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**REVIEW ARTICLE**

# CLASSIFICATION AND APPLICATIONS OF HYDROGEL AN OVERVIEW

Tahreem S.S.*

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**ABSTRACT:**

Hydrogels are a group of hydrophilic polymeric materials which has the capability to hold abundant water within their 3D networks. Research on hydrogels has been increased especially in biomedical application owing to their relatively high biocompatibility. At first hydrogels' only hydrophilic nature and large swelling properties were explored. Persistent and continuous research have resulted in various types of hydrogels. Literature on this subject is found to be expanding especially in the area of research. The article's primary objective is to review the literature concerning the hydrogels classification on the bases of their physical, chemical characteristics of the products, and technical feasibility of their utilization. Applications of hydrogels ranging from pharmaceutics, biomedical to biotechnology are summarized.

***Keywords:*** Hydrogels, crosslinking network, biomedical, biotechnology, 3D network.

**Corresponding author:** Ms. Shaikh Sana Tahreem
**Address:** Yash Institute of Pharmacy, Aurangabad.
**Email-** ssanatahreem@gmail.com


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## INTRODUCTION:

Hydrogels involves a hydrophilic polymers network arranged in a 3D network containing water. To maintain the 3D structure of a hydrogel the polymeric chain is usually cross linked chemically or physically. Chemically linked hydrogels are bonded covalently and therefore are more stable and difficult to change their shapes.

Alternatively, physically linked polymeric chain possesses non- covalent bonds viz. van der Waals interaction, ionic interactions, hydrophobic interactions or hydrogen bonding[i]. Physical gels possess sol-gel reversibility since the bonds involved in them are reversible.

In biomedical world the relevance of hydrogels was drastically increased by the landmark paper published by Wichterle and Lim on poly (2-hydroxyethyl methacrylate) or p (HEMA)[ii]. Since then the research work has been steadily increased on hydrogel. The research work on hydrogel began to take off in the end of 1970's. The number increased dramatically in 1994. The involvement of various scientists resulted in more understanding on the physicochemical properties of hydrogels and development of new types of hydrogels. [iii, iv]

## CLASSIFICATION OF HYDROGELS:

The classification of hydrogel products can be done on different basis as stated below:

**A. Classification based on the source:**

This classification can be done into two groups based on their origin i.e., natural or synthetic origins[v].

**Classification according to their polymeric composition:**

The different method of preparation paves the way to formations of several significant classes of hydrogels. These can be epitomized by the following:

a. Homopolymeric hydrogels are derived from a monomeric unit of single species of a polymer network, comprising of a basic structural unit[vi].
b. Homopolymers might have cross-linked skeletal framework depending on the polymerization technique and nature of the monomer.
c. Copolymeric hydrogels comprises of two or more different monomer species with at least a hydrophilic component, arranged in a random, block or alternating configuration all along the chain of the polymer network[vii].
d. Multipolymer Interpenetrating polymeric hydrogel (IPN) an essential class of hydrogels is prepared of two independent (cross-linked) polymers (synthetic and/or natural components) which are enclosed in a network form. One component is cross-linked polymer and other component is non-cross-linked polymer such networks are found in semi- IPN hydrogels[viii,ix].

**B. Classification based on configuration:**

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

a. Amorphous (non-crystalline).
b. Semi crystalline: A complex mixture of amorphous and crystalline phases.
c. Crystalline.

**C. Classification based on the type of cross-linking involved:**

Based on the cross-link junctions' hydrogels are divided into two categories i.e., chemical or physical nature. Permanent junctions are found in chemically cross-linked networks, whereas transient junctions are found in physical a network which arises from either physical interaction such as ionic interactions, hydrogen bonds, or hydrophobic interactions or polymer chain entanglementsix.

**D. Classification based on the physical appearance of hydrogels:**

The appearance of hydrogels as a matrix or a film, or a microsphere depends upon which technique of polymerization was used in that hydrogels preparation process.

**E. Classification based on the network electrical charge:**

Hydrogels may be sort out into four groups depending on the electrical charge's presence or absence of which is positioned on the cross-linked chains:

a. Nonionic (neutral).
b. Ionic (either anionic or cationic).
c. Amphoteric electrolytes (ampholytic) having both acidic-basic groups.
d. Zwitterionic (polybetaines) that contains both anionic-cationic groups in each of their structural repeating unit.

Hydrogel-forming natural polymers comprises of proteins such as collagen, gelatin and various polysaccharides. Traditional chemical polymerization methods are used to form hydrogels.

**NEW TYPES OF HYDROGELS:**

The capacity of hydrogels to perform additional functions is termed as 'smart' or 'intelligent' hydrogels. [x]

**a) Environment sensitive hydrogels:**

The capability of hydrogels to swell up in the water's presence and shrivel in the absence is inherent and cannot be particularly of great interest. Recent studies have proposed that hydrogels' swelling and shrinking property is well responsive to produce signals.

This property of hydrogels is used to determine alter in environmental conditions in which they swell, shrink, bend or degrade and therefore are very well known as 'environment sensitive hydrogels'.

The swelling ratio property which us the volume of the swollen hydrogel divided by the volume of dried hydrogel).The change in the swollen ratio changes as a result of only a minute change in environmental factors. [xi]

**b) Thermoplastic hydrogels:**

A unit of physical hydrogel possesses thermoplastic property.[xii] The thermoplastic hydrogels are found to be linear copolymers of hydrophobic and hydrophilic monomers.

They possess solubility in most of the organic solvents and swell only in water (insoluble). This serves advantageous in ease of processibility. Examples of thermoplastic hydrogels include copolymers of N-vinyl-2-pyrrolidine and methyl methacrylate which serves properties like film forming capability and melt processibility. [xiii]

**c) Hydrogel Foams:**

While hydrogels enlarge to a great extent in water, the equilibrium swelling usually gets tedious (from hours to days) depending on the size and shape of hydrogels. To trounce this leisurely swelling hydrogels, the hydrogel foam was lately developed. [xiv, xv] In the environment of gas bubbles hydrogels foams were prepared. The hydrogel foams prepared by means of macroscopic gas cells are poles apart from hydrogel sponges[xvi] or macro porous hydrogels[xvii]. The pores size in the hydrogel foam are in orders of magnitude larger than the pore size (which is typically a few micrometers) in hydrogel sponges or macro porous hydrogels. In addition, the kinetics and the amount of swelling of hydrogel foams are much faster and larger than others. Diffusion of water through glassy layer of the dried hydrogels is the rate limiting step. Therefore the swelling is tedious in many applications. It is also observed that the hydrogel foams swell rapidly as water is absorbed through pores (capillary reaction in the dried hydrogels) rather than the diffusion of a glassy layer. Recently developed comb-type grafted hydrogels [xviii] showed faster deswelling but the swelling was still quite slow. The hydrogel foams made of poly (acrylic acid) can swell more than thousand times its original size. The property of expeditious swelling with a very large swelling ratio of hydrogel foams should be useful in many bioapplications.

**d) Ligand specific Sol-Gel Phase Reversible Hydrogels:**

As mentioned earlier physically linked hydrogels possess a property of undergoing sol-gel phase transitions due to non-covalent crosslinking of polymer chains. There are only few hydrogels which undergoes such a phase change in response to interaction with specific molecules. Hydrogels made up of boronic acid involving polymers and polyvinyl alcohol) are known to degrade in the existence of glucose in the environment[xix,xx, xxi]

## e) Pharmaceutical applications:

Hydrogels' applications are involved in controlled drug delivery. While zero-order drug release is essential for most drugs, many drugs need to be delivered in a pulsatile fashion. The most widely used example is the delivery of insulin. Temporal control of insulin delivery can be achieved by utilization of smart hydrogels which release more insulin in response to increase in glucose level. Most glucose-responsive hydrogel systems are made of pH-sensitive polymers such as poly (diethylaminoethyl methacrylate) (PDEAEMA)[xxii,xxiii, xxiv] and glucose oxidase, which transforms glucose into gluconic acid. On the other hand, the presence of pH-responsive hydrogels, the discovery glucose-sensitive dissolvable hydrogels is used to control the insulin release. x, [xxv] Micro spherical hydrogels such as alginate micro particles have been used to encapsulate insulin-producing cells for the delivery of insulin[xxvi]. Pulsatile delivery of drugs can also be achieved by temperature-responsive hydrogels. Thermo-sensitive hydrogels are usually prepared with polyacrylamide derivatives with hydrophobic groups which help in promoting hydrophobic interactions which is necessary for shrinking at elevated temperatures. The volume collapse temperature can be adjusted by varying the hydrophobic groups. By altering the temperature around the thermo sensitive hydrogels, the release of drug from the gel can be turned on and off at will[xxvii, xxviii]

## BIOMEDICAL APPLICATIONS:

Hydrogels applications in biomedical world are sundry that can be ranging from diagnostic devices[xxix] to artificial muscles[xxx]. Application of hydrogels in preparation of contact lenses and intraocular lenses has a rather long history compared with other applications. Soft contact lenses made of hydrogels possess desirable properties such as high oxygen permeability, although they have problems of protein deposits and lens spoliation[xxxi]. Soft intraocular lenses possess advantages over rigid types. Their ability to be folded allows surgeon to use a much smaller surgical incision[xxxii]. The hydrogel contacts and intraocular lenses can be sterilized by autoclaving, which is more convenient than the sterilization by ethylene oxide needed for rigid lenses made of poly (methyl methacrylate). Hydrogels are commonly used as wound dressing materials, since they are flexible, durable, non-antigenic, and permeable to water vapor and metabolites, while securely covering the wound to prevent bacterial infection[xxxiii]. Methylcellulose hydrogel has been used to deliver allergens in skin testing. When test allergens are delivered in the hydrogel vehicle, less skin irritation was observed[xxxiv]. Hydrogels are also time and again coated on the urinary catheter surface to advance its biocompatibility[xxxv]. The hydrogel layer not only offers a smooth & slippery surface, but also inhibits bacterial colonization on its surface[xxxvi]. Hydrogel layers are formed on the internal surface of injured arteries are well-known to reduce thrombosis and intimae thickening in animal models[xxxvii]. Intimai thickening was prevented by inhibiting contact in between blood and sub endothelial tissue with a hydrogel layer. The pressure of swelling of p (HEMA) hydrogel was used to stabilize the bone implants[xxxviii]. Hydrogels are expected to be effectively used as interface stabilizer with enhanced design of implants. Hydrogels are also found to have its potential applications in sterilization and cervical dilation. An in situ plug of hydrogel was implanted into the fallopian tubes of rabbits through transcervical catheterization.[xxxix]. A hydrogel which forms an in-situ plug was placed into fallopian tubes of rabbits by transcervical catheterization, it was found that conception was prevented. With enhanced structurally rigid and biocompatible hydrogels the tubular sterilization system has been developed[xl]. Hydrogel rods were also developed to deliver hormones such as prostaglandin analogs furthermore to mechanically dilate the cervix. Cervical canal dilatation is essential for the first trimester-induced abortion by suction curettage [xxxix]. One of the major advanced applications of hydrogels is in the development of artificial muscles. Smart hydrogels which can transform electrochemical stimuli into mechanical work (i.e., contraction) can function like the human muscle tissue[xli]. Polymeric gels capable of reversible contraction and expansion under physicochemical stimuli are essential in the development of advanced robotics with electrically driven muscle-like actuators[xlii]. Smart materials that emulate the contractions and secretions of human organs in response to environmental conditions changes such as temperature, pH, or electric field may soon find a use in medical implants, prosthetic muscles or organs, and robotic grippers[xliii].

## APPLICATIONS IN BIOTECHNOLOGY:

Hydrogels is used as reactive matrix membranes in sensors. Hydrogels possess many advantageous properties, such as rapid and selective diffusion of the analyte, necessary for effective sensing. Hydrogels can also be made tough and flexible with desirable refractive indices[xliv]. Hydrogels made of p (HEMA) in an electrolyte solution were used as a salt bridge which separates the electrodes made of metallic compounds from the biological system for prevention of contamination via electrolysis products[xlv]. The p (HEMA) salt bridges are inexpensive, easy to make, easy to sterilize, very robust, and nontoxic to cell systems. They provide a viable and effective alternative to the widely used agar salt bridge. The ability of smart hydrogels in solutions to reversibly swell and shrink with small changes in the environment can be utilized to prepare purification devices[xlvi]. Smart hydrogels, especially thermo- and pH-sensitive hydrogels, have been used to concentrate dilute aqueous solutions of macromolecular solutes including proteins and enzymes, with no adverse effect on the activity of the enzyme[xlvii]. The size and net charge excludes the macromolecules from the hydrogel network while the absorption of water takes place[xlviii]. The absorbed water can be released from the hydrogel by altering temperature or pH of the environment, and thus the hydrogels can be reused repeatedly. Separation of bioactive proteins produced by recombinant DNA technology in a cost effective manner remains as a major huddles for the wide use of the technology. Separation of products by direct adsorption to adsorbents is attractive, but the adsorbents become fouled by colloidal contaminants and large macromolecules. This problem can be prevailing over by immobilizing the adsorbents into hydrogels like agarose and calcium alginate gel[xxxv]. Since the immobilized adsorbents do not interact with contaminants, separation turns out to be easier and more effective. The smart hydrogels can also be used to control the reactions of substrates with immobilized enzymes by controlling the substrate diffusivity via swelling changes[xlix]. A thermally reversible hydrogel was immobilized by which is known as Arthrobacter simplex and examined the temperature effect on steroid conversion. The steroid conversion was found to be high in high hydrophobic gels because of the elevated partition of water-insoluble steroids into the hydrophobic regions and the abridged product inhibition within the hydrophobic gel matrices[l]. Future of Hydrogels In the age of nanofabrication[li], the size of hydrogels in various applications is also expected to shrink. Gel electrophoresis is widely used for protein & DNA separation. Recent report showed that miniaturized electrophoresis gel instrument in the size of 25 mm long and 50 μm wide was constructed[lii]. The gels that can be used in the instrument are orders of magnitude smaller than the gels used in conventional instruments. Miniaturization of hydrogels is also important in all the areas mentioned above. For example, the ability to reproducibly prepare hydrogels in micro scale is essential in the preparation of glucose micro sensors[liii]. Hydrogels are generally biocompatible, but they are not perfect biomaterials, i.e., they still cause undesirable body reactions. Further improvement in biocompatibility will be critical in the wider hydrogels applications in biomedical and pharmaceutical areas. Hydrogels have rather less mechanical strength and durability for some applications. Enhancing these properties will make hydrogels more acceptable for many applications to come.

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