A REVIEW ON HYDROGEL

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ABSTRACT: Hydrogels are three-dimensional network structures able to imbibe large amounts of water. Hydrogels do not typically dissolve due to chemical or physical cross-links and/or chain entanglements. They exist naturally in the form of polymer networks such as collagen or gelatin, or can be made synthetically. Environmentally sensitive hydrogels can serve a wide variety of applications because of their ability to respond to environmental changes, typically by exhibiting changes in volume. Traditional stimuli that elicit hydrogel response are pH, temperature, and ionic strength. Analytes and biomarkers including glucose, proteins, and DNA also elicit hydrogel responses. Because of such a wide variety of response triggers, hydrogels can be incorporated into sensors or actuators, or can be utilized in controlled drug delivery systems, biosensors, tissue engineering scaffolds, artificial organs, wound healing bandages, physiological membranes, contact lenses, and microfluidic valves.

Keywords; Hydrogel, synthetic polymer, homo polymer, co-polymer.

INTRODUCTION

Hydrogels are three dimensional, cross-linked network of water–soluble polymers. Hydrogels can be made from virtually any water-soluble polymer, encompassing a wide range of chemical compositions and bulk physical properties. Furthermore, hydrogels can be formulated in a variety of physical forms, including slabs, micro-particles, nanoparticles, coating, and films. Hydrogels are commonly used in clinical practice and experimental medicine for a wide range of applications, including tissue engineering and regenerative medicine, diagnostics, cellular immobilization, separation of bio-molecules or cells, and barrier materials to regulate biological adhesions. The unique physical properties of hydrogels have sparked particular interest in their use in drug delivery application. Their highly porous structure can easily be tuned by controlling the density of cross-links in the gel matrix and the affinity of the hydrogels for the aqueous environment in which they swollen. Their porosity also permits loading of drugs into gel matrix and subsequent drug release at a rate dependent on the diffusion coefficient of the small molecule or macromolecule through the gel network. Indeed, the benefits of hydrogels for drug delivery may be largely pharmacokinetic specifically that a depot formulation is created from which drug slowly elute, maintaining a high local concentration of drug in the surrounding tissues over an extended period, although they can also be used for systemic delivery. Hydrogels are also generally highly biocompatible, as reflected in their successful use in the peritoneum and other sites in vivo. Biocompatibility is promoted by the high water content of hydrogels and the physiochemical similarity of hydrogels to the native extracellular matrix, both compositionally (particularly in the case of carbohydrate based hydrogels) and mechanically. Biodegradability or dissolution may be designed into hydrogel via enzymatic

DEFINITION

Hydrogels are three dimensional network of hydrophilic cross-linked polymer that do not dissolve but can swell in water or can respond to the fluctuation of the environmental stimuli.

Hydrogels are highly absorbent (they can contain over 90% water) natural or synthetic polymeric networks.

Hydrogel also possess a degree of flexibility very similar to natural tissue, due to their significant water content.

CLASSIFICATION OF HYDROGEL

The hydrogel products can be categorized on different bases as described below:

A. CLASSIFICATION BASED ON SOURCE

Hydrogel can be classified into two origins.

Natural origins:

Natural polymers occur in nature and can be extracted. They are often water-based.

E.g.: Natural origins; silk, wool, DNA, cellulose and proteins.

Synthetic polymers:

Include nylon, polyethylene, polyester, Teflon and epoxy.

B. CLASSIFICATION ACCORDING TO POLYMERIC COMPOSITION

The technique of preparation leads to formations of principal classes of hydrogel. These can be represented as following:

I) HOMOPOLYMERIC HYDROGELS

These are referred to polymer network which are derived from a single species of monomer, which is the basic structural unit comprising of any polymer network.

Homo polymers may have cross-linked skeletal structure dependent on the nature of the monomer and polymerization.

Cross linked homo-polymers are used in drug delivery system and in contact lenses.

Poly ethylene glycol (PEG) based hydrogels are responsive towards external stimuli and hence these smart hydrogels are widely used in drug delivery system.

eg; nylon6, nylon11, polyethylene, polypropylene.

II) COPOLYMERIC HYDROGELS

These are consisted of two or more distinct monomer species with at least one hydrophilic component, assembled in a random, block or alternating configuration along the chain of the polymer network.

eg; Acrylonitrile butadiene styrene, styrene – isoprene-styrene.

iii) MULTI-POLYMER

These are also called as interpenetrating polymeric hydrogel (IPN). An important class of hydrogels, which is made of two independent cross-linked synthetic and / or natural polymer component, confined in a network form. In semi-IPN hydrogel, one component is a cross-linked polymer and other component is a non-cross-linked polymer.

C) CLASSIFICATION BASED ON CONFIGURATION

These classification of hydrogels relies on their physical structure and chemical composition which can be illustrated as follows

- Amorphous (non- crystalline)
- Semi crystalline (A complex mixture of amorphous and crystalline phase.)
- Crystalline.

D. CLASSIFICATION BASED ON TYPE OF CROSS-LINKING

Hydrogel can be divided into two groups on the basis of cross-link junctions. Chemically cross-linked networks have stable junctions, while physical network have temporary junctions that results from either polymer chain entanglements or physical interactions, hydrogen bonds or hydrophobic interactions.

E. CLASSIFICATION BASED ON PHYSICAL APPERANCE

Hydrogels appearance as matrix, film or microsphere is dependent on the procedure of polymerization employed in the formulation process. Hydrogels may be classified into four groups on the basis of presence or

absence of electrical charges situated on the cross-linked chains.

1. Nonionic (neutral)
2. Ionic (including anionic or cationic)
3. Amphoteric electrolyte (ampholytic) comprising both acidic and basic groups.
4. Zwitter ionic (poly betaines) consisting of both anionic and cationic groups in each structural repeating unit.

ADVANTAGES OF HYDROGELS

1. Hydrogels possess a degree of flexibility very similar to natural tissue, due to their significant water content.
2. Entrapment of microbial cells within cells within hydrogel beads have advantage of low toxicity.
3. Environmentally sensitive hydrogels have the ability to sense changes of pH, temperature, or the concentration of metabolite and release their load as result of such a change.
4. . They are biocompatible.
5. . Hydrogels also possess good transport properties.
6. . Hydrogels are easy to modify.
7. . Timed release of growth factors and other nutrients to ensure proper tissue growth.
8. Hydrogel are biodegradable.
9. They can be injected.
10. More resistance to protein deposits.
11. Less drying of the lenses.
12. Lower risk of eye infection.
13. Easier handling due to increased rigidity of materials.
14. And much lower incidence of complications with extended wear use.
15. Soothing effect promotes patient acceptance.
16. Effective in hydrating wound surfaces and liquefying necrotic tissue on the wound surface.
17. Non-adherence and can be removed without trauma to the wound bed.
18. Hydrogels provide suitable semi-wet, three dimensional environments for molecular-level biological interaction.

19. Hydrogel mechanical properties are highly tunable.
20. Environment can protect cells and other substance (i.e. drugs proteins, and peptides).

DISADVANTAGE OF HYDROGELS

1. Hydrogels are expensive.
2. Hydrogels causes sensation felt by movement of the maggots.
3. Hydrogels causes thrombosis at Anastomosis sites.
4. The surgical risk associated with the device implantation and retrieval.
5. Hydrogels are non-adherent; they may need to be secured by a secondary dressing.
6. Hydrogels used as contact lenses causes lens deposition, hypoxia, dehydration and red eye reactions.
7. Hydrogels have low mechanical strength.
8. Difficulty in handling.
9. Difficulty in loading.
10. Difficulty in sterilization.
11. Difficult to co-ordinate degradation rate.
12. Mechanism of cross linking affects release profiles.
13. Toxicity posed by the chemical cross linkers.
14. Potential for maceration.
15. Requires daily changes.
16. Requires secondary dressing-unless bordered sheet.
17. Sheets cannot be used with heavy drainage.
18. Cannot act as a filler.
19. More difficult to characterize/ predict behavior.
20. Not as well defined as Stoichiometric compounds.
21. Poor oxygen transmission.
22. More dryness.
23. Greater care and maintenance.
24. Limited parameters available.

SIGNIFICANT PROPERTIES OF HYDROGEL

SWELLING PROPERTIES

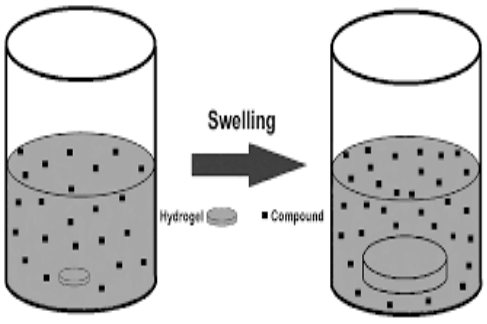
Hydrogels are the swollen polymeric network, interior of which is occupied by drug molecules, therefore, release studies are carried out to understand the mechanism of release over a period of application. Swelling property influenced by: Type and composition of monomers, Other environmental factors such as: temperature, pH, ionic strength, Cross-linking (mechanical strength and permeability).

Rs = (Ws-Wd)/ Wd

Rs = swelling ratio

Ws= weight of swollen hydrogels

Wd = weight of dried hydrogels



MECHANICAL PROPERTIES

Mechanical properties of hydrogels are very important for pharmaceutical applications. For example, property of maintaining its physical texture during the application of drug delivery. Changing the degree of cross-linking has been utilized to achieve the desired mechanical property of the hydrogel. However, a higher degree of cross-linking creates a more brittle structure.

BIOCOMPATIBLE PROPERTIES

It is important for the hydrogels to be biocompatible and non-toxic in order to make it applicable in biomedical field. Cell culture methods, also known as cytotoxicity tests, be used to evaluate the toxicity of hydrogel. Water holding capacity and permeability are the most important characteristic features of a hydrogels. Bio-compatibility is third most important characteristic property required for hydrogels.

PREPARATIONS OF HYDROGELS

On the whole, hydrogels can be formulated from either synthetic polymers or natural polymers. The synthetic polymers are hydrophobic in nature and chemically stronger in comparison to natural polymers. Their mechanical strength brings about slow degradation rate, but on the other hand, mechanical strength offers the sturdiness as

well. These two opposite properties should be balanced through optimum design. Water-soluble linear polymers of both natural and synthetic origin are cross-linked to form hydrogels in various ways

a. Linking polymer chain via chemical reactions.
b. Using ionizing radiation
c. Physical interactions such as entanglements, electrostatics and crystalline formation.

Generally, the three integral parts of the hydrogels preparation are monomer, initiator and cross linker. To regulate the heat of polymerization and the final hydrogels properties, diluents can be employed in the formulations, such as water or other aqueous solutions.

Hydrogels are normally prepared from polar monomers. According to their starting materials, they can be categorized into natural polymer, synthetic polymer and combinations of the two.

Bulk polymerization

Many vinyl monomers can possibly be employed for the fabrication of hydrogels. Bulk hydrogels can be obtained with one or more type of monomers. Ordinarily, a small amount of cross-linking agent is supplemented for hydrogel formulation. The polymerization reaction is typically initiated with radiation, ultraviolet or chemical catalysts. The selection of an appropriate initiator relies upon the type of monomers and solvents being used. The polymerized hydrogel may be yielded in a wide range of forms counting the films and membranes, rods, particles and emulsions. Bulk polymerization is the straightforward technique, which includes only monomer and monomer soluble initiators. The viscosity of reaction enhances significantly with the conversion which generates the heat during polymerization. These problems can be prevented by regulating the reaction. The bulk polymerization of monomers to make homogeneous hydrogel. Yields a glassy, transparent polymer matrix which is very tough. When placed in water, the glassy matrix swells to become soft and flexible.

Solution polymerization/ cross-linking

In solution copolymerization / cross-linking reactions, the ionic or neutral monomers are

blended with the multifunctional cross-linking agent. The polymerization is instigated thermally by UV/IR radiation or by a redox initiator system. The prepared hydrogels require washing with distilled water to eliminate the monomers, oligomers, cross-linked agent, the initiator, the soluble and extractable polymer and other impurities.

Phase separation takes place and the heterogeneous hydrogel is formed when the quantity of water during polymerization is more than the water content in proportion to the equilibrium swelling. Usual solvents utilized for solution polymerization of hydrogels include water, ethanol, water-ethanol mixtures and benzyl alcohol.

Suspension polymerization or inverse-suspension polymerization Dispersion polymerization is a worthwhile technique since the products are acquired as powder or microspheres (beads) and thus, grinding is not needed.

Since water-in-oil (w/o) process is selected in preference to the more common oil-in-water (O/W), the polymerization is denoted as "inverse suspension". In this method, the monomers and initiator are distributed in the hydrocarbon phase as a homogenous mixture. The viscosity of the monomer solution, agitation speed, rotor design and dispersant type chiefly regulates the resin particle size and shape. Several comprehensive discussions on hetero-phase polymerizations have been published previously. The dispersion is thermodynamically unsteady and necessitates both continuous agitation and addition of a low hydrophilic-lipophilic-balance (HLB) suspending agent Hydrogels are the organic polymer; two types of polymer are available

Natural polymers e.g. Dextran, Chitosan, Collagen, Dextran sulfate

Disadvantage:

- Low mechanical strength
- Batch variation
- Animal derived materials may pass on viruses.

Synthetic polymer e.g. Poly (vinyl alcohol)

Disadvantages:

- Low biodegradability
- Can include toxic substances

USES OF HYDROGELS

- Hydrogels are used dressings consist of 90% water in a gel base, serves to help monitor fluid exchange from within the wound surface.
- Used in diverse field of surgery and medicine.
- Mainly used for contact lenses.
- Successfully developed as drug delivery.
- Diagnostic labels detectable by CT or MR imaging technique.
- Administered intra-vascular as well as by implantation.
- Used in biotechnology that are responsive to specific molecules, such as glucose or antigens.
- Used in sanitary purpose in disposable diapers where they absorb urine, or in sanitary napkins.
- Used as medical electrodes in ECG
- Used as breast implants.
- Used in hygiene products.
- Used in tissue engineering.

APPLICATION OF HYDROGELS IN DRUG DELIVERY

- Transdermal drug delivery
- Perioral drug delivery
- Drug delivery in the oral cavity
- Ocular delivery
- Subcutaneous drug delivery
- Hydrogels to fix bone replacements
- Tissue engineering
- Protein drug delivery
- Topical drug delivery
- Drug delivery through the oral route has been the most common method in the pharmaceutical applications of hydrogels.
- In perioral administration, hydrogels can deliver drug to four major specific sites; mouth, stomach, small intestine and colon.
- Drug delivery in the oral cavity

Drug delivery to the oral cavity can have versatile application in local treatment of

disease of the mouth, such as periodontal disease, stomatitis, fungal and viral infection, and oral cavity cancers.

- Drug delivery in G.I.T

Hydrogel-based devices can be designed drugs locally to specific sites in the GI tract. e.g. specific antibiotic drug delivery systems for the treatment of H. pylori infection in peptic ulcer disease.

- Ocular delivery

Silicone rubber hydrogel composite ophthalmic insert extended the duration of the pilocarpine to 10 hr, compared to 3hr when pilocarpine nitrate was dosed as a solution.

- Trans dermal delivery

  Drug delivery to skin has been generally used to treat skin disease or for disinfections of the skin.Trans-dermal route is employed for systemic delivery of drugs.

- Subcutaneous delivery

  Subcutaneously inserted exogenous materials may more or less evoke potentially undesirable body responses, such as inflammation, carcinogenicity and immunogenicity.

- Hydrogels to fix bone replacements

  Provided orthopedic fasteners and replacements hip and knee replacements, etc. are coated with hydrogels which expand in the presence of liquids.

- Protein drug delivery
- Better patient compliance.
- Hydrogels form in-situ and release proteins slowly
- They are biodegradable and biocompatible.
- Topical drug delivery

  Hydrogels are used to deliver drug like desonide (synthetic corticosteroid) usually used as an anti-

inflammatory.Hydrogels with their moisturizing properties avoids scaling and dryness and has better patient compliance.

- Tissue engineering
- Micro-gels can be used to deliver macromolecules like phagosomes in to cytoplasm of antigen – presenting cells.

CONCULUSION

Novel hydrogel systems have been devised in current years. In terms of application, hydrogels are under research as matrices for the living cells encapsulation and for the pharmaceutically. Too many cross-linking methods have been devised and are currently available for hydrogel synthesis A number of physical cross-linking methods have been devised; there is undoubtedly a need for other methods. Supra –molecular chemistry principles will be used to devise new kind of gels with modifiable characteristics which may be synthesized preferably in aqueous environment.

Recently, many hydrogels based networks have been designed and tailored to meet the needs of different applications. The favorable property of these hydrogels is either ability to swell when put in contact with an aqueous solution. The presented review demonstrates the literature concerning classification of hydrogel on different bases, physical and chemical characteristics of these products and technical feasibility of their utilization.

REFERENCE

1. Sweta Garg, Ashish Garg. Hydrogel. Hydrogel: classification, properties, preparation and Technical Features, 2016; 2(6); page no.(164)
2. M. Ebara et al. classification of hydrogel. smart hydrogel, 2014; 5(2); page no.(11)Hennink WE, Van nostrum
3. CF. Smart hydrogel. Novel cross linking methods to design hydrogels, 2002; 9(12); page no. (54)
4. Ma Y, Lee P. Smart Hydrogel. hydrogel: preparation, characterization, and application: A review, 2009; 18(4); page no.(307)
5. Turakhiya jignesh M et al. A Super porous hydrogel. Approach for controlled drug delivery, 2013; 2(1); page no.(47-58).

6. Francis S, Mitra D, Dhanawade BR, Varshney L, sabharwal S. hydrogel. Gamma radiation synthesis of rapid swelling super porous polyacrylamide hydrogels, 2009; 78(11); page no.(951-3)
7. Zhang Ling et al. hydrogel. preparation of collagen- chondroitin sulfate- hyaluronic acid hybrid hydrogel scaffolds and cell compatibility in vitro,2001; 84(1); page no.(118-25).
8. Sun X, Zhang G, Shi Q, Tang B, Wu ZJ. Hydrogel. Preparation and characterization of water- swellable natural rubbers, 2002; 86(1); page no.(3212-717)'
9. Talaat HA et al. Hydrogel: preparation, characterization, and application. Development of a multi component fertilizing hydrogel with relevant techno-economic indicator. 2008; 3(5); page no.(764-70).
10. Ajji Z, Mirjalili G, Alkhatab A, Dada H. hydrogel. Use of electron beam for the production of hydrogel dressings, 2008; 77(2); page no.(200-2).
11. Y. S. Lipatov,―Polymer blends and interpenetrating polymer networks at the interface with solids,‖ Progress in Polymer Science (Oxford), 2002; 27(9): 1721–1801.
12. 12. A Singh, P. K. Sharma, V. K. Garg, and G. Garg, ―Hydrogels: a review.‖
13. T. Funami, M. Hiroe, S. Noda, I. Asai, S. Ikeda, and K. Nishinari, ―Influence of molecular structure imaged with atomic force microscopy on the rheological behavior of carrageenan aqueous system in the presence or absence of cations,‖ Food Hydrocolloids, 2007; 21; 617–629.
14. D. Magnin, J. Lefebvre, E. Chornet, and S. Dumitriu, ―Physicochemical and structural characterization of a polyionic matrix of interest in biotechnology, in the pharmaceutical and biomedical fields,‖ Carbohydrate Polymers, 2004; 55: 437–453.
15. C. Chang, L. Zhang, J. Zhou, L. Zhang, and J. F. Kennedy, ―Structure and properties of hydrogels prepared from cellulose in NaOH/urea aqueous solutions,‖ Carbohydrate Polymers, 2010; 82(1): 122–127.