

# HYDROGELS: A KEY PLAYER IN THE DEVELOPMENT OF ADVANCED THERAPIES AND DIAGNOSTICS

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**ABSTRACT:** - Hydrogels are versatile, three-dimensional networks of hydrophilic polymers that have garnered significant attention in recent years due to their unique properties and wide range of applications. This review article provides a comprehensive overview of the current state of hydrogel research, focusing on their synthesis, characterization, and applications in biomedical and pharmaceutical fields. We discuss the various types of hydrogels, including natural, synthetic, and hybrid systems, and highlight their advantages and limitations. The article also explores the latest advances in hydrogel technology, including stimuli-responsive, injectable, and wearable hydrogels. Furthermore, we examine the potential applications of hydrogels in drug delivery, tissue engineering, wound healing, and biosensing. With their enormous amenability to modification, hydrogels serve as promising delivery vehicles of therapeutic molecules in several disease conditions, including cancer and diabetes. This article presents an overview to the advances in hydrogel-based drug delivery that have become the interest of most researchers.

**KEYWORDS:** - hydrogels, biomedical applications, pharmaceutical applications, stimuli-responsive, drug delivery.

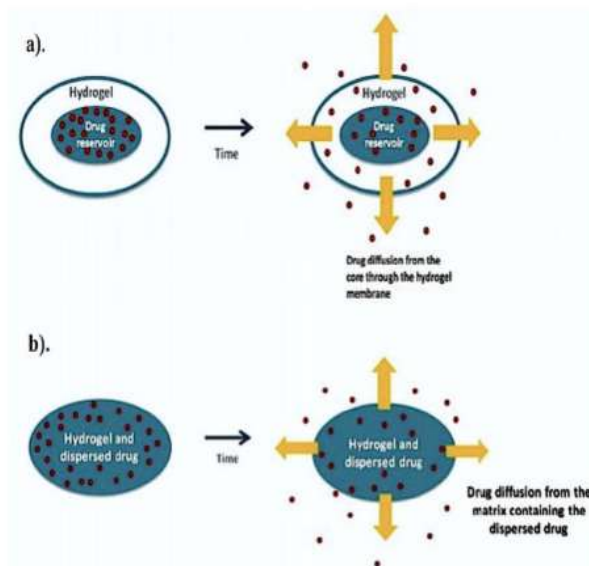
**INTRODUCTION:** - Wichterle and Lim first used the term "hydrogels" in the 1960s, and they proposed a biological use for it.[1] Since the beginning of earthly life. The extracellular matrix's constituents, the structure of plants, the biofilms of microorganisms found everywhere, and all of nature's swelling moist environments serve as evidence.[2] The first document noticed was written in 1936 for medicinal applications by a scientist named DuPont. This served as the impetus for research on poly (2-hydroxyethylmethacrylate) poly (HEMA) by Wichterle and Lim in 1960.[3] The polymeric chains' cross-linking results in the creation of a three-dimensional network. Physical interactions, covalent bonds, hydrogen bonds, and van der Waals interactions can all result in this cross linking.[4] The chemistry behind the interpenetrating hydrogel The presence of certain functional groups, such as -OH, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -CONH, and -COOR, which have a tendency to be hydrophilic and hence absorb water and biological fluids, is the best way to understand networks (IPN) Lately, biopolymers have become a wise choice for hydrogel production in drug delivery.[5]

In this brief review, the materials of interest are mostly hydrogels, which are networks of polymers that have been heavily inflated with water. Networks of polymer chains known as hydrophilic gels, or hydrogels for short, are occasionally discovered as colloidal gels with water acting as the dispersion medium.[6] Hydrophilic functional groups connected to the polymeric backbone provide hydrogels their capacity to absorb water, while cross-links between network chains give them resistance to disintegration. Numerous substances, both man-made and natural, meet the criteria for hydrogels.[7] Over the past 20 years, synthetic hydrogels with long service lives, high water absorption capacities, and high gel strengths have gradually supplanted natural hydrogels. Thankfully, synthetic polymers typically include distinct structures that can be altered to produce customized functionality and degradability. It is possible to create hydrogels using only synthetic ingredients. Additionally, it remains stable when temperatures fluctuate sharply and strongly.[8]

Since the early 1960s, hydrogels—a novel drug delivery method—have been investigated. First, Wichterle and Lim described a type of hydrophobic gel that was created for biological applications: cross-linked hydroxyethyl methacrylate (HEMA) hydrogels There are two types of hydrogels: physically cross-linked or reversible hydrogels, which dissolve and break down during water absorption, and chemically cross-linked or permanent hydrogels, which are stable to degradation during swelling.[9, 10] The polymers used to make hydrogels can come from synthetic or natural sources. Each type of polymer has advantages and disadvantages, so it's important to choose the right one based on the intended usage of the hydrogel and the drug delivery site.[11] According to Gibas and Janik [12], the swelling of hydrogels is a multi-step, intricate process. Water, in the form of primary bound water, hydrates the hydrogel matrix's polar hydrophilic groups in the first stage. The water interacts with the exposed hydrophobic groups in the second step as well, where they manifest as secondary bound water. Towards infinite dilution is resisted by the physical or chemical crosslinks, so additional water is absorbed. The water absorbed into the equilibrium swelling is called the bulk water or the free water, which fills the spaces between the network or chains and the center of the larger pores. The total bound water is made up of both the primary and secondary bound waters. In the third step, more water is absorbed as a result of the physical or chemical crosslinks resisting the network's osmotic pushing force toward infinite dilution. The water that fills the gaps between the network of chains and the center of the bigger pores is referred to as the bulk water or free water, and it is absorbed into the equilibrium swelling. The Flory–Huggins theory explains how temperature and the unique interaction between the water molecules and the

polymer chains affect how much water a hydrogel absorbs.[13] The hydrogels reported in this review are processed in various ways. The most common method is the one-step direct polymerization of the multifunctional monomer by crosslinking; alternatively, multistep procedures are used, wherein, as reported by Ahmed, the first polymer is synthesized with specific functional groups and then reacts with a crosslinking agent. When creating and processing a hydrogel specifically for a given purpose, different scientific methods must be used to demonstrate the hydrogel's maximum mechanical strength, chemical characteristics, responsiveness to stimuli, density, biodegradation, and biological and environmental response.[14] Super porous hydrogels (SPHs), a distinct class of water-absorbing polymer system, were identified in 1998 as having superior elastic qualities, mechanical strength, and water-holding capacity.[15] The literature for SAP and SPH evolution and differentiation is well reviewed in this review, providing material engineers with a useful path to process a hydrogel of their own choosing.[16]

Since many of the medications now utilized and effective in disease therapy are hydrophobic, it is challenging to keep incompatible hydrophobic pharmaceuticals in the water-loving polymeric core. These hydrogels have a low tensile strength, which can lead to the drug sometimes being released earlier than it reaches the intended location. [ (P.Torchilin, 2018 -19)] Reservoir or matrix devices that enable diffusion-based drug release through a hydrogel mesh or pores filled with water are used in diffusion-controlled drug delivery with hydrogels. To provide a consistent medication release rate, the hydrogel membrane in the reservoir delivery system is coated on a drug-containing core that creates capsules, spheres, or slabs with a high drug concentration at the system's center. Whereas the matrix system functions through the macromolecular pores or mesh, the reservoir delivery system generates a continuous and time-independent drug release. This kind of release is known as time-dependent drug release, in which the initial rate of release is not constant but rather relates to the square root of time.



**Figure 1:** - a) Drug containing core is coated with hydrogels membrane and the drug concentration is higher in the centre of the system to allow constant release rate of the same in Reservoir delivery system.

b) Uniform dissolution or dispersion of the drug throughout the 3d structure of hydrogels is achieved using matrix delivery.[18].

The method of controlling drug release from hydrogels through swelling involves the dispersion of pharmaceuticals within a glassy polymer, which initiates swelling upon contact with a bio-fluid. Beyond its limit, the expansion that happens during swelling facilitates both drug transport and polymer chain relaxation. Time-independent, continuous drug release kinetics are supported by the mechanism, also known as Case II transport. The process, which combines the processes of swelling and diffusion to enable drug release, is also known as anomalous transport because it permits the active ingredient to diffuse from a region of higher concentration within the hydrogel to a lower one due to the gradient between the dispersed drug and its surrounding environment.[19]

**CLASSIFICATION:** - Hydrogel are classified based on various factors like biodegradability type of cross-linking source, ionic charge and preparation method physical properties and the response nature of the hydrogel to external stimuli.[20] The complete classification of hydrogel.

**Cross linking hydrogel:** - Crosslinking of hydrogels refers to the process of creating chemical or physical links between polymer chains to form a network structure.

**a) Physical cross linking:** - Physical cross linking: -Polyethylene glycol forms compounds with polyacrylic and polymethacrylic acids. The carboxylic group of polyacrylic acid/polymethacrylic acid and the oxygen of the polyethylene glycol form hydrogen bonds in these complexes.[21]

Not only is there hydrogen bonding between polymethacrylic acid and polyethylene glycol, but poly (methacrylic acid-g-ethylene glycol) also contains hydrogen bonds.[22]

The formation of hydrogen bonds is contingent upon the protonation of carboxylic acid groups, resulting in pH-dependent gel expansion.

**b) Chemical cross linking:** -Using glutaraldehyde, hydrophilic polymers with -OH groups, such as polyvinyl alcohol, can be cross-linked. Tight circumstances (high temperature, quencher of methanol added, low pH) are used to create cross-linking. Alternately, under moderate circumstances where Schiff bases develop, polymers with amine groups can be crosslinked using the same cross-linker. It was created specifically for the manufacture of cross-linked proteins, such gelatin.[23] Hydrophilic polymers' functional groups can be reacted with by addition reactions using bis or higher functional cross-linkers. One method of cross-linking polysaccharides is using 1,6-hexamethylenediisocyanate.[24]. Condensation reactions between -NH<sub>2</sub> or -OH groups and -COOH or derivatives can be used to create polyesters and polyamides, respectively. The ionic charge of a hydrogel depends on the type of hydrogel and its composition. Hydrogels can be classified into three main categories based on their ionic charge:

**Ionic charge:** - The ionic charge of a hydrogel depends on the type of hydrogel and its composition. Hydrogels can be classified into three main categories based on their ionic charge

**1. Neutral hydrogels:** - These hydrogels have no net ionic charge, as they are composed of non-ionic polymers such as polyethylene oxide (PEO) or polyvinyl alcohol (PVA).

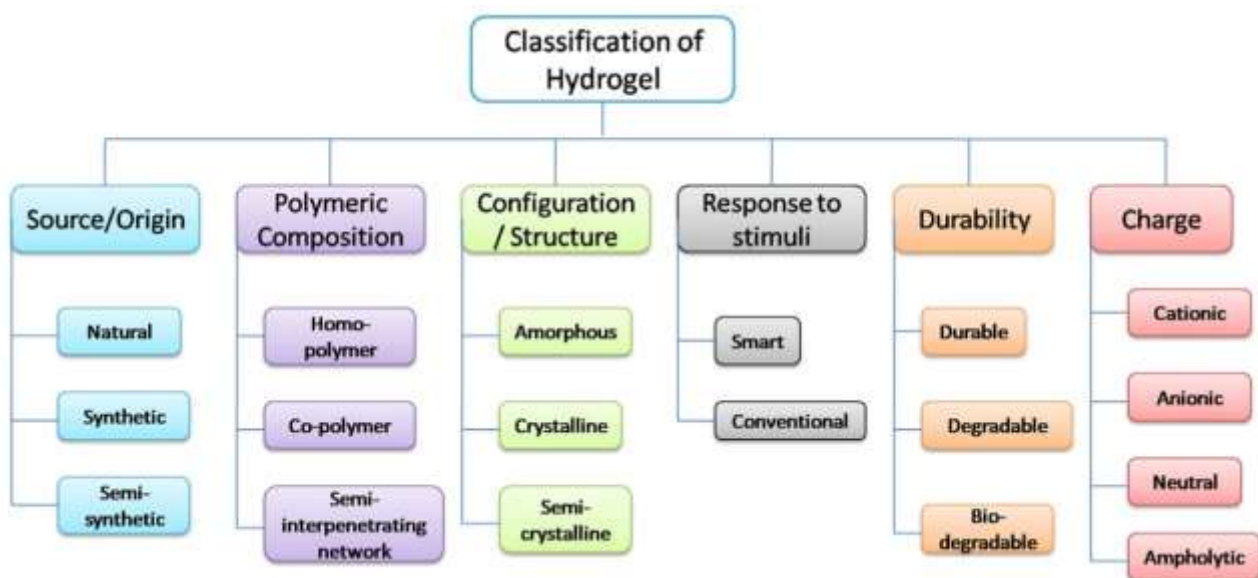
**2. Anionic hydrogels:** - These hydrogels have a negative ionic charge, as they are composed of anionic polymers such as polyacrylic acid (PAA) or polyvinyl sulfate (PVS).

**3. Cationic hydrogels:** - These hydrogels have a positive ionic charge, as they are composed of cationic polymers such as polyvinylamine (PVAm) or polyethyleneimine (PEI).

**Source:** - Natural hydrogels are three-dimensional polymeric networks derived from naturally occurring biomaterials. These materials can absorb and retain significant amounts of water or biological fluids, often exhibiting properties similar to natural tissues.

**1)Synthetic hydrogels:** - Synthetic hydrogels are three-dimensional, hydrophilic polymeric networks that are created artificially. These materials are designed to absorb and retain large amounts of water, often swelling significantly in aqueous environments. They are composed of synthetic polymers, which provides a level of control and customization that is often not possible with natural hydrogels.

**2)Hybrid hydrogels:** - Hybrid hydrogels are a class of materials composed of diverse building blocks, including biologically active proteins, peptides, or nano/microstructures. These components possess distinct chemical, functional, and morphological characteristics and are interconnected through physical or chemical methods.



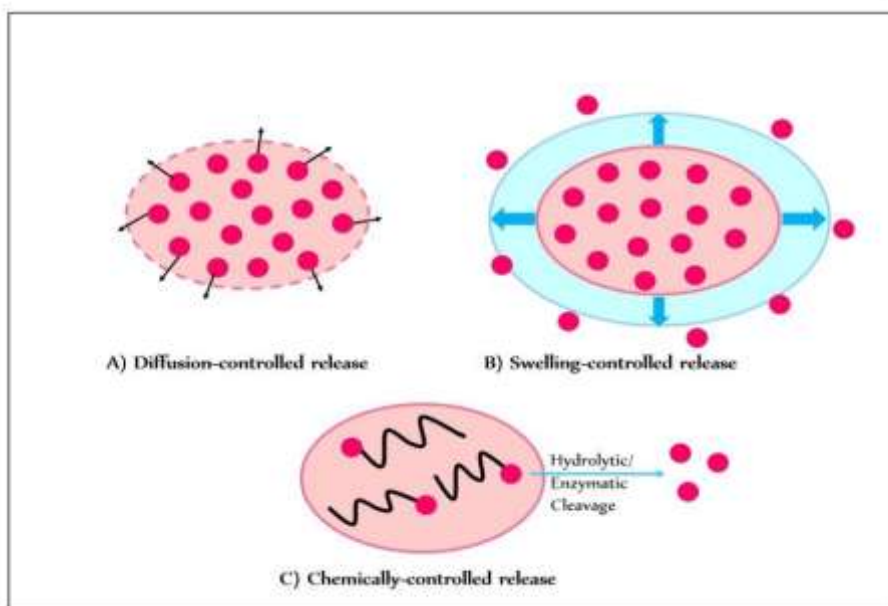
**RELEASE MECHANISM:** -

There are different release mechanisms of entrapped/encapsulated drug in hydrogels such as diffusion controlled, swelling controlled, and chemically controlled mechanisms. The diffusion-controlled mechanism is the most acceptable one and its drug release model follows Fick's law of diffusion. Porosity of the hydrogels is related to the diffusion coefficient of the hydrogels if the molecular dimensions of the drug molecules are much smaller than the pore size of the porous hydrogels. When the pore size in the hydrogels and the size of the drug molecules is comparable, the release of the drug molecules is hindered by the cross-linked polymer chains. As a result, the diffusion coefficient is decreased. If the rate of drug release exceeds the rate of swelling, then drug release follows a swelling controlled mechanism.[25] The solvent moving in develops a stress responsible for the increase in distance between the polymer chains (polymer chain relaxation) leading to swelling. This swelling process is accompanied by desorption of the drug and its controlled release. [26, 27]. If the entrapped molecules in the hydrogels network are smaller such as peptides/proteins, their diffusion is easy and their release takes place by a diffusion controlled mechanism whereas for larger entrapped molecules like plasmid DNA, diffusion is not easy and their release from the matrix follows a chemically controlled mechanism.[28] .It is further categorized as (i) a kinetically controlled release mechanism, and (ii) a reaction diffusion controlled mechanism. In the former case, there is negligible diffusion and the bond cleavage in the polymer chains (polymer degradation) dominates which is the rate determining step, whereas for the latter case diffusion as well as polymer reactions (polymer degradation) collectively explain the drug release.

**Diffusion control:** - Diffusion-controlled release is the most common mechanism of drug release from hydro-gels. In this type of drug release, Fick's diffusion theory is used for kinetic modelling. For porous hydrogels with pore sizes of larger than drug molecule dimensions, drug diffusion from hydrogels could be related to the porosity and also the tortuosity of hydrogels. Diffusion-controlled release hydrogels might be act as reservoir or matrix. In reservoir drug delivery systems, drug molecules are encapsulated and surrounded by polymeric hydrogels and so drug release mostly obeys the first law of Fickian diffusion. In matrix drug delivery systems, drug molecules are homogenously dispersed in polymeric hydrogels and drug release mostly follows the second law of Fickian Diffusion. Diffusion control of hydrogel refers to the ability of hydrogels to regulate the diffusion of molecules, such as drugs, nutrients, or waste products, through their network. This is achieved through various mechanisms, including:

**Swelling-controlled:** - Swelling-controlled drug release could occur when the rate of drug diffusion is faster than the rate of hydrogel swelling. For purely swelling controlled drug release, the kinetic model of release could be mostly fit to zero-order model. [29,30] Hydrogels may have swelling-induced transition phase (at glass transition temperature or T<sub>g</sub>) from glassy to rubbery state which causes faster drug diffusion and release from polymeric chains. In swelling-controlled delivery systems, the higher the rate of hydrogel swelling, the higher the rate of drug release, so the rate and ability of hydrogels' water absorption and the thickness of polymeric gels are important factors in swelling-controlled delivery systems. [31,32]

**Chemically-controlled:** - Chemically-controlled drug release mechanism explains the mechanism in which a reaction occurs within the hydrogel matrix. In these reactions enzymatic or hydrolytic cleavage of polymeric network is responsible for drug release. Drug release in chemically-controlled delivery systems could be occurred by cleavage of polymeric chains through bulk or surface erosion and following these mechanisms, the entrapped drug or tethered drug would be released from hydrogels. The polymer chain cleavage is the rate-limiting step of chemically-controlled.



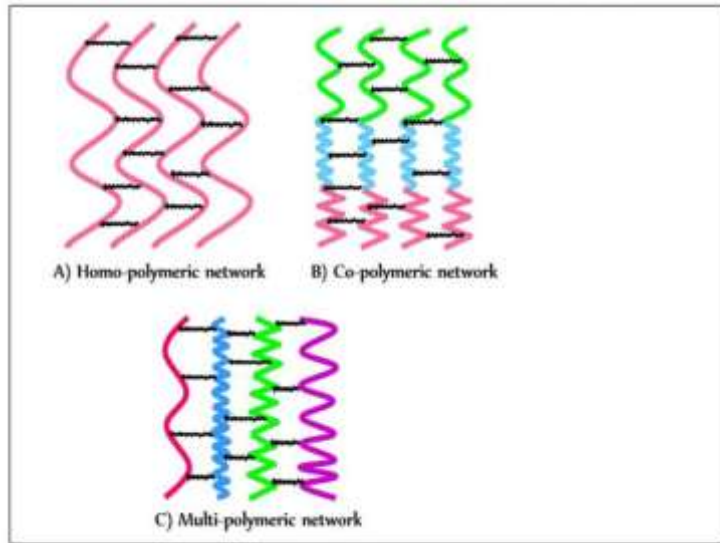
**Figure 2:** -Schematic view of drug release mechanism of hydrogels.

**STRUCTURE OF HYDROGELS: -**

Hydrogels could be prepared from natural or synthetic polymers.

**Homo-polymeric network:** - Homo-polymeric networks are formed from a single type of monomers. According to the nature of monomers and the polymerization technique, it would be possible for homo-polymers to have cross-linked structures.

**Co-polymeric network:** - Co-polymeric hydrogels are formed from two or more than two types of monomers. In these hydrogels, the presence of one or more hydrophilic component is necessary. **Multi-polymeric network:** - multi-polymeric hydrogels are formed from two independent cross-linked polymers.[33]



**Figure 3:** -Schematic view of hydrogels categories according to method of preparation

**POLYMERS USED IN HYDROGELS PREPARATION: -**

**Alginate:** - It's a natural polysaccharide. It is extracted from brown algae. It is mostly used in hydrogel preparation. Because, of its biocompatibility, biodegradability and its ability to form hydrogels with various properties.

**Methods of preparation: -**

**Alginate Solution Preparation:** - Alginate powder is dissolved into the solvent with which it is compatible such as water or a buffer solution. The properties of hydrogel based on the concentration of alginate. Higher the concentration stronger the hydrogel and less porous.

**b. Cross linking: -**

**Ionic cross linking:** - divalent cation is used (calcium chloride and calcium sulphate) in alginate solution. The alginate chain interacts with calcium ion and forms crosslinked network. **Chemical crosslinking:** - in these other crosslinking agents are used. Glutaraldehyde / genipin. It can also be used to create alginate hydrogels. These agents form covalent bonds between alginate chains.

**c. Gelation:** - After crosslinking alginate solution becomes gel or solidify into a hydrogel. The gelation time depends on the concentration of alginate and crosslinking agents.

**Applications of Alginate Hydrogels:**

**Drug Delivery:** - Alginate hydrogels can be used to encapsulate and release drugs in a controlled manner.

**Tissue Engineering:** - Alginate hydrogels are used as scaffolds for tissue regeneration.

**Wound Dressing:** - Alginate hydrogels are used as wound dressings due to their absorbent properties and ability to promote healing.

**Food Industry:** - Alginate hydrogels are used as thickeners, gelling agents, and encapsulants.[34]

**Gelatine:** - It is Protein derived from collagen which is major component of connective tissue. Widely use in hydrogel preparation because biocompatibility, biodegradability ability to form hydrogel with various properties

**Method of Preparation:** -

**1. Gelatin solution preparation:** -

**Methods of preparation:** -

**a) Gelatine Solution Preparation:** - Gelatine powder is dissolved into the solvent with which it is compatible such as water or buffer solution. The properties of hydrogel based on the concentration of gelatine. Higher the concentration stronger the hydrogel and less porous.

**2. Cross-linking:** -

**Chemical cross-linking:** - Gelatin hydrogels cross-linked using chemical agents glutaraldehyde/genipin form covalent bond between chain and strengthening hydrogel structure

**3. Gelation:** - After cross linking alginate solution become gel or solidify into a hydrogel. The gelation time depend on the concentration of alginate and cross-linking agent

**Applications of Gelatin Hydrogels:** -

**Drug Delivery:** - Gelatin hydrogels can be used to encapsulate and release drugs in a controlled manner.

**Tissue Engineering:** - Gelatin hydrogels are used as scaffolds for tissue regeneration.

**Wound Dressing:** - Gelatin hydrogels are used as wound dressings due to their absorbent properties and ability to promote healing.

**Food Industry:** - Gelatin hydrogels are used as thickeners, gelling agents, and encapsulants.[35]

**Fibrin:** - It is a protein that forms during blood clotting from fibrinogen it is widely used in hydrogel preparation due to its ability to promote cell adhesion and migration and biocompatibility and biodegradation

**Method of preparation:** -

**1. Fibrinogen Isolation:** - It can be obtained commercial or from blood plasma

**2. Clot formation:** -

Fibrinogen mixed with thrombin. Thrombin is enzyme that converts Fibrinogen into fibrin process is known as clot formation.

**Applications of fibrin hydrogel:** -

**Drug Delivery:** - Fibrin hydrogels can be used to encapsulate and release drugs in a controlled manner.

**Wound Healing:** - Fibrin hydrogels are used as wound dressings due to their ability to promote cell migration and tissue repair.

**Biomaterials:** - Fibrin hydrogels are used in various biomaterials applications, such as cell culture and biosensors.

**Tissue Engineering:** - Fibrin hydrogels are used as scaffolds for tissue regeneration, particularly in cardiovascular and neural.[36]

**Chitosan:** - It is derived from chitin the main component of crustacean shells. It is positively charged polymer it can form hydrogel from various method. It is Natural Polysaccharides. Hydrogels are known for their antimicrobial properties

**Methods of preparation:** -

**A) Ionic Cross Linking:** -

**Tripolophosphate (TPP):** - Interaction of TPP and chitosan from hydrogel. It creates cross-linked network by positive and negative interaction. Chitosan (Positive), TPP (Negative)

**Other Polyanions:** - Other Polyanions like alginate or carboxy methyl cellulose can be used to cross link chitosan.

## **B) Chemical Cross-linking: -**

**Glutaraldehyde:** - It is very commonly used cross-linking agent for chitosan hydrogel. It forms covalent bond between chitosan chain

**Other cross-linking agent:** - Genipin or Formaldehyde are also used as cross-linking agents.

**C) Physical cross-linking:** - Temperature Induced Gelation: - Chitosan can form hydrogel by temperature induced Gelation, specially when combine with additive.

## **Applications of Chitosan Hydrogels: -**

**Drug Delivery:** - Chitosan hydrogels can be used to encapsulate and release drugs, especially those with positive charges.

**Tissue Engineering:** - Chitosan hydrogels are used as scaffolds for tissue regeneration, particularly in wound healing and cartilage repair.

**Biomedical Devices:** - Chitosan hydrogels are used in various biomedical devices, such as contact lenses, wound dressings, and filters.

**Food Industry:** - Chitosan hydrogels are used as thickeners, gelling agents, and encapsulants.[37]

## **Hyaluronic acid: -**

Natural Polysaccharide found in various tissues of body like skin, cartilage, synovial fluid.

## **Method of preparation: -**

### **1) Chemical Cross-linking: -**

**Glutaraldehyde:** - Common cross-linking agent used to create hyaluronic acid hydrogel. It forms covalent bond between HA chain.

**Other cross-linking agent:** - Genipin and Formaldehyde

### **2) Physical cross-linking: -**

**Freezing -Thawing:** - Repeating freezing and thawing cycle can form hydrogel

This process aggregates the HA molecules and forms network

**Ionic Crosslinking:** - HA Cross-linking with divalent cations and forms hydrogels

divalent cation (calcium/copper)

## **Applications of Hyaluronic Acid Hydrogels**

**Tissue Engineering:** - HA hydrogels are widely used in tissue engineering, particularly for cartilage repair, wound healing, and skin regeneration.

**Drug Delivery:** - HA hydrogels can be used to encapsulate and release drugs, especially those for ophthalmic and joint applications. **Biomedical Devices:** HA hydrogels are used in various biomedical devices, such as contact lenses, wound dressings, and medical implants.

**Cosmetics:** - HA hydrogels are used in skincare products due to their hydrating and anti-aging properties.[38]

## **APPLICATIONS: -**

### **Pharmaceutical Applications: -**

- Wound Healing
- Colon specific drug delivery
- Cosmetology
- Industrial applicability
- Topical drug delivery
- Ocular drug delivery
- Tissue engineering
- Protein drug delivery

## **DIFFERENT ROUTES OF ADMINISTRATION: -**

Hydrogels could be used as drug delivery systems through different routes of administration.

### **Parenteral route: -**

For many drugs such as peptide and protein, parenteral route is the most favorite route of administration. Hydrogels as controlled drug delivery systems could be used for parenteral drug delivery.

### **Nasal route: -**

Nasal drug delivery has the advantages of high patient compliance and prevention of hepatic first pass effect which could increase drug bioavailability.

### **Ocular route: -**

Ocular drug delivery via eye drops is a common route of topical administration which is not efficient enough and may cause systemic adverse reactions.

### **Topical route: -**

Topical drug delivery is one of the favorite routes of administration which is used to reduce adverse effects and to localize high amounts of drug at target site.

### **Brain delivery: -**

Drug delivery to brain is still associated with so many challenges and the most important problem is the presence of blood brain barrier.

### **Tissue engineering: -**

Hydrogels have many advantages for tissue engineering purposes such as similarity to the extracellular matrices of tissues, induction of cell proliferation, negligible irritation to adjacent tissues and sustained release of incorporated growth factors.

### **Gene delivery: -**

Gene delivery through hydrogel scaffold is delivery of DNA or RNA for the purpose of genetic modification. Hydrogels are capable to increase gene therapy efficacy especially in cancer therapy.

## **TYPES: -**

**Homopolymeric hydrogels:** - Made from a single type of monomer, these hydrogels have a uniform structure and properties.[39]

**Copolymeric hydrogels:** - Composed of two or more types of monomers, these hydrogels exhibit unique properties due to the combination of different monomers.[40]

**Multipolymeric hydrogels:** - Made from three or more types of monomers, these hydrogels offer enhanced properties and functionality.[41]

**Interpenetrating network (IPN) hydrogels:** - Consist of two or more independent polymer networks that are intertwined, providing improved mechanical strength and stability.[42]

**Semi-interpenetrating network (SIPN) hydrogels:** - Comprise a polymer network that is interpenetrated by a linear polymer, offering a balance between mechanical strength and flexibility.[43]

**Biodegradable hydrogels:** - Composed of biodegradable polymers, these hydrogels can break down naturally in the body, making them suitable for biomedical applications.[44]

**Hybrid hydrogels:** - Combine different materials, such as polymers and ceramics, to create hydrogels with unique properties and functionality.[45]

**Double-network hydrogels:** - Consist of two independent polymer networks with different properties, providing enhanced mechanical strength and toughness.[46]

#### **pH sensitive or ion sensitive hydrogels: -**

These hydrogels respond to changes in pH of the external environment. These gels have ionic groups (which are readily ionizable side groups) attached to impart peculiar characteristics. Some of the pH sensitive polymers used in hydrogels' preparations are polymethyl methacrylate (PMMA), polyacrylamide (PAAm), polyacrylic acid (PAA), poly dimethylaminoethylmethacrylate (PDEAEMA) and polyethylene glycol. These polymers though in nature are hydrophobic but swells in water depending upon the pH prevalent in the external environment. pH sensitive hydrogels have also been used to encapsulate proteins in acrylamide polymer cross-linked with bisacrylamide acetal cross linkers.

**Temperature sensitive hydrogels:** - The hydrogels being cross-linked polymers are temperature sensitive. These hydrogels are pharmaceutically well accepted owing to large number of temperature sensitive drugs being delivered in these dosage forms. The release as well as mechanical characteristics of drug and hydrogels are altered with the change in the temperature of external environment (Prabaharan and Mano, 2006)

**Glucose sensitive hydrogels:** - These hydrogels are sugar sensitive and show variability in response depending upon the presence of glucose. One of such pharmaceutical hydrogel system is the cross-linked poly (methacrylamido phenylboronic acid)-coacylamide hydrogel which liberates the drug in a controlled manner only when the concentration of glucose is high in the surrounding environment causing swelling of the hydrogel (Pluta and Karolwicz, 2004;

**Nanohydrogels:** - Nanohydrogels are the hydrogels which are prepared in water by self aggregation of polymers of natural origin like dextran. These types of hydrogels are formed from natural polysaccharides like dextran, pullulan, or cholesterol-containing polysaccharide.

**CONCLUSION:** - Hydrogels have emerged as a versatile and dynamic class of materials with vast potential in biomedical and pharmaceutical applications. Their unique properties, such as high-water content, biocompatibility, and tunable functionality, make them an attractive platform for drug delivery, tissue engineering, wound healing, and biosensing. These hydrogels being biocompatible and biodegradable in nature have been used in the development of nano biotechnology products and have marvelous applications in the field of controlled drug delivery as well. That is why these turn-able biomedical drug delivery devices are gaining attention as intelligent drug carriers.

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