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Review Article

Hydrogels as Effective drug Delivery Systems

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Abstract: Hydrogels are crosslinked polymer networks that absorb substantial amounts of aqueous solutions. Hydrogels can be divided into two categories based on the chemical or physical nature of the crosslink junctions. Chemically crosslinked networks have permanent junctions, while physical networks have transient junctions that arise from either polymer chain entanglements or physical interactions such as ionic interactions, hydrogen bonds, or hydrophobic interactions .Hydrogels, the swellable polymeric materials, have been widely investigated as the carrier for drug delivery systems. These biomaterials have gained attention owing to their peculiar characteristics like swelling in aqueous medium, pH and temperature sensitivity or sensitivity towards other stimuli. Hydrogels being biocompatible materials have been recognized to function as drug protectors, especially for peptides and proteins, from *in vivo* environment. Also these swollen polymers are helpful as targetable carriers for bioactive drugs with tissue specificity. This article presents an overview to the advances in hydrogel based drug delivery that have become the interest of most researchers.

Keywords: Hydrogels, pH sensitivity, temperature sensitivity, glucose sensitivity, biodegradable.

INTRODUCTION

According to the latest medical and pharmaceutical encyclopaedias, there is still no precise and limiting definition of the term *hydrogel*. Most often, a hydrogel is considered to be a material made when a water-insoluble polymer absorbs a large amount of water, or else it is simply a water-swollen polymer network. Hydrogels have attracted tremendous research interest over many years, in part for fundamental reasons and in part because of the potential for a wide range of applications [1]. Hydrogels have been successfully used in biomedical fields due to their high water content and the consequent biocompatibility. Successful examples include soft contact lenses, wound dressings, super absorbents and drug-delivery systems. The most recent and exciting applications of hydrogels are cell-based therapeutics and soft tissue engineering. The biomaterial used to grow the first living, tissue-engineered skin product was a collagen hydrogel [2]. Although the success of skin tissue engineering is encouraging, efforts to engineer other soft tissues have not achieved similar success. The progress in large measure is limited by inappropriate properties of the biomaterials currently available. To elicit desired cell response and coax cells to assemble into functional tissues, the materials that support and contact the cells need to be carefully designed. Hydrogels have been used as drug delivery system due to following reasons [3]:

- Hydrogels provide suitable semi-wet, three-dimensional environment for molecular-level biological interactions.
- Hydrogel's mechanical properties are highly tunable, for example elasticity can be tailored by modifying cross-link densities.

Hydrogels can be designed to change properties (e.g. swelling/ collapse or solution-to-gel transitions) in response to externally applied triggers, such as temperature, ionic strength, solvent polarity, electric/magnetic field, light, or small (bio) molecules.

PREPARATION OF HYDROGELS [4]

Isostatic ultra-high pressure (IUHP)	Use of cross linkers	Use of nucleophilic substitution reaction	Use of gelling agents
Here the suspension of natural biopolymers like starch, are subjected to ultrahigh pressure of 300-700 MPa for 5 or 20 min in a chamber which brings about changes in the morphology of the polymer (i.e. gelatinization of starch molecules occur). It is different from heat-induced gelatinization where a change in ordered state of polymer occurs. Usually the temperature within the chamber varies from 40 to 52°C.	Since hydrogels are the polymers which swell in presence of water and they entrap drug within their pores; therefore, to impart sufficient mechanical strength to these polymers, cross linkers are incorporated like glutaraldehyde, calcium chloride and oxidized konjac glucomannan (DAK). These cross linkers prevent burst release of the medicaments. Hydrogels of gelatin has been prepared with DAK. Some researchers have *reported in situ* hydrogel formation by incorporating lactose along with sodium azide that results in formation of azide groups along with amino groups in polymers like chitosan and thus a photo cross linkable chitosan (Az-Ch- LA) is formed which has desired integrity	Hydrogels of N-2-dimethylamino ethyl-methacryalmide (DMAEMA), a pH and temperature sensitive hydrogel has been prepared by nucleophilic substitution reaction between methacyloyl chloride and 2-dimethylamino ethylamine. The synthesized hydrogel was characterized for its swelling behaviour	Gelling agents like glycophosphate, 1-2 propanediol, glycerol, trehalose, mannitol, etc, have been used in formation of hydrogels. Usually the problem of turbidity and presence of negative charged moieties which are associated with this method pose problem of interaction With the drug.

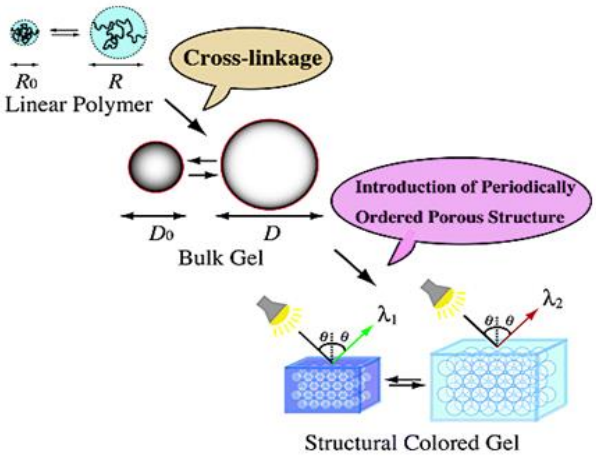

Fig-1: Porous structure in Hydrogel

Hydrogel (also called Aquagel) is a network of polymer chains that are water-insoluble, and found as a colloidal gel in which water is the dispersion medium. Hydrogels are magnificent absorbent (they can contain over 99% water) natural or synthetic polymers. Hydrogels also acquire a degree of flexibility very indistinguishable to natural tissue, due to their remarkable water content. The hydrogels discovery by "Wichterle and Lim" in 1960 of poly (2-hydroxyl ethyl methacrylate) have been of great engrossment to biomedical scientists. Hydrogels are 3-D hydrophilic polymer networks capable of swelling in water or biological fluids, and reserve a large amount of fluids in the swollen state. The water content in the hydrogels influence different properties like mechanical properties, permeability, biocompatibility and surface properties. Hydrogels have similar physical properties as that of living tissue and this resemblance is due to the high water content, soft and rubbery uniformity and low

interfacial tension with water or biological fluids. The potential of molecules with varying size to diffuse into (drug loading) and out (release drug) of hydrogels, allow the use of hydrogels as delivery systems. Since hydrogels have elevated permeability for water soluble drugs and proteins, the most typical mechanism of drug release is diffusion. Factors like polymer composition, cross-linking water content, density, and crystallinity, can be used to control the release rate and release mechanism from hydrogels [5].

Benefits of using hydrogels as controlled drug delivery system are as follows:

(I) Biocompatible and degradated products have no noxious effect.
(II) Soft rubbery nature of hydrogel reduces mechanical irritation by *in-vivo* implant.
(III) Low hydrogel water interfacial tension decreases protein adsorption and cell adhesion.
(IV) Release can be synchronized by controlling water swelling and cross-linking density.
(V) Applicable for both hydrophilic and hydrophobic drugs and charged solutes.

Common uses for hydrogels include [6, 7].

- Recent the hydrogel used as scaffolds in tissue engineering. Scaffolds hydrogels may contain human cells in order to renovate tissue.
- Environmental sensitive hydrogels. These hydrogels have the ability to perception changes of temperature, pH, or the concentration of metabolite and release their load as reverberation of such a change.
- Sustained-release delivery approach.
- Impart absorption, desloughing and debriding capacities of necrotic and fibrotic tissue.
- Used as biosensors as well as in drug delivery systems.
- Used in replaceable diapers where they absorbed urine, or in sanitary napkins
- Contact lenses (polyacrylamides, silicone hydrogels etc.)
- Hydrogel used as medical electrodes composed of cross linked polymers (polyethylene oxide and polyvinylpyrrolidone)
- Breast implants
- Granules for holding soil moisture in tedious areas
- Dressings for healing of burn or wounds. Wound gels are excellent for helping to create or maintain a moist environment.
- Act as reservoirs in topical formulation.

Common ingredients are e.g. sodium polyacrylate, polyvinyl alcohol, acrylate polymers and copolymers with an ampleness of hydrophilic groups. Natural hydrogel materials are being explored for tissue engineering, these materials include methylcellulose, and agarose and other naturally procure polymers.

CLASSIFICATION OF HYDROGEL

Nature of Cross linked

a. Chemically cross-linked networks having enduring junctions.
b. Physical networks have momentary junctions drive from polymer chain complexation or physical interactions through, ionic interactions, hydrogen bonds, or hydrophobic interactions.

On the basis of origin

On the basis of origin hydrogel may be classified as [12]

Natural origin	**Synthetic polymer**
By the use of natural polymer	through chemical polymerization
Advantages : Biocompatible Biodegradable Maintain cellular activities	Advantages : Intrinsic bioactive properties absent
Examples: Gelatin polysaccharides like alginate and agarose and Proteins like collagen	Examples: Vinyl acetate , Hydroxyethyl methacrylate (HEMA) and Acrylic acid

BONDING IN HYDROGELS [8]

- Covalent
- Ionic
- Hydrogen bonding
- Polypeptide complexation (e.g. coiled coils)

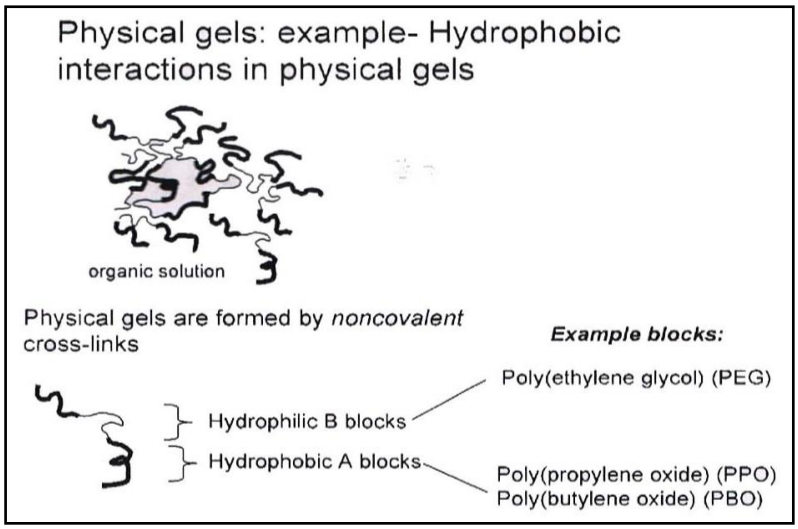

Fig-2: Hydrophobic Interaction of Hydrogels

CHARACTERISTIC OF HYDROGEL

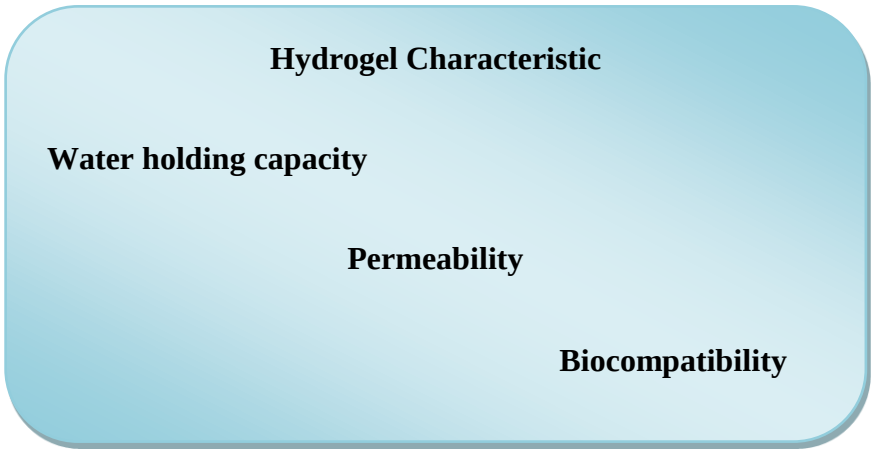

Fig-3: Characteristic of Hydrogel

The salient features of a hydrogel are illustrated as

Hydrations of the polar hydrophilic groups occur as they association with water which promote to the formation of primary bound water which result the network swells and exposes the hydrophobic groups which are also competent of interacting with the water molecules. This resulting to the formation of hydrophobically-bound water, also termed as 'secondary bound water'. Primary and secondary bound water are frequently combined and called 'total bound water'. The cross linked network will absorb ancillary water, due to the osmotic driving force of the network chains towards infinite dilution. This additional swelling is incompatible by the covalent or physical cross-links, essential to an elastic network retraction force. Thus, the hydrogel will attain an equilibrium swelling state. The additional absorbed water is so called 'free water' assumed to pack the space between the network chains, and the centre of larger pores or voids. On the basis of nature and composition of the hydrogel the next step is the disintegration and/or dissolution if the network chain or cross-links are decomposable. Biodegradable hydrogels, containing labile bonds, are therefore beneficial in applications such as wound healing, tissue engineering and drug delivery system. These bonds can be available either in the polymer backbone or in the cross-links used to prepare the hydrogel. The labile bonds can be burst under physiological conditions either enzymatically or chemically hydrolysis [9]. Biocompatibility is the third most important salient property required by the hydrogel. Biocompatibility stands for compatibility with the immune system of the hydrogel and its degradation products are also non toxic. Ideally they should be metabolized into safe products or can be eliminated by the renal filtration process. Predominantly, hydrogels acquire a good biocompatibility because their hydrophilic surface has a low interfacial free energy when in association with body fluids, which resulting in a low tendency for proteins and cells to adhere to the surfaces.

Moreover, the soft and rubbery nature of hydrogels reduced irritation to surrounding tissue [10].

SUMMARY AND CONCLUSION

There is adequate scientific validation for the potentiality of hydrogels in delivery of drug molecules to a desired site by triggering the release through an external stimulus such as temperature, pH, glucose or light. These hydrogels being biocompatible and biodegradable in nature have been used in the development of nano biotechnology products and have stunning applications in the field of controlled drug delivery as well.

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