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A Review on Hydrogels in Drug Delivery Systems

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ABSTRACT

Hydrogels are materials composed of polymers, either synthetic or natural, that exhibit a wide range of chemical and physical characteristics. To create 3D networked tissues with a lot of water, these polymers are interlocked molecular networks that are crosslinked chemically or physically. It can occasionally be found as a colloidal gel with water acting as the dispersion medium. Crosslinked polymer networks, or hydrogels, are able to absorb large volumes of aqueous liquids. When exposed to water, these translucent, very soft materials absorb and release water, causing them to expand or contract and hold a significant amount of water without losing their structural integrity.

Drug release from hydrogels can be triggered by a variety of chemical, physical, and environmental factors. Hydrogels can be manufactured as films, coatings, slabs, microparticles, and nanoparticles, among other physical forms. Hydrogels are therefore employed in a wide range of clinical settings and medical fields, such as tissue engineering and regenerative medicine, cell immobilization, biomolecular or cell separation, and barrier materials that control biological adhesions. Hydrogels having various applications in drug delivery, protein drug delivery, wound healing, tissue repair and also in cosmetology.

Keywords: Hydrogels, classification of hydrogel, Applications, polymers

Introduction

Hydrogels are highly absorbent three-dimensional, crosslinked structures of water-soluble polymers capable in retaining a lot of water or biological liquids. They have a degree of flexibility fundamentally equivalent to standard tissue due to their enormous water content.

The hydrophilic functional groups attached to the polymeric backbone constitute the basis for water retention by these hydrogels while intermolecular chains among network chains lead to their resistance against dissolution. Hydrogels can be synthesized from nearly all types of water-soluble polymers ranging across various chemical compositions and bulk properties. Furthermore, hydrogels can be arranged in various genuine designs, including pieces, microparticles, nanoparticles, coatings, and films. Accordingly, hydrogels are typically used in clinical practice and preliminary medicine for some applications, including tissue planning and regenerative prescription, diagnostics, cell immobilization, division of biomolecules or cells, and provision of biological barriers to prevent adhesions. Such gels are known as “physical” or “reversible” hydrogels since entanglement between polymer chains is facilitated by secondary interactions including hydrogen bonding ionic interactions van der walls forces etc.[5]

Hydrogels are polymers that can hold ordinarily their own load in water. The compound design of the hydrogel, its morphology and balance expanding influence properties like mechanical strength and intracellular and extracellular vehicle. Due to low surface tension, biocompatibility, water absorption capacity, a soft structure that allows for low protein ad-sorption, which is similar to ECM structure and attraction to different medical applications such as tissue engineering, release of therapeutic agents (proteins, drugs, genes) Contact lenses and wound coverings. Hydrogels can be made from various angles like; main source of the hydrogel (natural or synthetic polymer (hydrogel structure), homopoly-mer network, copolymer network and permeable network. Physical and chemical cross-links (anionic and cationic (and biodegradable) hydrogen gel loads (and biodegradable). Hydrogels have emerged as important frames in biochemistry due to their inherent biocompatibility, tunable properties, comparison to tissue or cell environments. They have moved from being static materials over decades into “smart” responsive materials that mimic the real-world scenarios such as pH simulations, temperature fluctuations among others. Their responsiveness together with programmable functions increases versatility outside biomedical sector thus they can be used in fields such as catalytic agent chemical sensors, and carbon-capture absorbents.[4]

Advantages [5,6]

1. Hydrogel is more flexible and stronger in nature.

2.Hydrogel can be more more flexible and durable than other hydrogels of similar, Poly (methyl acrylate-cohydroxyethylacrylate) hydrogel implant material that has strength and softness.

3. Hydrogel-based micro valves have a number of advantages over conventional micro-valves, including relatively simply.

4. Environmentally sensitive hydrogels. Specifically, these gels respond to changes in pH, temperature or concentration of metabolite by releasing load associated with the changes.

5.Researchers are studying natural hydrogel materials for tissue engineering purposes such as agarose, methylcellulose, and other biopolymers obtained in nature.

6. Hydrogels possess nice transparency while being easy to modify.

7. Due to their significant water content they possess a degree of flexibility very similar to that which is present in the most natural tissues.

8. They are compatible with human body tissues, can decompose after use and are injectable

9. Such a change detectable by sensing systems incorporated into these hydrogels can cause them to release their content as result constituents such as temperature and pH alter.

10.Time and again medicines or nutrients release only at the right moment.

Classification

a) Classification based on source

1. Natural hydrogels: These hydrogels are biodegradable, biocompatible and great cell

bond properties. There are two significant kinds of regular polymers which are utilized to

produce regular hydrogels are proteins like collagen, gelatin and, polysaccharides, for example, hyaluronic corrosive, alginate and Chitosan.[7]

2. Synthetic hydrogels: They are more valuable as contrast with regular hydrogels since they

can be designed to have a lot more extensive scope of mechanical and synthetic properties than their normal partners. Polyethylene glycol-based hydrogels are one class of the generally

involved material in biomedical application because of their non-harmfulness there similarity and low immunogenicity.[7]

3. Hybrid hydrogels: They are the blend of natural and synthetic polymer hydrogels.

To normally consolidate the benefits of both engineered and regular hydrogels numerous

happening biopolymers, for example, dextran, collagen, Chitosan, have been joined with

synthetic polymers, for example, poly (N-isopropylacrylamide) and polyvinyl alcohol.

b) Based on biodegradability [7,8]

1. Biodegradable hydrogels: Hydrogels are biodegradable numerous polymers made commonly are biodegradable, like Chitosan, fibrin and agar. Poly (aldehyde guluronate),

Polyanhydrides are instances of manufactured biodegradable polymers.

2. non-biodegradable hydrogels: Different vinylated monomers or macromers like 2-

hydroxyl ethyl methacrylate, 2-hydroxyl propyl methacrylate and acryl amide are generally applied in the arrangement of non-biodegradable hydrogels.

c) Classification based on configuration

The classification of hydrogels depends on their physical structure and chemical composition they can be

1. Amorphous (non-crystalline).

2. Semi crystalline: A complex mixture of amorphous and crystalline phases.

3. Crystalline.[2]

d) Classification based on physical appearance.

Hydrogels appear as matrix, film, or microsphere based on the preparation process.[2]

e) Classification by sort of cross-linking

Hydrogels can be separated into two classes based on synthetic or actual nature of the cross

linking. Synthetically interconnected networks have extremely durable associations, while actual organizations have transient associations that are not because of polymer chain trap or actual communications, for example, ionic collaborations, hydrogen bonds or hydrophobic interactions. [11]

f) Characterization as per network electrical charge

Hydrogels might be classified into four gatherings based on presence or absence of electrical charge situated on the cross-connected chains:

1. Nonionic

2. Ionic (counting anionic or cationic).

3. Amphoteric electrolyte (ampholytic) containing both acidic and fundamental gatherings.

4. Zwitter ionic containing both anionic and cationic gatherings. [11]

g) Classification according to the mechanism controlling the release of drug

1. Diffusion Controlled Release Systems:

There are two varieties of diffusion-controlled release systems:

-Reservoir devices

-Matrices devices

Reservoir devices

- Drug-containing cores surrounded by polymeric membranes make up reservoir devices.
- Diffusion via the device's outer membrane is the rate-limiting stage for medication release.

Matrix devises

- In matrix devices, the medication is distributed over the hydrogel's three-dimensional structure.
- The medication diffuses across the water-filled pores or the macromolecular mesh, causing release. [10]

2. Swelling Controlled Release Systems:

- This type of drug release involves the medication being distributed throughout a glassy polymer. The polymer swells when it comes into touch with biological fluid.
- The penetrant lowers the polymer's glass transition temperature as it penetrates the glassy polymer, allowing the macromolecules to relax. [12]

3. Stimuli-sensitive Swelling-controlled Release Systems

When the pH or ionic strength of the surrounding biological fluid or temperature changes, environmentally sensitive hydrogels can react to these changes by exhibiting dramatic changes in their swelling behavior, network structure, permeability, or mechanical strength. Some hydrogels can react to changes in the concentration of glucose or to applied magnetic or electrical fields. These materials' nature allows for a wide range of applications, including

medication delivery devices, chemical valves, artificial muscles, biosensors, and separation membranes. [13]

4. Hydrogels Sensitive to pH:

Acidic or basic groups may be found in the ionic networks of hydrogels that display pH-dependent swelling behavior. These groups can also be found in aqueous environments with the proper pH and ionic strength.

• These groups ionize and form fixed charges on the gel in aqueous solutions with the proper pH and ionic strength. The electrostatic repulsions cause the solvent to be absorbed more fully into the network.

• The amount of fixed charges rises with increasing degree of ionization (higher system pH), increasing electrostatic repulsions between the chains.

5. Temperature-sensitive Hydrogels:

The capacity of temperature-sensitive hydrogels to swell or deswell in response to changes in the surrounding fluid's temperature has gathered significant interest for these gels.

• Often utilized in biosensors, intelligent cell culture dishes, and on-off medication release restrictions.

• Systems that are temperature-sensitive either positively or negatively can be categorized as thermosensitive hydrogels.

• An upper critical solution temperature (UCST) exists for a positive temperature-sensitive hydrogel. [12,14]

6. Other Stimuli-sensitive Hydrogels:

- Drug release from a depot can be triggered by a number of stimuli besides pH and temperature.

• These include externally applied physical stimuli that may be applied to the systems, such as light, magnetic fields, electric currents, and ultrasound.

• Chemical stimuli, such as biological components, specific chemical substances, and ionic species.

Applications

1) Transdermal delivery:

A number of hydrogel-based drug delivery systems have been created to administer medications transdermally. To improve the penetration of goods like hormones and nicotine by transdermal iontophoresis, hydrogel formulations are being researched. [3]

2)Drug Delivery in the GI Tract

The gastrointestinal tract is the most often used route for medication delivery due to its wide surface area for absorption and simplicity of administration. But it's also a very complicated pathway, requiring adaptable drug delivery strategies for successful therapy.

Devices based on hydrogel may be created to locally administer medication to certain Gl tract locations. Particular delivery methods for antibiotics to treat Helicobacter pylori infections in peptic ulcer disease. Before the medication is released in the small intestine, these hydrogels shield the insulin from the stomach's acidic environment.

Currently, a number of hydrogels are being researched as possible colon-specific medication delivery tools. They are intended to decompose or swell dramatically when exposed to intestinal enzymes or micro flora, providing colon- specificity in drug delivery. [15]

3) Ocular drug delivery

The eye's defense systems, such efficient tear drainage, blinking, and poor corneal permeability, make it challenging to administer drugs to the eye.

As a result, medication solutions contained in eye drops often leave the eye quickly and have poor absorption, which results in low ocular bioavailability. For the requisite therapeutic effectiveness, a frequent dosage schedule is required because of the short retention duration.

When pilocarpine nitrate was dosed as a solution, the duration of the drug was just 3 hours; with this technique, it was prolonged to 10 hours. The formation of hydrogels in situ is interesting. [15]

4)Wound healing

Hydrogels are able to retain water and drugs due to their cross-linking structure.

Due to its ability to retain moisture, it can maintain and maintain wounds. Hydrogel have been produced to cure cartilage abnormalities by using a modified polysaccharide found in cartilage.

Hydrogels made of honey have been used to speed up wound healing. These hydrogels include a transparent, readily peelable matrix that contains cross-linked honey.

Blood coagulant and a hydrogel consisting of gelatin and polyvinyl alcohol have been prepared. In terms of blood coagulation control, the cell adhesive hydrogel guaranteed a superior result than the similar gel or ointment. Polyacrimides and polyvinyl alcohols are used to retain water and helps in wound healing. [17]

(5) Topical medication administration

Hydrogels exhibit superior compliance compared to traditional creams. Patient because of the moisturizing qualities of these hydrogels, scaling and dryness are not anticipated while using this medication delivery method. Hydrogel formulations containing antifungal medications, such as clotrimazole, have been created to treat vaginitis. It has demonstrated improved absorption. [16]

6) Gene delivery

Changes in hydrogel structure lead to the targeting and delivery of nucleic acids to specific cells for gene therapy. Hydrogels have many uses in the treatment of various inherited or acquired diseases. [4]

7) Hydrogel Application for Fixing Bone Replacements

The orthopedic fasteners and replacements offered, such as knee replacements, screws, pins, and nails, are covered with hydrogels and other biocompatible and biodegradable polymers that expand when liquids are present. Once introduced into bone material, the fastener or replacement is securely secured into place due to the swelling of such coatings.

Methacrylate, hyaluronic acid esters, and crosslinked hyaluronic acid esters—which are produced when hyaluronic acid is esterified with polyhydric alcohols—are useful coating materials. A technique for using coated orthopedic fasteners or replacement to secure a bone or bone replacement in place is also offered. [16]

8) Cosmetics

A special kind of gel made of water, hydrogel can retain 500 times its own weight in water. Because hydrogel's molecular structure is equal to that of human skin cells, some of the greatest skincare products contain it—without getting too technical. The performance of all the other healthy elements in a skincare product will improve if it contains hydrogel.

Hydrogels are used as new cosmetic products as beauty masks, anti aging products, sunscreen usually made with engineered collagen, hyaluronic acid, or polyvinyl pyrrolidone. Mask of hydrogel hydrate skin as they have more water content.

9)Tissue engineering

Tissue engineering is a medical intervention that aims to replace or repair missing, damaged, or wounded tissues to their original anatomical form and function. This will enable the replacement of complete organs. Among the many applications the scientists see for the new technique are the regeneration of healthy tissue in a liver afflicted with cancer, the healing of a biopsy site, and the provision of painkilling, infection-fighting medical therapy to injured warriors.

A network of very absorbent, chain-like polymers is what forms hydrogels. Despite not being soluble in water, they absorb a lot of it, and nutrients and cell wastes may easily travel through them due to their porous nature. [12]

10) Contact lenses

In order to create contact lenses, hydrogel is the perfect material because it is highly water-soluble, oxygen-permeable, mechanically sound, wettable on the surface, stable against hydrolysis and sterilization, non-toxic, and has a sufficient biological tolerance for living cells. [18]

11) Restoration of the environment

Heavy metals and dyes found in the wastewater from several industrial activities are extremely dangerous to natural systems and public health. Researchers have discovered a method for cleaning water that is both ecologically benign and effective. It's referred to as hydrogel material water filtration. [18]

11) Additional applications

Other drug delivery methods, such as oral or pulsatile drug administration, also employ hydrogels.

Drug delivery for cancer is also being studied with injectable hydrogels. Long-term in situ gel-forming hydrogels have also been stated.[16]

Marketed products of hydrogels

Eligard - Leuprolide acetate(drug) used for treatment of advanced prostate cancer.

Sandostatin- Octreotide acetate(drug) used for Acromegaly.

Timoptic-XE- Timolol malate(drug) used for glaucoma.

POSIDUR – Bupivacaine (drug) used for Post-operative pain.

Relday- Risperidone(drug) for Schizophrenia and bipolar disorder.

Conclusion

Networks of cross-linked polymers called hydrogels are able to absorb vast volumes of aqueous liquids. These days, it mimics natural biological tissue more than other synthetic biological materials because of its high water content. Because of a special set of characteristics, hydrogels can be applied to the delivery of drugs. Large volumes of water may be absorbed by hydrogels because of their hydrophilic nature. Therefore, hydrogels molecule transport strategy differs greatly from hydrophobic polymers. Numerous hydrogel networks have been developed recently to satisfy the demands of many applications. This hydrogel has a tendency to expand when it comes into touch with an aqueous solution. This paper outlines the different bases hydrogel categorization, as well as their chemical and physical characteristics and prospective applications.

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