Review Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: **www.ijrpns.com**

A REVIEW ARTICLE ON HYDROGELS

Pulasani Sowjanya*[1], Boddu Venkata Komali [1], CH. Ajay Babu[1]

[1*]Department of Pharmaceutics, Narasaraopet Institute of Pharmaceutical Sciences, Narasaraopet, Guntur (Dt), Andhra Pradesh, India.

ABSTRACT

For the treatment of many diseases large molecular weight protiens are required. These can be available with the availability of Hydrogels. Hydrogels are hydrophilic, three-dimensional networks, which are able to imbibe large amounts of water or biological fluids, and thus resemble, to a large extent, a biological tissue. They are insoluble due to the presence of chemical (tie-points, junctions) and/or physical crosslinks such as entanglements and crystallites. These materials can be synthesized to respond to a number of physiological stimuli present in the body, such as pH, ionic strength and temperature. The main aim of the current article is to describe about all the information of Hydrogels.

KEYWORDS

Hydrogels, Crystallites, Hydrophilic, Biological tissue and Proteins.

Author for Correspondence:

Pulasani Sowjanya,

Department of Pharmaceutics,

Narasaraopet Institute of Pharmaceutical Sciences, Narasaraopet, Guntur, Andhra Pradesh, India.

Email: sowjanya.pulasani@gmail.com

INTRODUCTION[1,2,3]

By definition, hydrogels are polymeric networks with three-dimensional configuration capable of imbibing high amounts of water or biological fluids. Their affinity to absorb water is attributed to the presence of hydrophilic groups such as –OH, –CONH–, –CONH2–, and –SO3H in polymers forming hydrogel structures. Due to the contribution of these groups and domains in the network, the polymer is thus hydrated to different degrees (sometimes, more than 90%wt.), depending on the nature of the aqueous environment and polymer composition. They are insoluble due to the presence

of chemical and/or physical crosslinks such as entanglements.

The term hydrogels implies that the material is already swollen in water, the dried hydrogels is called a xerogels. During the drying process, water evaporate from the gel and the surface tension causes collapse of the gel body, if water is removed without disturbing the polymeric network, either by lyophilization or by extraction with organic solvents, then the remaining material is extremely light with a porosity as high as 98%, such a dehydrated hydrogel is called aero gel. Hydrogels have been widely used as a drug carrier due to its ease in manufacturing and self-application. The production of a large and constant surface area is one of the major merits for them to be widely used for clinical and fundamental applications. Various combinations of polymers are made into hydrogel formulations to investigate their potential as a drug delivery system. The combination of natural and synthetic polymers may provide mechanical stability and biological acceptability, acquiring from synergistic properties of both materials. The Hydrogels were found stable and resilient .The existence of Hydrogels dates back to 1960, when Wichterle and Lim first proposed the use of hydrophilic networks of poly(2-hydroxyethyl methacrylate) (PHEMA) in contact lenses. Since then, the use of Hydrogels has extended to various biomedical and pharmaceutical applications. Antibiotics loaded interpenetrating network hydrogel based on poly(acrylic acid) and glutaradehyde for treatment of experimental H pylori. IPN Hydrogels such as gelatin and dextran are widely used as a drug carrier due to their biodegradability and removable versatility in terms of composition and size. Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fuids.[6,7] The networks are composed of homopolymers or copolymers, and are insoluble due to the presence of chemical crosslinks (tie-points, junctions), physical crosslinks, such as entanglements or crystallites.8-15 The latter provide the network structure and physical integrity. These Hydrogels exhibit a thermodynamic compatibility with water which allows them to swell in aqueous media. [6,7,15-16]

There are numerous applications of these Hydrogels in particular in the medical and pharmaceutical sectors.[17-18] Hydrogels resembles natural living tissue more than any other class of synthetic biomaterials. This is due to their high water contents and soft consistency which is similar to natural tissue.[17] Furthermore, the high water content of the materials contributes to their biocompatibility. Thus, Hydrogels can be used as contact lenses, membranes for biosensors, linings for artificial hearts, materials for artificial skin, and drug delivery devices.[17-19] Hydrogels are also used as carriers that can interact with the mucosa lining in the gastrointestinal (GI) tract, colon, vagina, nose and other parts of the body due to their ability to prolong their residence time at the delivery location. The interaction between such carriers and the glycoprotein's in the mucosa is thought to occur primarily via hydrogen bonding. Therefore, materials containing a high density of carboxyl and hydroxy groups appear to be promising for this type of application. Monomers most often used for the synthesis of mucoadhesive polymers include acrylic and methacrylic acid (MAA). The idea of adhesion promoters diffusing across the polymer/mucin interface has also been introduced.[21] Chains of polymerized ethylene glycol either freely loaded in the carrier or grafted to the polymer surface, have been utilized as adhesion promoters.[21]The `stealth' properties of poly(ethylene glycol), known also as PEG, have also been used to reduce the uptake of particulate carriers by the reticuloendothelial system.[22] PEG has also been shown to both lengthen the biological half-life and reduce the immunogenicity of high molecular weight substances, such as adenosine de-aminase (ADA) and asparaginase.[23]

CLASSIFICATION[5,6,7]

Hydrogels can be classified as follows:

- Based on the nature of the side group: Neutral or Ionic
- Based on their mechanical and structural

characteristics: Affine or Phantom networks.

- Based on the method of preparation: Homopolymer or Copolymer networks.
- Based on the physical structure of the networks: Amorphous, semi crystalline, Hydrogen bonded super molecular structures or Hydro colloidal aggregates.
- Based on the mechanism controlling the drug release: Diffusion controlled, swelling controlled, chemically controlled or environmentally responsive release systems.

METHOD FOR PREPARATION OF HYDROGEL

Cross-linked networks of synthetic polymers such as polyethylene oxide (PEO), polyvinyl pyrollidone (PVP), polylactic acid (PLA), polyacrylic acid (PAA) polymethacrylate (PMA), polyethylene glycol (PEG), or natural biopolymers such as alginate, chitosan, carrageenan, hyaluronan, and carboxymethyl cellulose (CMC) have been reported. The various preparation techniques adopted are physical cross-linking, chemical cross-linking, grafting polymerisation, and radiation cross-linking. Such modifications can improve the mechanical properties and viscoelasticity for applications in biomedical and pharmaceutical fields.

SYNTHETIC POLYMER HYDROGELS FOR BIOMEDICAL APPLICATIONS[10]

Poly (hydroxyethyl methacrylate)

Known for many years, poly (hydroxyethyl methacrylate) (polyHEMA, PHEMA) (Fig. 1) is one of the most important and most widely applied hydrogel biomaterials. Since 1955 it has been modified with many natural and synthetic substances and by various methods, and has been applied in the production of contact lenses and dressings, and for drug delivery and tissue engineering purposes.

Polyethylene Glycol and Derivatives

Poly (ethylene glycol) (PEG), otherwise known as poly (oxyethylene) or poly (ethylene oxide) (PEO), is one of the most widely used hydrogels in medicine and biomedicine. Hydrogels based on its derivatives – polyethylene glycol methacrylate (PEGMA), polyethylene glycol dimethacrylate (PEGDMA) and polyethylene glycol diacrylate (PEGDA) – are likewise widely applied.

PEG hydrogel drug release systems are stimuli sensitive and react in the presence of a physical or chemical (biological) agent. Because of their unique properties, hydrogels used for these kinds of drug release systems are called “smart” or “intelligent gels”. Physical stimuli include temperature, solvent, light, radiation, pressure, a magnetic, acoustic or electrical field, while the chemical and biological stimuli include pH, specific ions, and molecular recognition events

Poly (vinyl alcohol)

Beyond the advantages of typical hydrogel materials (ability to absorb water, gas permeability, soft tissue imitation, flexibility and biocompatibility), polyvinyl alcohol (PVA)-based hydrogels are distinguished by their good mechanical properties and the ability to retain water in the structure, which ensures a prolonged moist environment. PVA hydrogels are used in contact lens production, cartilage reconstruction and regeneration, artificial organs, drugs systems and wound dressings, providing the humid environment beneficial for wound healing

Polyvinylpyrrolidone

Next to PVA hydrogels, another group widely used in biomedical applications is hydrogels based on polyvinyl pyrrolidone (PVP). They are present in DDSs and wound dressings and are usually obtained with the radiation technique, an apparently simple, efficient, clean and environmentally friendly process. The application of radiation in the formation of hydrogels for biomedical use offers a unique opportunity to combine the formation and sterilization of a product in one single technological step. PVP hydrogels can thus be regarded as advantageous owing to their simple formation and lower production costs, softness and elasticity; their ability to store large amounts of liquid while retaining quite good mechanical properties makes them optimal candidates for the manufacture of dressings.

Polyimide

Like PVA hydrogels, polyimide (PI) hydrogels are used mainly in plastic and reconstructive surgery. They can imitate soft tissue, contain a great amount of water, and have the required mechanical strength and a high level of biocompatibility. They are soft, transparent and have good permeability – oxygen passes through them especially easily.

Polyacrylate

Polyacrylate (PA) hydrogels, mainly polyacrylamide (PAA), are used in many branches of industry, most commonly as agricultural gels. They also play an important role in biomedical applications in aesthetic corrections, as soft tissue fillers and augmentation materials.

Polyurethane

Recent years have witnessed an upsurge in interest in polyurethane (PU) hydrogels. The specificity of PU hydrogels is based on their wide variety of final product properties depending on their chemical structure and monomers, which also makes for extensive bio-applications.

CHARACTERIZATION OF HYDROGELS[11,12]

Morphological characterization Hydrogels are characterized for morphology which is analyzed by equipment like stereomicroscope. Also the texture of these biomaterials is analyzed by SEM (Scanning Electron Microscope) to ensure that hydrogels, especially of starch, retain their granular structures.

Fourier Transform Infrared Spectroscopy (FTIR)

Analysis FTIR spectra of hydrogel are recorded using FTIR spectrophotometer to determine their structure and intermolecular interactions. Thoroughly ground IPN samples are mixed with dried KBr and discs are be prepared by compression under vacuum. Spectra are recorded with a resolution of 1 cm-1.

Swelling Studies of IPN hydrogel

The swelling studies of IPN hydrogel are studied by placing a known weight of hydrogels in 0.1 N HCl at 370 C. During swelling the gels are removed every 1 hr interval and their surface are dried and a low equilibrium degree of swelling and thus may filter paper weight are recorded. The swelling process is characterized by following relationship:

Swelling ratio% = Ws-Wd/Wd * 100,

Where Ws- Weight of swollen hydrogels

Wd- weight of dry hydrogels

HYDROGELS IN DRUG DELIVERY

Hydrogels were studied as antibiotics and anticancer drug delivery depots soon after their discovery. Initial studies concentrated on polyHEMA, with later studies focused on hydrogels based on HEMA copolymers, polyacrylamide, N-vinylpyrrolidone copolymers, and polyvinylalcohol. HEMA hydrogels were studied as matrices for protein delivery. Different chemical structures have been tailor-made to match the physiological need. For example, HPMA copolymer based hydrogels were synthesized with entrapped anticancer drugs or containing degradable oligopeptide crosslinks and the drug (DOX) bound via a degradable oligopeptide spacer. Various natural polysaccharides were used for drug delivery; poly-alginate hydrogels were designed to permit combination delivery of anticancer drugs with different release profiles.

Crosslinking hydrogels with compounds that contain an aromatic azo-bond endows them with colon-specific degradability. Due to a low proteolytic activity in the colon, these hydrogels are being developed for protein delivery. Changes in pH affect the ionization state and hydrophilic/hydrophobic balance in these hydrogels, shifting the LCT above or below ambient temperature. Also, ionized monomer units and their counter ions engender an osmotic pressure that affects swelling equilibrium. For example, copolymers of *N*,*N*- dimethyl acrylamide with acrylic acid (to introduce pH-sensitivity), *N*-tert.-butylacrylamide (to improve mechanical properties), and a crosslinking agent such as 4,4′-di(methacryloylamino)azobenzene are suitable for colon delivery of proteins. Following oral administration, the hydrogel delivery system reaches first the stomach; at the low pH, the hydrogels have protect the peptide or protein drug against digestion

by proteolytic enzymes. As the gels pass down the GI tract, swelling increases due to ionization of carboxylic acid groups in response to pH increase. Finally, in the colon, the aromatic azo bonds are reduced, the hydrogel disintegrates and the protein is released into an environment of low proteolytic activity. Dextran hydrogels are also suitable as colon-specific drug delivery systems, due to microbial dextranase activity in the colon.

An example of a combination of stimuli-sensitivity and drug delivery are hydrogel-based mimics of secretory granules containing the anticancer drug doxorubicin (DOX). A microgel prepared by copolymerization of methacrylic acid with methylene-bis-acrylamide was loaded with DOX and then coated with a phospholipid bilayer. The hydrogel microspheres exhibited pH- and ion-dependent volume phase transitions and were suitable for triggered DOX release.

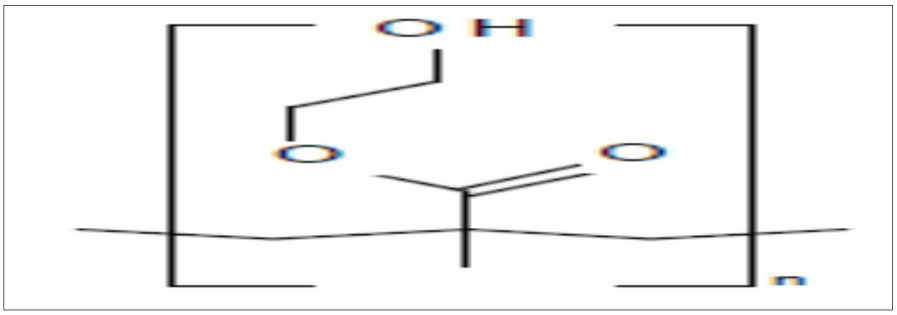

Figure No.1: Chemical structure of Poly (hydroxyethyl methacrylate)

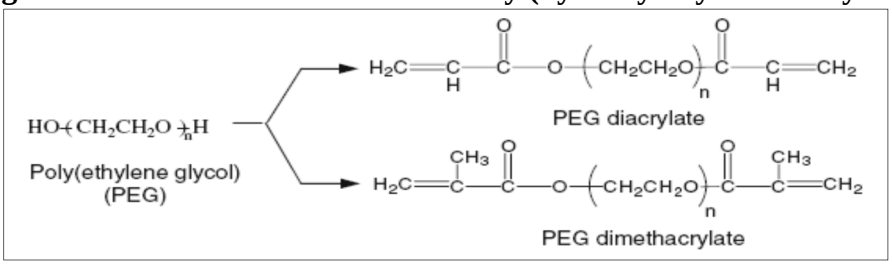

Figure No.2: Polyethylene glycol and its derivatives

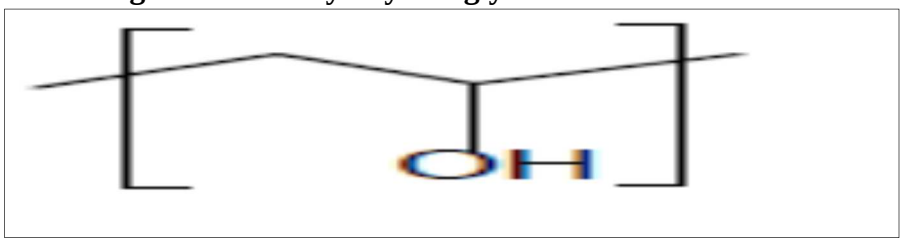

Figure No.3: Poly (vinyl alcohol)

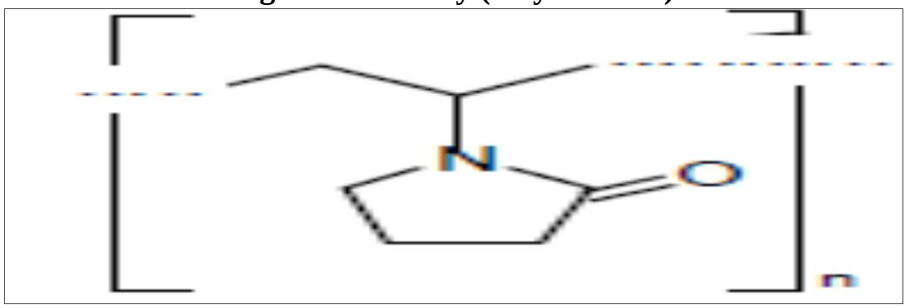

Figure No.4: Poly vinyl pyrrolidone

CONCLUSION

The goal of drug delivery is to maintain the drug concentration in the body (plasma) within therapeutic limits for long periods of time. However, the high water content of most hydrogels results in relatively rapid release of drugs from the gel matrix, particularly in the case of hydrophilic drugs for which hydrogel delivery is typically applied. In this context, a range of strategies have been explored to reduce the release rate of drug from hydrogels either by enhancing the interactions between the drug and the hydrogel matrix and/or by increasing the diffusive barrier to drug release from the hydrogel.

ACKNOWLEDGEMENT

The authors are sincerely thanks to the Narasaraopet Institute of Pharmaceutical Sciences, Narasaraopet, Guntur (Dt), AP, India for providing the facilities to complete this review work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Lee K Y, Mooney D J. Hydrogels for Tissue Engineering. *Chemical Reviews*, 101(7), 2001, 1869-1880.
2. Dagani, R. Intelligent gels, *Chem. Eng. News*, 75(23), 1997, 26–36.
3. Harvey J A. Smart materials, In Encyclopedia of Chemical Technology, 2nd edition, 1995, 502–514,
4. Kost J. Intelligent drug delivery systems, *In Encyclopaedia of Controlled Drug Delivery*, 1(2), 1999, 445–459.
5. Todd R. Hoare, Daniel S Kohane, Hydrogels in drug delivery: Progress and challenges Polymer. 3rd edition, 49(8), 2008, 1993-2007.
6. Park K, Shalaby W S W, Park H. Editors, Biodegradable Hydrogels for Drug Delivery, *Technomic, Lancaster, PA*, 14, 1993, 1065-1072.
7. Harland R S, Prud homme R K. Editors, Polyelectrolyte Gels: Properties, Preparation, and Applications, *American Chemical Society*, Washington, DC, 1992.
8. Ulbrich K, Subr V, Podperova P, Buresova M. Synthesis of novel hydrolytically degradable hydrogels for controlled drug release. *J. Controlled Release,* 34(2), 1995, 155–165.
9. Hoffman A S. Intelligent polymers, In Controlled Drug Delivery, *American Chemical Society*, Washington, DC, 15(9), 1997, 364-9.
10. Hoffman A S. Hydrogels for biomedical applications, *Advanced Drug Delivery Reviews*, 54(1), 2002, 3-12.
11. Wichterle O, Lim D. Hydrophilic gels in biologic use. *Nature*, 185(4706), 1960, 117.
12. Campoccia D, Doherty P, Radice M, Brun P, Abatangelo G, Williams D F. Semisynthetic resorbable materials from hyaluronan esterification. *Biomaterials,* 19(23), 1998, 2101–2127.
13. Pal K, Banthia A K, Majumdar DK. Preparation of novel pH-sensitive hydrogels of carboxymethyl cellulose acrylates, A comparative study. *Materials and Manufacturing Processes*, 21(8), 2006, 877-882.

Please cite this article in press as: Pulasani Sowjanya. *et al.,* A review article on hydrogels, *International Journal of Research in Pharmaceutical and Nano Sciences,* 2(5), 2013, 548-553.