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(REVIEW ARTICLE)



A review article on PH- sensitive Hydrogel

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Abstract

Hydrogels are a type of hydrophilic network that can be cross-linked through physical or chemical means. They are a three-dimensional network. Hydrogels are also known as hydrophilic gels due to their significant water absorption capacity. Hydrogels are known for their swelling, mechanical qualities, biodegradability, elasticity, biocompatibility, ease of modification and flexibility, among other attributes. This article discusses general hydrogels knowledge, including its significance, preparation process, synthesis, chemical and physical properties, features, benefits, and drawbacks. Hydrogels that are sensitive to pH have advanced significantly in the last few years. The creation of novel hydrogel systems with higher sensitivity has made this possible. Up to 10-5 pH units of sensitivity have previously been determined. Applications for hydrogen in medicine include tissue engineering, contact lenses, wound dressings, and the release of medicinal agents. We talk about hydrogels, their varieties, their qualities and their uses in medicine.

Keywords: Applications; Preparation Method; Hydrogel Properties; pH-sensitive; Tissue design

1. Introduction

The skin serves as a vital barrier to human defense and is essential both preserving homeostasis, defending the body against mechanical harm, detecting outside stimuli, and triggering immunological responses ^[1]. While hydrogels offer numerous benefits, these materials are accompanied as well by certain drawbacks. Their low tensile strength may restrict their application in drug loading scenarios and cause the hydrogel to prematurely dissolve or drain from the intended tissues and organs. This disadvantage is important for several common topical and subcutaneous drug delivery methods ^[2]. Particularly hydrogels have attracted a lot of interest in the fight against oral disorders because of their superior drug delivery capabilities, affordability and biocompatibility. Moreover, hydrogels have outstanding bioadhesive, which enables them to stick to oral tissues and provide long-term medication release ^[3]. Hydrogel materials find extensive applications in the medical, cosmetic, textile, agricultural and more recently, food industries, hydrogels are a subject of extensive research due to their wide range of possible applications. hydrogels have been widely used as delivery system scaffolds for cell cultivation and tissue engineering in the pharmaceutical and biomedical industries ^[4]. hydrogel DDSs can be produced from natural, semi-synthetic and synthetic polymers [5]. To meet specific needs like tissue engineering, a wide variety of hydrogels have been created using blends, derivatives and natural and synthetic polymers ^[6]. By grafting or cross-linking monomers with different functional groups, the characteristics of these soft materials can be enhanced [7]. Consequently, medication administration drug delivery applications require carriers such as beads, tablets, cross linked hydrogels made of natural materials and microparticles. Among these, hydrogels are crucial since of their stability, degradability and is responsiveness ^[8]. We examine the following as unique viewpoint characteristics for the use of organogels: i) response to multiple stimuli; ii) long-term environmental stability and durability; iii) capacity to absorb and release substances; iv) unique wettability; and v) actuation ^[9]. The synthesis of hydrogels can be done via several "classical" chemical methods. These comprise both multi-step processes involving the synthesis of polymer molecules with reactive groups and their subsequent cross-linking, potentially also by reacting

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polymers with appropriate cross-linking agents and one-step processes such as polymerization and parallel crosslinking of multifunctional monomers ^[10]. Hydrogels that are thermos-sensitive, pH-sensitive or analytic-sensitive are the several types of physical gels referred to as stimuli-sensitive or smart gels ^[11]. A variety of techniques and precursors can be used to create hydrogels, enabling the modification of various characteristics such pore size, mechanical strength, degradability and rate of degradation ^[12]. Mechanical strength, intracellular and extra cellular transport and other characteristics are influenced by the hydrogels chemical structure, shape and equilibrium swelling ^[13]. Hydrogels are often made using starch, a popular biocompatible polymer ^[14]. When it comes to the medicinal application of pre-formed hydrogels, injectable hydrogels offer advantages over these drawbacks ^[15]. Hydrogel currently has several potential applications after years of development ^[16]. For wastewater treatment to be efficient, robust hydrogels with high adsorption capacities must be built ^[17]. Hydrogels can be made from a variety of polymers in different formats (such as coatings and slabs) and shapes (such as spherical, cylindrical) ^[18]. Food safety applications for hydrogel-based sensors are still in their infancy ^[19]. Depending on the disease's stage, liver cancer can be treated with a variety of methods and strategies, such as immunotherapy, gene therapy, radiation, chemotherapy, surgery and targeted therapy ^[20].

2. History of Hydrogel

Hydrogels have been used for more than 50 years in a variety of biological fields, including ophthalmology (for contact lenses) and a wide range of clinical settings to treat conditions like diabetes mellitus, osteoporosis, asthma, heart disease and neoplasms. The first hydrogel, synthetic poly-2-hydroxyethyl methacrylate, was created for use in the production of contact lenses and has biomedical uses ^[21]. Professors lim and wichterle of prague, czech republic, created the first hydrogel with possible uses in medicine in 1955. That was artificial poly-2-hydroxyethyl methacrylate, which was utilized to make contact lenses not long after it was discovered ^[22].

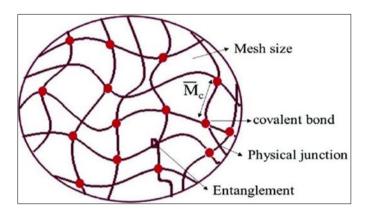


Figure 1 Structure of hydrogel [23]

3. Advantages of Hydrogel: [24, 25, 26, 27]

- Hydrogels are biocompatible
- Making changes is simple.
- Hydrogels have good transport properties as well.
- Extremely comparable to the flexibility of natural tissue.
- Release of medicines or nutrients timely.
- They are biocompatible, biodegradable and can be injected.
- Injectable
- Easy to modify
- Timing the release of nutrients and growth substances to assure proper tissue growth
- The polyurethane hydrogel beads that encase the microbial cells have the advantage of being very little toxic.
- Simple to adjust.
- Good transparent characteristics.

4. Disadvantages of Hydrogel: [24, 28, 29]

- High cost.
- Can be hard to handle.

- Low mechanical strength.
- They are non-adherent and may need to be secured by secondary dressings and also cause sensation felt by movement of the maggots.
- Difficult to sterilize.
- In contact lens less deposition hypoxia, dehydration and red eye reactions .
- Noncompliant.
- Tough to sanitize.

5. Hydrogel techniques features: [24, 11]

- The higher absorbency under load (AUL).
- The lowest price and highest absorption capacity in saline.
- The lowest soluble content and residual monomer.
- The highest biodegradability without formation of toxic species following the degradation.
- pH-neutrality after swelling in water.
- Colorlessness, colorlessness, and absolute non-toxic.
- Photo stability.

6. Classification of Hydrogel:

6.1. Natural Hydrogels

Natural hydrogels, such as cellulose, alginate, chitosan and their derivatives, are generally extracted from renewable resources ^[30]. Natural polymers include Polysaccharides and their proteins, which are widely used as carriers for the release of substance ^[31].

6.2. Natural Polymer Hydrogels

6.2.1. Gelatin

Gelatin is a natural and economical vascular polymer whose properties, such as minimal immunogenicity and substantial decomposition, make it one of the best options for tissue engineering. This polymer is obtained through dissolving the triple helical conformation of collagen, there are two types of gelatins derived from 2 different treatments: Gelatin a examined by acids (pH 1–3) and gelatin b processed with An alkaline approaches, type a being the most preferable for scaffold building. Gelatin has been utilized as a coating agent to enhance cell attachment as a technique of vascular tissue regeneration [³²].

6.2.2. Collagen

One of the most prevalent proteins in animal anatomy is collagen, which is an essential part of the extra-cellular matrix. Its remarkable tensile strength is imparted by its tightly packed triple helix structure, which surpasses that of steel wire with an equivalent cross-section. Like gelatin, collagen contains the RGD sequence, which promotes higher integrin subunit expression. This characteristic establishes a high affinity for adherent cells and fosters the conditions necessary for cell adhesion [³³].

6.2.3. Alginate

Alginate is a polymer found in brown algae cell walls and certain bacteria capsules. Its structure is built from blocks of two distinct monomers, D-manuronate (M) and L-Glucoronate (G). Alginate's substantial G block concentration may produce stiff hydrogels When bound to divalent cations like Ca2+. This is referred to as the "egg-box model". Alginate with an elevated M block concentration demonstrates reduced adhesiveness and immunostimulatory properties ^[34]. Alginate gel is relatively weak, with a compressive they are more useful as compared to natural hydrogels because they can be engineered to have a much wider range of mechanical and chemical properties than their natural counterparts. Polyethylene glycol (PEG) based hydrogels are one class of the widely used material in biomedical application due to their non-toxicity their compatibility and low immunogenicity ^[24]. Unlike DNA-based hydrogels, gelatin and alginate are commercially available with well documented functionalization in the range 1–8 kPa ^[35].

6.2.4. Hyaluronic Acid

Hyaluronic acid offers many advantages as a scaffold including biodegradability, a primary intracellular component of connective tissues, creating an environment conducive for cell infiltration and taking part in key cellular activities such as proliferation, tissue regeneration, and wound repair. Hyaluronic-acid-based polymers have been explored as cell carriers for bone, nerve, soft tissue and smooth muscle engineering applications. Different chemical modifications on hyaluronic acid are performed to create new bio-compatible, biodegradable mechanically strong scaffolding materials [36].

6.2.5. Synthetic Hydrogels

They are more useful as compared to natural hydrogels because they can be engineered to have a much wider range of mechanical and chemical properties than their natural counterparts. Polyethylene glycol (PEG) based hydrogels are one class of the widely used material in biomedical application due to their non-toxicity their compatibility and low immunogenicity ^[24]. For synthetic hydrogels, in addition to single network hydrogels, hydrogels consisting of two independently crosslinked polymer networks attracted wide attention recently, for which tough gels Can be formed even with a less crosslinked "second work" within a more highly crosslinked "first Network". The molar ratio of the second network repeat units to the first network needs to be >5 ^[37]. Unlike DNA-based hydrogels, gelatin and alginate are commercially available with well documented functionalization techniques and biological relationships ^[38].

6.3. Polyvinyl alcohol (PVA)

Based hydrogels as well stand noteworthy for their outstanding mechanical characteristics along with their ability to hold water throughout the structure, which leads to an environment that is permanently wet. These advantages go beyond those of typical hydrogel materials, which include the ability to absorb water, gas permeability, soft tissue imitation, flexibility and biocompatibility [³⁹].

6.3.1. Polyethylene Glycol

The U.S. food and drug administration (FDA) has approved polyethylene glycol for use in human medicine. It is a hydrophilic, non-toxic, biocompatible polymer with minimal immunogenicity. Polyethylene glycol is mutable due to its two free hydroxyl groups in its structure ^[33]. To improve the stability of PLGA–PEG–PLGA-based hydrogel, Hennink's group prepared a PCLA–PEG–PCLA-based hydrogel by replacing PLGA block with Poly(E-caprolactone-co-lactide) (PCLA) ^[40].

6.3.2. Polyimide

Hydrogels are primarily used in plastic and reconstructive surgery, much as PVA hydrogels. They have a lot of water, the necessary mechanical strength, a high degree of biocompatibility and the ability to mimic soft tissue. They have good permeability oxygen flows through them and very easily they are transparent and soft. The polyalkylimide (PAI) hydrogel, which contains 96% water, is one example ^[22].

6.4. Smart Hydrogels

Researchers in academia and business have focused their efforts on creating "smart" biomaterials in general and hydrogels in particular due to the variety of therapeutic obstacles and the advancement of treatment standards ^[12]. Certain processes, such regulated drug release, protein separation, muscle contraction and in situ gelling systems, are facilitated by environmental triggers ^[2].

6.5. Hybrid hydrogels

These are formed by combining hydrogels made of natural and artificial polymers. Natural biopolymers including collagen, chitosan and dextran have been combined with synthetic polymers like poly (N-isopropylacrylamide) and polyvinyl alcohol ^[41].

6.6. Physical Hydrogel

The items are reasonably priced, biocompatible, and have low toxicity. Alginate hydrogel can help encapsulated chondrocytes grow and proliferate while still preserving their chondrogenic character. After injection of chondrocytes for 21 to 28 days ^[31].

7. Properties of Hydrogel

7.1. Swelling Properties

Rapid and reversible changes in hydrogel can be triggered by little variations in the surrounding environment. The hydrogels physical texture may be changes in environmental factors like temperature, pH, electric signal and the presence of enzymes or other ionic species ^{[42].} Hydrogels are composed of polymers that have undergone different cross-linking procedures. As such, they are all considered to be single molecules ^[41].

7.2. Mechanical properties

By varying the degree of crosslinking, the hydrogel's desired mechanical attributes could be achieved, and a stronger hydrogel could be produced by adding the percentage of crossing. Achieved though the higher degree of crosslinking decreases the % elongation of the hydrogels creates a more brittle Structure ^[24].

7.3. Biocompatible properties

Non-toxic and biocompatible in their behavior are hydrogels. Most polymers are employed in vitro toxicological and cytotoxity tests. Biosafety and Bio-functionality are the two polymers that make up biocompatibity ^[23]. the biological and physical properties of the electrospun hydrogel may be changed by adjusting the exposure duration ^[42].

8. Method for preparation of Hydrogel

In the creation of hydrogels, both hydrophilic and hydrophobic monomers are occasionally utilized to control the characteristics for certain uses. Hydrogels are formulated using a variety of techniques. For preparation, polymers that are natural or synthetic can be utilized. Synthetic polymers are chemically stronger and hydrophobic in contrast to natural Polymers ^[26]. By employing copolymerization or cross-linking free-radical polymerizations, hydrophilic monomers and multifunctional cross-linker can react to produce hydrogels. Water-soluble linear polymers, both synthetic and natural, are connected to form hydrogels. This can be accomplished in several ways.

- Creating main-chain free radicals with ionizing radiation that can recombine to form cross-link junctions.
- Chemically joining polymer chains together.
- Physical interactions, including crystallite formation, electrostatics and entanglements ^[23].

8.1. Bulk polymerization

The most basic method, bulk polymerization, uses simply monomers and monomer-soluble initiators. Due to the high monomer concentration, there is a high rate and degree of polymerization. However, the conversion that produces the heat during polymerization causes the reaction's viscosity to significantly increase. When monomers are bulk polymerized to create a homogenous hydrogel, a glassy, transparent. The glassy matrix swells to become soft and flexible when submerged in water ^[10]. Numerous shapes and sizes of the polymerized hydrogel can be created, such as emulsions, films, particles, rods and membranes ^[26].

8.2. Free radical polymerization

Acrylates, vinyl lactams and amides are the principal monomers utilized in this process to make hydrogels. These polymers have been functionalized with radically polymerizable groups or they have appropriate functional groups. The chemistry of common free-radical polymerizations, including propagation, chain transfer, initiation and termination Steps, is applied in this procedure ^[27]. Many thermal, ultraviolet, visible and redox initiators can be used for the radical generation in the initiation step; the radicals react with the monomers to change them into active forms ^[25].

8.3. Optical Polymerization

One technique for chemical cross-linking in the synthesis of hydrogen is optical polymerization, which has the benefits of low energy consumption and no solvent requirement for reaction execution. Hydrophilic polymers with light-sensitive molecules are used in this method. Free radicals and the optical decomposition initiator are created when the polymer solution is exposed to UV or visible light, which starts the polymerization process. Light polymerizes groups of acrylates and methacrylates, which are present in polymers that cross-link in this manner [41].

8.4. Suspension polymerization

The method of dispersion polymerization is useful. There is no need to crush the items because they are purchased as powder or microspheres (beads). Since an emulsion (W/O) a position has been chosen over the more conventional oil-in-water (O/W) method, the method used for polymerization is commonly referred to as "inverse suspension." this technique, a uniform mixture of monomers and initiator is distributed throughout the hydrocarbon phase. The main factors influencing the size and form of resin particles are the dispersant type, rotor design, agitation speed, and monomer solution viscosity ^[42].

8.5. Solution polymerization:

The multifunctional cross-linking agent is combined with either neutral or ionic monomers in these cases. The polymerization process is initiated by thermal initiators, such as redox initiator systems or UV radiation. Solution polymerization has a major benefit due to the presence of a solvent that acts as a heat sink. Above the bulk polymerization. The produced hydrogels are washed with distilled water to remove the initiator, soluble monomers, oligomers, cross-linking agent, extractable polymer, and other impurities. Water, ethanol, benzyl alcohol and water-ethanol mixes were used as solvents ^[25].

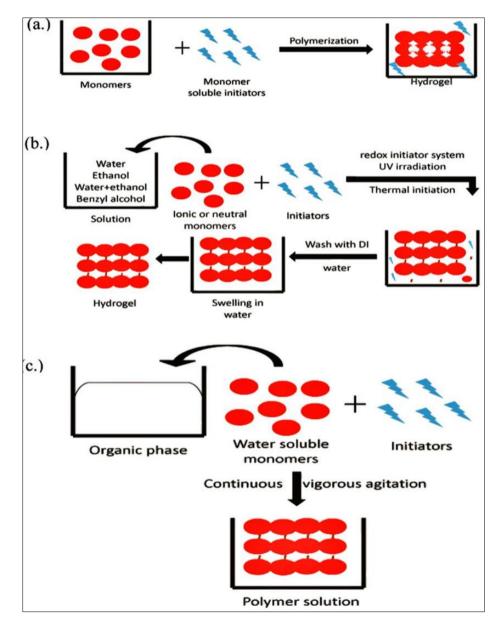


Figure 2 Different polymerization techniques in hydrogel preparation. (a) Bulk polymerization, (b) cross-linking polymerization, (c) network formation of water-soluble polymers (or inverse Suspension polymerization) [43]

8.6. Grafting to a support

Hydrogels made through bulk polymerization typically have a weak structure inherent to them. A hydrogel can be surface coated onto a more robust substrate to enhance its mechanical properties [10]. The three methods are poly (acrylic acid), poly (ethylene glycol) and poly (vinyl alcohol). The creation of comparatively clean and initiator-free hydrogels is the main advantage of radiation initiation over chemical initiation ^[42].

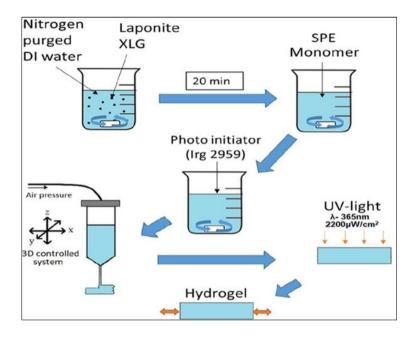


Figure 3 Block diagram for the preparation of the high swelling Hydrogel [44]

9. Chemical cross-linking

This method involves grafting monomers onto the polymers backbone and using a crosslinking agent to join two polymer chains. By reacting their functional groups (such as OH, COOH, and NH2) with cross-linker like aldehyde (e.g., glutaraldehyde, adipic Acid dihydrazide), natural and synthetic polymers can be cross-linked. To create an interpenetrating network structure, a polymerized monomer is placed into another solid polymer ^[24].

9.1. Physical cross-linking

By adjusting intramolecular forces such as hydrogen bonding, electrostatic ionic force and hydrophobic contact hydrogels can be produced physically by bonding. This technique avoids the possible increase in cross linker toxicity linked to the chemical process while allowing for the simple and safe synthesis of hydrogel. Physical cross-linking techniques come in three varieties: ionic, temperature-dependent and pH-dependent^[41].

10. Characterization of Hydrogel

10.1. Fourier Transform Infrared Spectroscopy (FTIR)

The structure and intermolecular interactions of hydrogel, FTIR spectra are captured using an FTIR spectrophotometer. Dehydrated KBr is employed to completely convert some ground IPN situations and spheres are produced via extension. Beneath a blank area. Spectra are recorded with a 1 cm-1 conclusion ^[39].

10.2. Rheological measurement

An essential parameter for an embolic material's viability in transcatheter delivery administration is its rheological characteristics. Thus, using a dynamic mechanical analyzer (Bohlin Rotational Rheome-Ter, Malvern Instruments, UK), the viscosity variation of PCL-PEG-SM solutions in response to temperature change was investigated. With a 250-Im gap, samples were positioned between two plates with a 20 mm upper diameter and a 100 mm bottom diameter ^[45].

11. PH-Sensitive Hydrogel

Ionic groups in pH-sensitive hydrogels allow them to either donate or take protons in response to changes in the pH of their surroundings. A pH variation affects the degree of ionization (pKa or pKb). A quick volume transition brought on by a pH shift produces a significant osmotic swelling force ^[2]. The radiopaque embolic compositions that were developed had a low viscosity at pH 8.0 making injection simple. Using a microcatheter, they demonstrated a sol-to-gel phase transformation. the tumor site's lower ambient pH creates a stable hydrogel DOX depot to enable the regulated release of DOX ^[46]. acryl amide, acrylic acid and methacrylic acid are a few examples of polymers ^[47]. Among the physiologically responsive hydrogel varieties that have been explored the most are pH-sensitive hydrogels. These hydrogels are inflated networks of ions that have basic or acidic pendant groups in them. The pendant groups have the ability to ionize and form fixed charges on the gel in aqueous solutions with the proper pH and ionic strength. Every ionic material has sensitivity to both pH and ionic strength. In comparison with non-ionic materials, these systems create greater swelling forces ^{[48].}

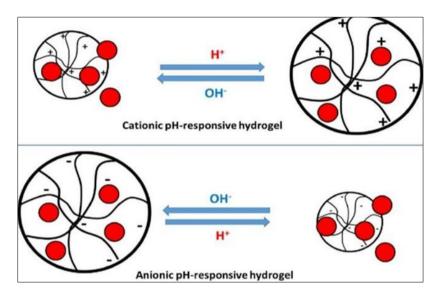


Figure 4 Schematic representation of a general behavior of pH-responsive polymer hydrogel for a drug delivery application. The cationic hydrogel swells at acidic pH and shrinks at basic pH and releases its cargo. The opposite is true for anionic hydrogels ^[49]

11.1. Principle of Operation for pH-Sensitive Hydrogels

Hydrogels that are sensitive to stimuli change their volume in reaction to changes in the surroundings. It has been observed that these volumetric changes are greater than a hundredfold. Water makes up the polymer matrix in weight amounts ranging from at least 20% to 99%. The degree of water retention in a hydrogels volume directly affects its biocompatibility; hydrogels with more than 95% of their volume retained in water are thought to have good biocompatibility ^[48].

11.2. Ph-Based Drug Release Mechanism Careful Hydrogels

Different release mechanisms, such as diffusion controlled, swelling controlled and chemically controlled mechanisms, are available for drugs entrapped or encapsulated in hydrogels. Spread the most practical mechanism is the controlled one and Fick's rule of diffusion governs its drug release model. If the drug molecules have considerably smaller molecular dimensions than the porous hydrogels pores, the hydrogels porosity and diffusion coefficient will be correlated. The cross-linked polymer chains impede the release of the drug molecules when the hydrogel pore size and the drug molecule size are similar. The diffusion coefficient is lowered. If the rate of medication release surpasses edema, after which a swelling-controlled mechanism governs medication release [^{50]}. a chance to create a responsive carrier for AgNPs to be released on demand. When bacteria are present in a wound, the pH of healthy skin is higher than normal, typically falling between 4-6. 7.3–9.8 is the alkaline pH, depending on the severity of the infection [^{47].} The main factors to consider should be the properties of the polymeric material, such as its ionic strength, hydrophilicity or hydrophobicity, dose, crosslinker concentration and solubility. The secondary factor to be considered includes the various states of the swelling solution, such as the ionic concentration, environmental pH, repulsive ions and the valence of the particular polymer [^{46].}

Natural polymers	Functional groups.	Swelling PH
Chitosan (CS).	-NH2, -OH	Acidic
Guar gum (natural semi-solid)	-СООН	Basic
Alginic acid hyaluronic acid. (HA)	СООН, ОН	Basic
Carboxymethyl dextran. (CM-Dex)	СООН, -ОН	Basic
Carboxymethyl cellulose	-СООН, -ОН	Basic
Gelatin A and B	NH2, -OH, COOH	Acidic and basic
Starch ether with tertiary amine.	-N, -OH	Acidic

Table 1 Enumeration of natural and semi-natural polymers that respond to pH [51]

12. Hydrogel Application

12.1. Drug delivery

Local treatment of oral conditions such as periodontal disease, stomatitis, viral and fungus infections and oral malignancies can greatly benefit from the introduction of drugs to the mouth cavity ^[28].

12.2. Delivery via Rectal

Rectal medication administration is the primary usage for hydrogels with bioadhesive properties ^[26].

12.3. Transdermal Application

In the field of wound dressing, swollen hydrogels can be employed as controlled release mechanisms. Formulations based on hydrogel are being investigated for transdermal iontophoresis to achieve improved product penetration, namely for hormones and nicotine ^[29].

12.4. Drug administration in the mouth

Medication is delivered to specific GIT sites using hydrogels. Colon-specific hydrogels containing microbial drugs show tissue specificity, a pH shift or an enzymatic action that breaks down the drugs ^[25].

12.5. Topical drug delivery

Hydrogels have been utilized to apply active ingredients such as synthetic corticosteroid desonide, which is typically used as an anti-inflammatory. the hydrogels' moisturizing qualities and improved patient compliance, scaling and dryness are not anticipated with this medication delivery method ^[24].

12.6. Drug distribution through the eyes

The most common application for hydrogels is in ocular medication delivery systems. Hydrogel exhibits sustained or controlled release to lessen dosage frequency or to improve the drug's efficiency by delivering the medication consistently, lowering the dose needed or localizing it to the site of action ^[26].

12.7. Tissue Engineering

Using biology and engineering, tissue engineering is a multidisciplinary branch of research and technology that aims to regenerate failing or damaged tissues. In a nutshell, autologous or allogenic cells are planted into biocompatible and biodegradable materials to create porous scaffolds. After that, the cell-filled constructs are either implanted directly into the patient's intended site or grown in vitro for maturation ^[52]. The goal of tissue engineering research and development is to create biological substitutes that will help injured tissues and organs function better and return to their original morphology ^[53].

12.8. Wound healing

Hydrogels, which are materials composed of cross-linked polymers, possess the capacity to retain both water and drugs. They are able to retain wound exudates. When applied, hydrogels based on gelatin and sodium alginate can cover and shield the site from bacterial infection. For instance, polyacrylamide or polyvinyl pyrrolidine in the form of a gel that contains 70–95% water ^[26]. The goal of wound healing is to hasten the body's natural healing process to facilitate the regeneration and repair of damaged tissues. Dressings, biomaterials and medications that control hemostasis, inflammation, proliferation and remodeling phases are used in this ^[54].

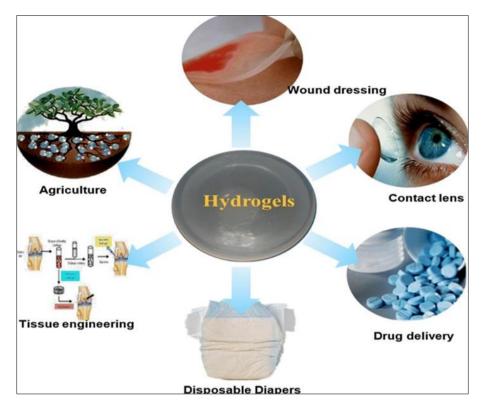


Figure 5 An illustration of possible health application of pH- sensitive Hydrogel sensor drug delivery in the human body $^{[25]}$

13. Applications in electronics

Given the excellent tunability and accuracy of capacitors using hydrogel dielectrics, the use of hydrogels as matrices in electronics is particularly promising. High-performance, low-cost capacitors can be constructed by varying the polymer and the solution carried. Organic polymers may be used to make these hydrogel electrolytes ^[55].

Agriculture sector: Reducing irrigation frequency by 50% can improve soil's ability to retain water over several years.

- A reduction in the amount of water and nutrients leached.
- Reducing the amount of water evaporating from the soil.
- Increasing aeration to enhance the physical characteristics of dense soils.
- Promote the development of plants. In the root zone, nutrients and water are always available for plants to absorb to their full potential.
- Preserving the environment against contaminants in groundwater and drought [31].

14. Miscellaneous applications

Cellulose-based SAHs are also used in construction, electrical applications, water swelling rubbers, artificial snow, packaging, refreshing systems, enzyme and catalyst supports, sludge/coal dewatering, body water retainers, stomach bulking agents and food preservatives, among other miscellaneous applications ^[56].

15. Biomedical applications

A variety of biomedical applications have utilized hydrogel delivery of RNA therapies. Hydrogels are mainly employed to protect RNA from innate immune responses and to facilitate the local administration of RNA therapies to the illness site. To optimize the effectiveness of RNA therapies, hydrogels can be altered to provide different release profiles based on the pathophysiology of the disease. The paragraphs that follow describe the use in RNA delivery hydrogels in recovering from wounds, bone regeneration, cancer treatment and cardiovascular repair ^[57]. For biomedical companies for using hydrogel, they enhanced mechanical and antibacterial features. Semi-IPN hydrogels were created using bacterial cellulose (BC), chitosan (CS) and glutaraldehyde crosslinker ^[58].

16. Conclusion

Drug development has advanced quickly thanks to site-specific delivery and controlled drug delivery. Numerous researches demonstrated the value of gels, particularly hydrogels. Hydrogels maintain a long-term therapeutic balance in the body's medication concentration. Hydrogel-based delivery systems with a high-water content and a soft consistency can be applied orally, ocularly, topically or subcutaneously. The information in this overview covers the many categories of hydrogels, as well as their chemical and physical characteristics, uses and technological viability of use. Hydrogels can currently be prepared in a variety of ways. Hydrogels that the had been generated by boiling displayed a macro porous structure, whilst those that those developed by frozen displayed a structure approximating fibers.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

- [1] Guo W, Ding X, Zhang H, Liu Z, Han Y, Wei Q, Weaba O, Okora V, Shavandi A, Nie L. Recent advance of chitosanbased hydrogel for skin -wound Dressings. Journal of gel. 2024; 10(175): 1-26.
- [2] Raza F, Zafar H, Zhu Y, Ren Y, Ullah A, Ullah Khan A, He X, Han H, Aquib Md, Yiadim KB, Ge L. A Review on Recent advance in stabilizing peptide/protein upon fabrication in Hydrogel from biodegradable polymers. Journal of pharmaceutical. 2018; 10(16):1-21.
- [3] Conte R, Valentino A, Romoano S, Margarucci S, Portillo O, Calarco A. Stimuli-Responsive Nano-composite hydrogel for oral diseases. Journal Of gel. 2025; 10(478): 1-15.
- [4] Hilal A, Florowska A, Wroniak M. Hydrogel Induction method and Recent Application progress as food Matrices for Bio active compound Delivery -A Bibliometric Revie. Journal of gel. 2023; 9(68): 1-26.
- [5] Sobczak M. Enzyme-Responsive Hydrogels as Potential Drug Delivery Systems-State of Knowledge and Future Prospects. International Journal of moleculer science. 2022; 23(8): 1-18.
- [6] Khodadadiyazdi M, Vatanpour V, taghizadeh A, Taghizadeh M, Muhammad GM, Muhammad TM, Habibzadeh S, Mohammad RS, Ghaedi M. Hydrogel membrance material science and engineering. 2020. 114: 111023.
- [7] Monir T, Aforz S, Khan RA, Muhammed YM, Takafuji M and Alam A. pH-Sensitive Hydrogel from polyethylene oxide and acrylic acid by gamma radiation. Journal of composite science. 2019; 3(2): 58.
- [8] Rao KM, Rao KSVK, Palem RR, Uthappa UT, Ha CS, Han SS. pH-Sensitive drug delivery behaviour of Polymers palm kernel, Hydrogel of chemotherapeutic agent. Journal of gel. 2023; 9(38): 1-10.
- [9] Kuzina M, Kartsev D, Stratonovich A, Levkin P. Organogels versus Hydrogel, advantages, chellengs and application. Advanced functional materials published. 2023; 33(27): 27 2301421
- [10] Ahmed EM. Hydrogel preparation characterization and application. A review Journal of advanced research. 2013; 6(2): 105-121.
- [11] Doost mohammadi M, Ameri A, mohammadinejad R, Dehghannoudeh N, Banat I, Ohadi M, Dehaghannouldeh G. Hydrogel for peptide hormones delivery therapeutic and tissue engineering. drug design development and therapy. 2019; (23): 3405-3418.

- [12] Sosnik A, Sereneta KP. Polymeric Hydrogel as technology platform drug delivery application. Journal of gel. 2017; 3(3): 25.
- [13] [13] Chamkouri H, Chamkouri M. A review of Hydrogel their properties and applications in medicine. American journal of biomedical sciences and rest. 2021; 485-496.
- [14] [14] Narayanaswamy R, Torchillin V. Hydrogel and their application in targeted drug delivery. Journal molecules. 2019; 24(3): 603.
- [15] [15] Nur B, Mohammad S, Mohamad A, Mohamad N, Mohamad I. Review on starch-based Hydrogel and its application for drug delivery of peramotal. progress in petrochemical science. 2022; 4(4): 425-428.
- [16] [16] Lee JH. Injectable hydrogels delivering therapeutic Agents for disease treatment and tissue Engineering. Biomaterials Research. 2018; 26(22): 27.
- [17] Ahmadi S, Pourebrahimi S, Malloum A, Pirooz M, Osagie C, Ghosh S, Muhammad ZM, Mohammad DM. Hydrogelbased materials as antibacterial agents and super Adsorbents for the remediation of emerging pollutants. A Comprehensive r Emerging Contaminants. 2024; 10(3): 100336
- [18] Abune L, Wang Y. Affinity Hydrogels for Protein Delivery. HHS Public Access. 2024; 42(4): 300-312
- [19] Lin X, Yan H, Zhao L, Duan N, Wang Z, Wu S. Hydrogel-integrated sensors for food safety and Quality monitoring. Fabrication strategies and Emerging applications. Critical Reviews in Food Science and Nutrition. 2023; 64 (18): 6395-6414.
- [20] Far FB, Ali AI, Nasiriyan E, Pourmolaei A, Mahmoudvand G, Rouzbahani AK, Mohamme AN, Mohammad RJ. An Updated Review on Advances in Hydrogel-Based Nanoparticles for Liver Cancer Treatment. Journal livers. 2023; 3(2): 161-189
- [21] Saini k. Preparation method, properties and cross-Linking of Hydrogel. A review. Pharma tutor. 2017; 5(1): 27-36.
- [22] Gibas I, Helena J. Synthetic polymer Hydrogel for biomedical applications chemistry and chemical technology. 2010; (4): 298-304.
- [23] Yadav S, madan J. Hydrogel A review. International journal of pharmacy and life science. 2020;11(6): 6711-6717.
- [24] Singh S, Dhyani A, Juyal D. Hydrogel preparation, characterization and application. the pharma innovation journal. 2017; 6(6): 25-32.
- [25] Mitkari DS, More AK, Joshi D. A review-hydrogel. International journal of research. 2023; (4): 719-726.
- [26] Dcosta P, Shabaraya A, Miranda FC. Hydrogel in novel drug delivery. International journal of pharmaceutical research and application. 2022; 7(4): 527-535.
- [27] Bhalerao SB, Mahajan VR, Maske RR. Hydrogel Based drug delivery systems, World journal of biology pharmacy and health science. 2022; 12(3): 039-053.
- [28] Malpure PS, Patil SS, More YM, Nikam PP. A review on Hydrogel. American journal of pharmtech research. 2018; 8(3): 42-61.
- [29] Singh A, Sharma P, Garg V, Garg G. Hydrogel a review. International journal of pharmaceutical sciences review and research. 2010; 4(2): 97-105
- [30] Zhou P, Zhang Z, Mo F, Wang Y. A Review of Functional Hydrogels for Flexible Chemical Sensors. Advanced Sensor Research. 2023; 3(3): 2300021.
- [31] Dastanaei P, Ghazinezhad M. Varied application of Hydrogel Based on their smart Properties a review. International journal of new chemistry. 11(4): 284-310.
- [32] Catoira M, Fasara L, Francesco D, Ramella M, Boccufoschi F. Overview of natural Hydrogel for regenerative medicine and application. Journal of materials science material in medicine. 2019; 30(10):115.
- [33] Chen X, Jing S, Xue C, Guan X. Progress in the application of Hydrogel in intervrtebral disc repair a comprehensive review. current pain and headache reports. 2024.
- [34] Gounden V, Singh M. Hydrogels and Wound Healing. Current and Future Prospects. Journal of gels. 2024; 10(1):
 43.
- [35] Gibbs D, Black C, Jonathon I, Dawson and oreffo R. A review of Hydrogel in fracture healing and bone regeneration. Journal of tissue engineering and regenerative medicine. 2016.10(3):187-98

- [36] Jacob S, Nair A, Sreeharsha N, Gupta S, Shinu P. Emerging role of Hydrogel in drug delivery systems tissue engineering and wound management. journal pharmaceutical. 2021; 13(3): 357.
- [37] Chai Q, Jiao Y, Yu X. Hydrogel for biomedical applications their characteristics and mechanisms behind them. Journal of gel. 2017; 3(1): 6.
- [38] Richbourg N, Wechsler ME, Rodriguez-Cruz JJ, Peppas AN. Model-based modular Hydrogel design. nature reviews bioengineering. 2024. 16(36);46988–47002.
- [39] Sowjanya P, komali V, Babu A. A review article on Hydrogel. International journal of research in pharmaceutical and nano science. 2013; 2(5): 548-553.
- [40] Yu H, Gao R, Liu Y, Lu Y, Fu L, Zhou J, Li L. Stimulus-Responsive Hydrogels as Drug Delivery Systems for Inflammation Targeted Therapy. Advanced Science published. 2023; 11(1): 2306152.
- [41] Bharati R, Pal S, Prasad N, Kumar Y, Joseph B, Sharma H, Saha G. A comprehensive review on Hydrogel. Acts scientific pharmaceutical sciences. 2024; (8): 64-75.
- [42] Sahu N, Gupta D, Nautiyal U. Hydrogel preparation, characterization and application, Asian Pacific journal nursing and health science. 2020; 3(1): 2581-7442.
- [43] Weerasundara L, Gabriele B, Figoli A, Yong-Sik Ok, Bundschuh J: Hydrogels: Novel materials for contaminant Removal in water. Critical Reviews in Environmental Science and Technology. 2020. 51(1):1-45.
- [44] Sallstrom N, Capel A, Lewis M, Engstrøm D, Martin S: 3D-printable zwitterionic Nano-composite hydrogel system for Biomedical applications. Journal of Tissue Engineering. 2020. 11: 2041731420967294.
- [45] Lym JS, Nguyen QV, Ahn DW, Huynh CT, Jae HJ, Kim Y, Lee DS. sulfamethazine based pH-Sensitive Hydrogel with potential applications for tran-scatheter arterial chemoemboliszation therapy act biomaterials. 2016; (41): 253-263.
- [46] Chuang E, Chiang C, Wong P, Chen C. Hydrogels for the Application of Articular Cartilage Tissue Engineering. A Review of Hydrogels, Advances in Materials Science and Engineering. 2018;(12): 1340893.
- [47] Haidari H, Kopecki Z, Sutton A, Gary S, Cowin A, Vasilev K. PH sensitive Smart Hydrogel controlled delivery of silver nanoparticles to inflated wound. Journal antibiotic. 2021; 10(1): 49.
- [48] Hendi A, Hassan M, Elsherif M, Alqatten B, Park S, Yetisen A, Butt H. Health care application of pH-Sensitive Hydrogel based device. International journal of Nanomedicine. 2020; 3887-3901.
- [49] Abdalla H and Lee D. A Review on the Design and Hydration Properties of Natural Polymer-Based Hydrogels. Journal of material. 2021; 14(5): 1095.
- [50] Rizwan M, Yahya R, Hassan A, Yar M, Azzahari A, Selvanathan V, Sonsudin F, Abouloula C. pH-Sensitive Hydrogel in drug delivery brief history properties, swelling and release mechanism, material selection and application. Journal polymer. 2017; 9(4): 137.
- [51] Kocak G, Tuncer C and Butun V. pH-Responsive polymers. Polymer Chemistry. 2017; 8(1): 144-176.
- [52] Mellati A, Akhatari J. Injeatable Hydrogel a review of injectability mechanisms and biomedical applications. Research in molecular medicine. 2018; 6(4): 1-19.
- [53] Wang K, Hao Y, Wang Y, Chen J, Mao J, Deng Y, Chen J, Yuan S, Zhang T, Ren J, Liao W. Functional Hydrogels and Their Application in Drug Delivery, Biosensors, and Tissue Engineering. International Journal of Polymer Science. 2019; (1): 3160732.
- [54] Ye R, Liu S, Zhu W, Li Y, Haung L, Zhang G, Zhang Y. Synthesis, Characterization Properties, and Biomedical Application of Chitosan-Based Hydrogels. Journal of polymers. 2023; 15(11): 2482.
- [55] Chirani N, Yahia L, Gritsch L, motto F, Chirani S, Fare S. History and application of Hydrogel. Journal of biomedical sciences. 2015; (4): 1-25
- [56] Kabir SM, Shikdar PP, Haque B, Bhuiyan MA, Ali A, Islam MN. Cellulose based hydrogel material chemical, properties and their prospective application. progress in biomaterials. 2018; (7): 153-174.
- [57] Zhong R, Talebian S, Mendes B, Wallace G, Langer R, Conde J, Shi J. Hydrogel for RNA delivery, Natrure material. 2023; (22): 818-831.
- [58] Cona C, Bailey K, Barker E. Characterization Methods to Determine Interpenetrating Polymer Network (IPN) in Hydrogels. Journal of Polymers. 2024; 16(14): 2050.