REVIEW ARTICLE Am. J. PharmTech Res. 2019; 9(01) ISSN: 2249-3387

AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

A Review On Hydrogel

A. B. Danole*, B.K. Kothali, A.K. Apte, A.A. Kulkarni, V.S. Khot, A.A. Patil, S. S. Upadhye

Dr. J.J. Magdum Pharmacy College, Jaysingpur, Tal-Shirol, Dist-Kolhapur, Maharashtra, India

ABSTRACT

Hydrogels are three-dimensional, hydrophilic & polymeric networks capable of absorbing large amounts of water or biological fluids. Due to their high water content, porosity & soft consistency, they closely simulate natural living tissues, more so than any other class of synthetic biomaterials. Hydrogels can be formulated in a variety of physical forms, including slabs, micro-particles, Nano-particles, coatings and films. As a result, hydrogels are commonly used in clinical practice & medicine for a wide range of applications, including Tissue engineering & Regenerative medicine, Diagnostics, Cellular immobilization, separation of biomolecules or cells, & barrier materials to regulate biological adhesions. Hydrogels are also relatively deformable & can conform to the shape of the surface to which they are applied. In the latter context, the bioadhesive properties of some hydrogels can be advantageous in immobilizing them at the site of application or in applying them on surfaces that aren't horizontal. They have started to create a niche in several fields of medicine like in specific site drug delivery, tissue reconstruction & tissue engineering and even as biosensors. In this review article an attempt has been made to explain the properties of hydrogels, their methods of preparation & its applications.

Keywords: Hydrogel Properties, Classification, Technologies adopted, Applications.

*Corresponding Author Email: hemanthhemu63639@gmail.com
Received 01November 2018, Accepted 20 November 2018

Please cite this article as: Danole AB *et al* A Review On Hydrogel. American Journal of PharmTech Research 2019.

INTRODUCTION

Hydrogels are polymeric networks that take in & keep huge quantities of water. There are hydrophilic groups in the polymeric network which become hydrated in aqueous media thus forming hydrogel structure.[1] Another definition is that it is polymeric material that exhibits its ability to swell & retain a significant fraction of water within its structure, but it will not dissolve in water. They possess a degree of flexibility very similar to natural tissue due to their large water content. The ability of hydrogel to absorb water arises from hydrophilic functional group attached to a polymeric backbone, while their resistant to dissolution arises from cross links between network chains.[2]

Hydrogels are three-dimensional, hydrophilic & polymeric networks capable of absorbing large amounts of water or biological fluids. Due to their high water content, porosity & soft consistency, they closely simulate natural living tissues, more so than any other class of synthetic biomaterials. Hydrogels may be chemically stable or they may degrade & eventually disintegrate and dissolve [1].

They are prepared from materials such as gelatin, polysaccharides, cross-linked polyacrylamide polymers, polyelectrolyte complexes, & polymers or copolymers derived from methacrylate esters. They are insoluble in water & are available in dry or hydrated sheets or as a hydrated gel in drug delivery systems designed for a single use [4].

Furthermore, hydrogels can be formulated in a variety of physical forms, including slabs, microparticles, nanoparticles, coatings, & films. As a result, hydrogels are commonly used in clinical practice & medicine with a wide range of applications, including Tissue Engineering & Regenerative Medicine, Diagnostics, and Cellular immobilization, Separation of biomolecules or cells & barrier materials to regulate biological adhesions [3].

These unique physical properties of the hydrogels have stimulated particular interest in their use in drug delivery applications. Their highly porous structure can easily be tuned by controlling the density of cross-links in the gel matrix & the affinity of the hydrogels for the aqueous environment in which they are swollen [3].Their porosity also permits loading of the drugs into the gel matrix & subsequent drug release in a rate dependent on the diffusion coefficient of a small molecule or a macromolecule through the gel network [3]. Since the polymer cannot dissolve due to the covalent cross links & water uptakes far in excess of those achievable with hydrophilic linear polymers can be obtained [5].

Advantages of hydrogels:

1. Due to their significant water content they possess a degree of flexibility very similar to the natural tissue.
2. It Release medicines or nutrients timely.
3. They are biocompatible, biodegradable & can be injected.
4. Hydrogels have the ability to sense changes of pH, temperature, or the concentration of metabolite & release their load as a result of such a change.
5. Hydrogels also possess good transport properties & easy to modification.

Disadvantages of hydrogels

1. It has High cost.
2. It can be hard to handle.
3. It has Low mechanical strength.
4. They are non-adherent & may need to be secured by secondary dressing & also cause sensation felt by movement of the maggots.
5. Difficult to load with drugs or nutrients. [6]

Properties of Hydrogel:

Hydrophilic gels called hydrogels receive considerable attention for their use in the field of pharmaceutical & biomedical engineering.

Swelling properties:

A small change in environmental condition may trigger fast & reversible changes in hydrogel. The alteration in environmental parameters like electric signal, pH, temperature & presence of enzyme or other ionic species may lead to a change in physical texture of the hydrogel.

Mechanical properties:

The desired mechanical property of the hydrogel could be achieved by changing the degree of Cross-linking & by increasing the degree of cross linking a stronger hydrogel could be achieved through the higher degree of cross linking decreases the percentage elongation of the hydrogels creates a more brittle structure. [7]

POLYMERS USED IN HYDROGELS:

Hydrogels are prepared from natural and synthetic polymers.

Biocompatible properties:

Biocompatibility is the ability of material to perform with an appropriate host response in a specific application. Biocompatibility consists basically of two elements (a) bio-functionality i.e. the ability of material to perform the specific task for which it is intended & (b) bio-safety i.e.

appropriate host response not only systemic but also local (the surrounding tissue), the absence of mutagenesis, cytotoxicity, and carcinogenesis .[8]

CLASSIFICATION OF HYDROGEL PRODUCTS:

The hydrogels can be broadly classified on different bases as detailed below:

Classification based on source:

Hydrogels can be classified into 2 groups based on their natural or synthetic origins. [9]

Classification according to polymeric composition:

The method of preparation leads to formations of some important classes of hydrogels. These can be exemplified by the following:

Homopolymeric hydrogels

These are referred to polymer network derived from a single species of a monomer, which is a basic structural unit comprising of any polymer network. Homopolymers may have cross-linked skeletal structure depending on the nature of the monomer & polymerization technique. [9]

Copolymeric hydrogels

These are comprised of two or more different monomer species with at least one hydrophilic component, arranged in a random, block or alternating configuration along the chain of the polymer network .[9]

Multi-polymer interpenetrating polymeric hydrogel (IPN)

This is an important class of hydrogels, is made of two independent cross-linked synthetic and natural polymer components, contained in a network form. In semi-IPN hydrogel, one component is a cross-linked polymer & other component is a non-cross-linked polymer. [9]

Classification based on configuration:

The classification of hydrogels depends on their physical structure & chemical composition can be classified as follows:

Amorphous (non-crystalline)

Semicrystalline: A complex mixture of amorphous & crystalline phases Crystalline. [9]

Classification based on type of cross-linking:

Hydrogels can be divided into two categories based on the chemical or physical nature of the cross-link junctions.

- Chemically cross-linked networks have permanent junctions.
- While physical networks have transient junctions that arise from polymer chain entanglements / physical interactions such as ionic interactions, hydrogen bonds or hydrophobic interactions. [9]

Classification based on physical appearance:

Hydrogels appearance as matrix, film, or microsphere depends on the technique of polymerization involved in the preparation process. [9]

Classification according to network electrical charge:

Hydrogels may be categorized into 4 groups on the basis of presence or absence of electrical charge located on the cross-linked chains:

I. Nonionic (neutral).
II. Ionic (including anionic or cationic).
III. Amphoteric electrolyte (ampholytic) containing both acidic & basic groups.
IV. Zwitterionic (polybetaines) containing both anionic & cationic groups in each structural repeating unit [5].[9]

Classification according to mechanism controlling the drug release they are classified into:

I. Diffusion controlled release systems
II. Swelling controlled release systems
III. Chemically controlled release systems
IV. Environment responsive systems. [9]

TECHNOLOGIES ADOPTED IN HYDROGEL PREPARATIONS:

Hydrogels are the polymer networks having hydrophilic properties. Hydrophilic monomers & hydrophobic monomers are sometimes used in hydrogel preparation to regulate the properties for specific applications. Hydrogels can be produced by reacting hydrophilic monomers with multifunctional cross-linkers by using Copolymerization or cross-linking free-radical polymerizations. Water-soluble linear polymers of both natural & synthetic origin are cross-linked to form hydrogels in a number of ways:

1. Using ionizing radiation to generate main-chain free radicals which can recombine as cross-link junctions.
2. Linking polymer chains via chemical reaction.
3. Physical interactions such as entanglements, electrostatics & crystallite formation.

In general, 3 integral parts of the hydrogels preparation are monomer, initiator, and cross-linker.

Bulk polymerization:

The Bulk hydrogels can be formed with one or more types of monomers mainly include vinyl monomers for the productions of hydrogels. Usually, small amount of cross-linking agent is added in any hydrogel formulation. Radiation, ultraviolet or chemical catalysts is used for the initiation of the polymerization reaction. The initiator is chosen which depends upon the type of monomers &

solvents being used. The polymerized hydrogel may be produced in a wide variety of forms including rods, particles, films, membranes & emulsions. [10]

Free radical polymerization:

The main monomers which are used in this method for the preparation of hydrogels are such as acrylates, vinyl lactams & amides. These polymers have the suitable functional groups or have been functionalized with radically polymerizable groups. This method involves the chemistry of typical free-radical polymerizations, which includes propagation, chain transfer, and initiation & termination steps. For the radical generation in the initiation step a wide variety of thermal, ultraviolet, visible & redox initiators can be utilized, the radicals react with the monomers which convert them into active forms. [11]

Solution polymerization or cross-linking:

In this polymerization ionic /neutral monomers are mixed with the multifunctional crosslinking agent. The polymerization is initiated thermally by UV-irradiation or by redox initiator system. The major advantage of this polymerization over the bulk polymerization is the presence of solvent serving as a heat sink. The prepared hydrogels are washed with distilled water to remove the initiator, the soluble monomers, oligomers, cross-linking agent and extractable polymer, and other impurities. Solvents used water–ethanol mixtures, water, ethanol, and benzyl alcohol.

Suspension polymerization or inverse-suspension polymerization:

The advantages of this method are that the products obtained as powder or microspheres (beads), so grinding is not required. Since water-in-oil (W/O) process is chosen instead of the more common oil-in-water (O/W), the polymerization is referred to as ‘‘inverse suspension’’. In this technique, monomers & initiators are dispersed in the hydrocarbon phase as a homogenous mixture. The resin particle size & shape is used to govern the viscosity of monomer solution, rotor design, agitation speed & dispersant type. The dispersion is thermodynamically unstable and requires both continuous agitation and addition of a low hydrophilic– lipophilic balance (HLB) suspending agent.

Grafting to a support:

Due to the weak structure of hydrogels prepared by bulk polymerization it is necessary to improve the mechanical properties of the hydrogel so it can be grafted on the surface coated onto a stronger support. This involves the generation of free radicals onto a stronger support surface & then polymerizing monomers directly on to it to form chain of monomers which are covalently bonded to the support. [12]

Polymerization by irradiation:

For the preparation of hydrogels of unsaturated compounds the initiators such as the ionizing high energy radiation like gamma rays and electron beams are used. The irradiation of the aqueous polymer solution results in the formation of radicals on the polymer chains. Recombination of macro-radicals on different chains results in the formation of covalent bonds & finally, a cross-linked structure is formed. Poly vinyl alcohol, poly ethylene glycol, poly acrylic acid is used for polymerization by irradiation. Relatively pure and initiator-free hydrogels is produced by this method. [13]

Physical cross-linking:

It is the most common and easy routes for hydrogel formation by cross linking of polymers through physical interactions. This physical cross linking includes interaction of ions such as hydrogen bonding, polyelectrolyte complexation & hydrophobic association. The various methods used in physically cross-linked hydrogels preparation are: -

Heating/cooling a polymer solution:

It is prepared by cooling hot solutions of gelatin or carrageenan to form physically cross-linked gels. The gel formation is due to association of helices, helix-formation & forming junction zones. Some of the examples are polyethylene glycol-polylactic acid hydrogel & polyethylene oxide, polypropylene oxide.

Complex coacervation:

Formation of complex coacervate gels by mixing of polyanions with a polycations. The underlying principle of this method is that polymers with opposite charges stick together & form soluble & insoluble complexes depending on the concentration & pH of the respective solutions. For example coacervating polyanionic xanthan with polycationic chitosan. [14]

Ionic interaction:

Addition of di- or trivalent counter ions in ionic polymer leads to cross linking between polymers. This method underlies the principle of gelling polyelectrolyte solution (e.g. sodium alginate) with a multivalent ion of opposite charges (e.g. Ca^{2+} + $2Cl^{-}$). Some other examples are chitosan-polylysine, chitosan-glycerol phosphate salt & chitosan dextran hydrogels.

Hydrogen Bonding:

A hydrogen bond is formed through the association of electron deficient hydrogen atom and a functional group of high electron density. For Example, a hydrogel can result from hydrogen bond formation between PA and PNVP. The factors which affect the hydrogels are the molar ratio of each polymer, polymer concentration, the type of solvent, the solution temperature and the polymer structure.

Chemical cross-linking:

In this process the use of a crosslinking agent to link two polymer chains and grafting of monomers on the backbone of the polymers takes place. The cross-linking of natural and the synthetic polymers can be achieved through the reaction of their functional groups (such as OH, COOH, NH2) with cross-linkers such as aldehyde (e.g. glutaraldehyde, adipic acid dihydrazide). IPN is a polymerize monomer within another solid polymer to form interpenetrating network structure.[15]

APPLICATIONS:

Wound healing:

Hydrogels have ability to hold water and drug in them due to their cross linked structure. Due to their water holding capacity they can hold and retain wound exudates. Polyvinyl pyrrolidine or polyacrylamide in the form of a gel containing 70-95% water. [16]

Colon Specific Hydrogels:

The Colon specific hydrogels of polysaccharide have been specifically designed because of presence of the high concentration of polysaccharide enzymes in the colon region of GI. Dextran hydrogel is formulated for colon- specific drug delivery.

Drug delivery in Gastro Intestinal tract:

Hydrogels delivers drugs to specific site in the Gastro Intestinal tract. In presence of micro flora, the drug loaded with colon specific hydrogels show tissue specificity and change in the pH or enzymatic action which causes degradation of drug. [17]

Rectal Delivery:

Hydrogels showing bio adhesive properties are used for rectal drug delivery. [18]

Transdermal Delivery:

The various hydrogel based drug delivery device are formed to deliver drug through transdermal route. Hydrogel based formulations are being explored for the transdermal iontophoresis to obtain enhanced permeation of products viz. hormones and nicotine.

Drug delivery in the oral cavity:

Drug is incorporated into hydrogels and delivers to oral cavity for local treatment of diseases of the mouth like stomatitis, fungal diseases, periodontal disease, viral infections & oral cavity cancers. [19]

Gene delivery:

Change in composition of the hydrogels leads to effective targeting and delivery of nuclei acids to specific cells for gene therapy. Hydrogels has more potential application in the treatment of many genetic o acquired diseases. [16]

Tissue Engineering:

Micronized hydrogels are used to deliver the macromolecules into cytoplasm of antigen presenting cells. Natural hydrogel material is used for tissue engineering include agarose, methylcellulose and other naturally derived products. [20]

Ocular drug delivery:

Hydrogels are mostly used in ocular drug delivery system. Hydrogel shows Controlled or sustain release in order to reduce the frequency of dosing or to increase the effectiveness of the drug by localization at its site of action, decreasing the dose required or providing uniform drug delivery. [21]

Figure 1 Applications of hydrogel

REFERENCES:

1. Caló E., Khutoryanskiy V.V., Biomedical applications of hydrogels: A review of patents and commercial products,Volume 65, April 2015: 252-267
2. Ahmed EM. Hydrogel: Preparation, characterization and applications: A review. Journal of Advance Research 2015; 6: 105-121.

3. Hoare T.R., Kohane D.S., Hydrogels in drug delivery: Progress and challenges,Polymer, Volume 49, Issue 8,15 April 2008:1993–2007
4. Swarbrick J., Encyclopedia Of Pharmaceutics, 4thedition,Vol II, D-F, 6000 Broken Sound Parkway NW, Suite 300, Boca Raton, FL 33487-2742, Taylor & Francis Group,, 2013
5. Robinson J., Lee V., Controlled Drug Delivery, Fundamentals and Applications, second edition, New York, 52 Vanderbuilt Avenue,Informa Healthcare USA, Inc,, 2009
6. Devi A, Nautiyal U, Kaur SK. Hydrogels: a smart drug delivery device, Asian Pacific Journal of Health Sciences. 2014; 1(4S):93-94.
7. Flowerlet M, Arya S, Mini A, Nayir SS, Joseph J, Vineetha VC *et al*. Hydrogel - A Drug Delivery Device**,** International Journal of Universal Pharmacy and Bio Sciences. 2014; 3(2):2-4.
8. Shetye SP, Dr. Godbole A, Dr. Bhilegaokar S, Gajare P. Hydrogels: Introduction, Preparation, Characterization and Applications, International Journal of Research of Research Methodology. 2015; 1(1):51-55.
9. Ahmed E.M., Hydrogel: Preparation, characterization and applications, Journal of advanced research, Volume 6, Issue 2, March 2015:105–121
10. Enas MA. Hydrogel: Preparation, characterization, and applications: A review. Journal of Advanced Research. 2015; 6:105-121.
11. Shuanhong M, Bo Y, Xiaowei P, Feng Z. Structural hydrogels, Polymer. 2016; 98:516-535.
12. Das N. Preparation Methods and Properties of Hydrogel: A Review, International Journal of Pharmacy and Pharmaceutical Sciences. 2013; 5(3):1-2.
13. Flowerlet M, Arya S, Mini A, Nayir SS, Joseph J, Vineetha VC *et al*. Hydrogel - A Drug Delivery Device**,** International Journal of Universal Pharmacy and Bio Sciences. 2014; 3(2):2-4.
14. Madolia H, Sheo DM. Preparation and Evaluation of Stomach Specific IPN Hydrogels for Oral Drug Delivery: A Review. Journal of Drug Delivery & Therapeutics. 2013; 3(2):131-140.
15. Chauhan S, Harikumar SL, Kanupriya. Hydrogels, a Smart Drug Delivery System, International Journal of Research in Pharmacy and Chemistry. 2012; 2(3):604-615.
16. Khapare SS, Bhandare MG, Talele SG, Jadhav A. An Emphasis on Hydrogels for Pharmaceutical Applications. American Journal of Pharmatech Research. 2016; 6(3).
17. Remington, the Science and Practice of Pharmacy. 21st ed., Delhi: Wolters Kluwer health Pvt. Ltd; 2006: 884.

18. Bindu SM, Ashok V, Chatterjee A. As a Review on Hydrogels as Drug Delivery in the Pharmaceutical Field. International Journal of Pharmaceutical and Chemical Science. 2012; 1(2).
19. Azevedo EPD. Chitosan Hydrogels for drug delivery and Tissue engineering applications. International journal of Pharmacy and Pharmaceutical science. 2015; 7(12).
20. Calo E, Vitaliy V, Khutoryanskiy. Biomedical applications of hydrogels: A review of patents and commercial products. European polymer journal. 2015; 65: 252-267.
21. Dubey A, Prabhu P. Formulation and evaluation of stimuli-sensitive hydrogels of timolol maleate and brimonidine tartrate for the treatment of glaucoma. International Journal of Pharmaceutical investigation.2014; 4 (3).

AJPTR is

- **Peer-reviewed**
- **bimonthly**
- **Rapid publication**

Submit your manuscript at: editor@ajptr.com