a big role in many scientific and practical applications, from cleaning to advanced drug delivery and biotechnology.

4] CROSS LINKED MICELLES –

Cross-linked micelles are special types of micelles that have stronger and more stable structures due to the formation of **chemical bonds (cross-links)** between their molecules. Normally, regular micelles are formed by surfactant molecules that come together in water, but they can easily break apart if the conditions change (like pH, temperature, or dilution). To make them more stable, scientists use cross-linking — a process that connects the molecules in the micelle with strong chemical bonds, either in the **core**, the **shell**, or both.

Cross-linked micelles are especially useful in **drug delivery systems** because they can hold and protect drugs more effectively and release them in a controlled way at the target site. They are also less likely to fall apart in the bloodstream, which helps the medicine stay active for a longer time. In addition, these micelles can be designed to respond to specific conditions like changes in pH or temperature, allowing the drug to be released only where it is needed, such as in cancerous tissues.

In summary, **cross-linked micelles** are advanced, stable versions of normal micelles that are widely used in **nanomedicine**, **drug delivery**, and **biotechnology**, offering better control, safety, and efficiency in therapeutic applications.

5] FILMS –

Films are thin layers or sheets of materials that can be made from natural or synthetic substances. They are usually flexible and can vary in thickness, depending on their use. Films are widely used in many fields, including packaging, medicine, electronics, and biotechnology. In **pharmaceutical and biomedical applications**, films are often used as **drug delivery systems**, where a drug is incorporated into a thin layer that can release the medicine slowly and in a controlled manner. These are called **drug-loaded films** or **polymer films**.

Films can be made from different **polymers** such as cellulose, chitosan, gelatin, or synthetic materials like polyethylene and polyvinyl alcohol. In **medical use**, films are applied to wounds or skin to protect the area, deliver drugs, or help in healing. For example, **wound-healing films** keep the injury moist and allow the drug to reach the affected area. In **oral drug delivery**, thin films that dissolve in the mouth are used for faster absorption of medicines.

In general, films are simple but very useful materials because they are **easy to apply, lightweight, and can control how a drug is released**. Their flexibility and biocompatibility make them an important part of modern medicine, packaging, and industrial applications.

6] BIOSENSING –

Biosensing is a technique used to detect and measure biological substances such as glucose, proteins, toxins, or bacteria by converting a biological response into an electrical or optical signal. The main tool used for this purpose is called a **biosensor**. A biosensor has two main parts — a **bioreceptor** and a **transducer**. The **bioreceptor** (like enzymes, antibodies, DNA, or microorganisms) specifically recognizes the target substance, while the **transducer** converts this biological interaction into a measurable signal that can be read by a device.

Biosensing plays an important role in many fields. In **medicine**, it is used for monitoring blood glucose levels in diabetic patients, detecting infections, and diagnosing diseases quickly. In **environmental science**, biosensors help detect pollutants, toxins, and harmful microorganisms in water or air. In **food industries**, they are used to check freshness and detect contamination. Biosensors are popular because they provide **fast, accurate, and sensitive** results, often using very small samples.

7] DRUG DELIVERY –

Drug delivery is the process of transporting a medicine to a specific part of the body so it can work effectively. The main goal of drug delivery is to make sure that the right amount of drug reaches the right place at the right time. Traditional drug delivery methods, like tablets or injections, release the medicine throughout the whole body, which can sometimes cause side effects or reduce effectiveness. Modern drug delivery systems are designed to control how, when, and where the drug is released, improving treatment and reducing unwanted effects.

There are many types of **drug delivery systems**, such as **nanoparticles**, **micelles**, **liposomes**, **hydrogels**, **films**, and **implants**. These systems can protect the drug from being destroyed inside the body and help it reach the target site more safely. For example, in **targeted drug delivery**, the medicine is directed only to diseased cells, like cancer cells, without harming healthy ones. Some systems are also designed to respond to specific conditions like temperature, pH, or enzymes, releasing the drug only when needed.

Overall, **drug delivery** is an important part of modern medicine because it improves the effectiveness of treatments, reduces side effects, and enhances patient comfort and compliance.

With the help of **biotechnology and nanotechnology**, drug delivery continues to advance, offering smarter and more precise ways to treat diseases.

With the help of **nanotechnology** and **microelectronics**, modern biosensors are becoming smaller, more efficient, and portable. For example, wearable biosensors can continuously monitor health conditions in real time. Overall, **biosensing** is a powerful and growing technology that connects biology and engineering to improve healthcare, safety, and environmental protection.

FUTURE PERSPECTIVAS

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

Integration with Biosensors and Wearables

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

Smart Polymer–Drug Conjugates

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

Personalized Nanomedicine Platforms

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

Clinical Translation and Regulatory Advances

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

CONCLUSION

the advancement of novel drug delivery systems, smart polymeric drug delivery systems provide a link between therapeutic need and drug delivery. This review highlights the current literature and describes the principles and mechanisms of smart materials. Various stimuli are utilized to attain the controlled and site-specific delivery of drug. Inherent limitations of this drug delivery system are slow response times. While there are many exciting challenges facing this field, there are a number of opportunities for the development of smart polymeric drug delivery systems. Smart polymeric drug delivery systems have a very wide range of applications and are likely to have an exciting future.

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