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Original Research Article

Current Scenario of Hydrogel as Drug Delivery System

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Abstract: Crosslinked polymer networks known as hydrogels are capable of absorbing large volumes of water liquids. Depending on whether the crosslink connections are chemical or physical, hydrogels can be categorised into two groups. Physical networks feature temporary junctions that result from either polymer chain entanglements or physical interactions like ionic contacts, hydrogen bonds, or hydrophobic interactions, as opposed to chemically crosslinked networks, which have permanent junctions. Swellable polymeric polymers called hydrogels have received a lot of attention as potential drug delivery system carriers. These biomaterials have drawn attention because of their unusual properties, such as swelling in aqueous media, sensitivity to pH and temperature, or sensitivity to other stimuli. Because they are made of biocompatible materials, hydrogels are known to protect drugs from the in vivo environment, particularly peptides and proteins. Moreover, these swelling polymers are useful as tissue-specific targetable carriers for bioactive medicines. This article provides a summary of the developments in hydrogel-based drug delivery that have captured the attention of the majority of researchers.

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

INTRODUCTION

Several medical and pharmaceutical encyclopaedias claim that the term "hydrogel" still lacks a clear, restrictive definition. A hydrogel is typically thought of as a substance created when a water-insoluble polymer absorbs a significant amount of water, or else it is just a network of water-swollen polymers. Over the years, hydrogels have gained a lot of scientific attention, partly for theoretical reasons and partly due to the promise for a wide range of applications [1]. Due to their high water content and resulting biocompatibility, hydrogels have found success in the biomedical field. Effective examples include super absorbents, soft contact lenses, wound dressings, and medication delivery methods. Cell-based therapies and soft tissue engineering are two of hydrogels' most recent and interesting uses. A collagen hydrogel was the biomaterial used to generate the first living, tissue-engineered skin product. Although hopeful, efforts to engineer other soft tissues have not been as successful as those for the skin. The unsuitable qualities of the biomaterials that are now accessible severely restrict advancement. The materials that support and contact the cells must be carefully designed in order to induce the proper cell response and induce cells to assemble into functioning tissues. Due of the following factors, hydrogels have been employed as medication delivery systems [3]:

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

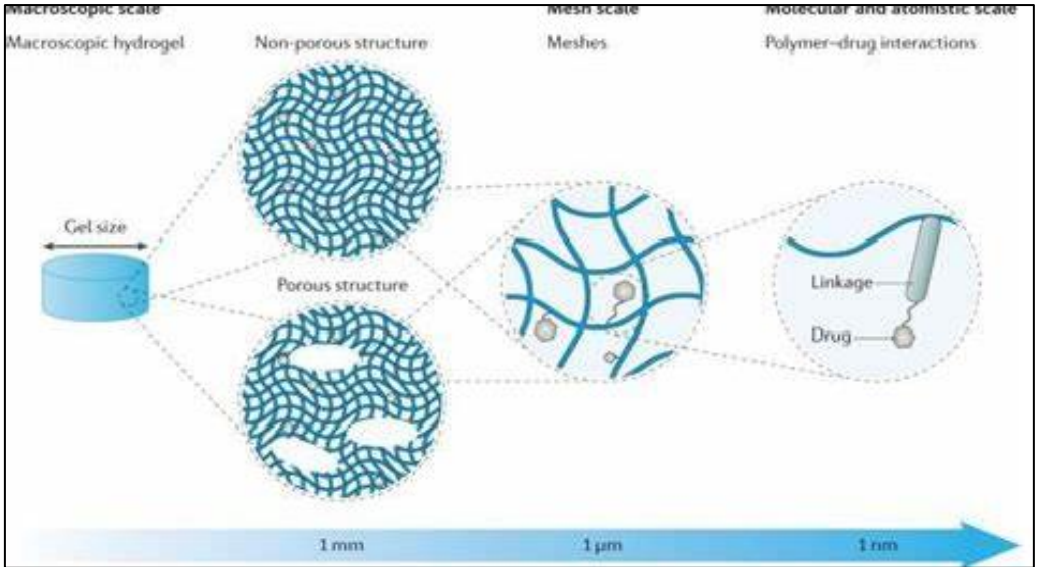
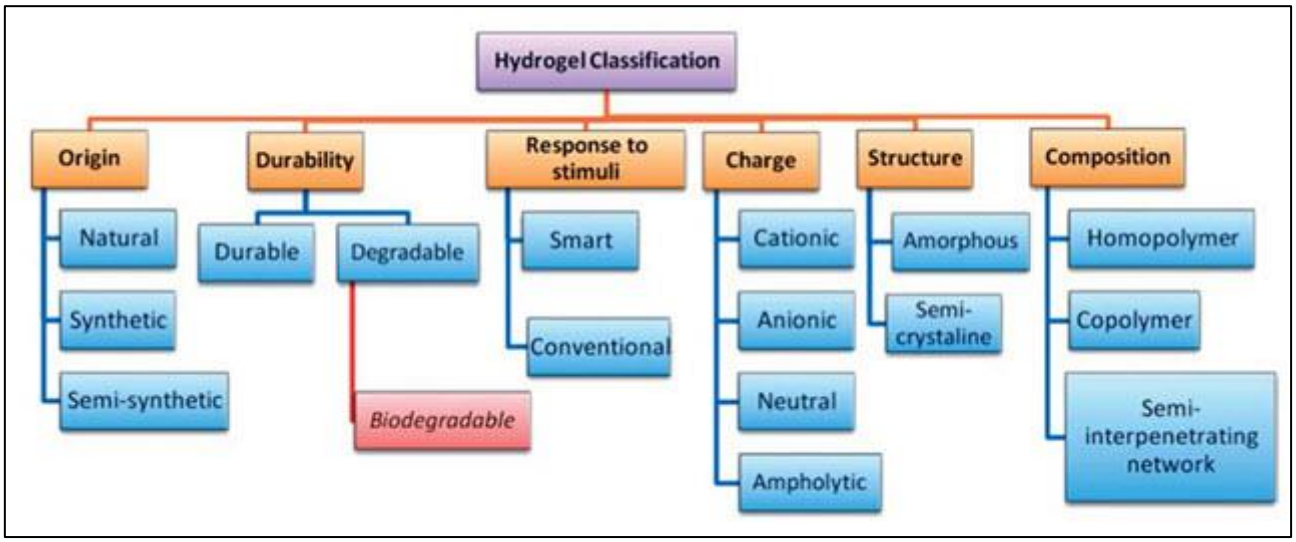


Fig. 1: Hydrogel



Common types of Hydrogel

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.

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, 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).

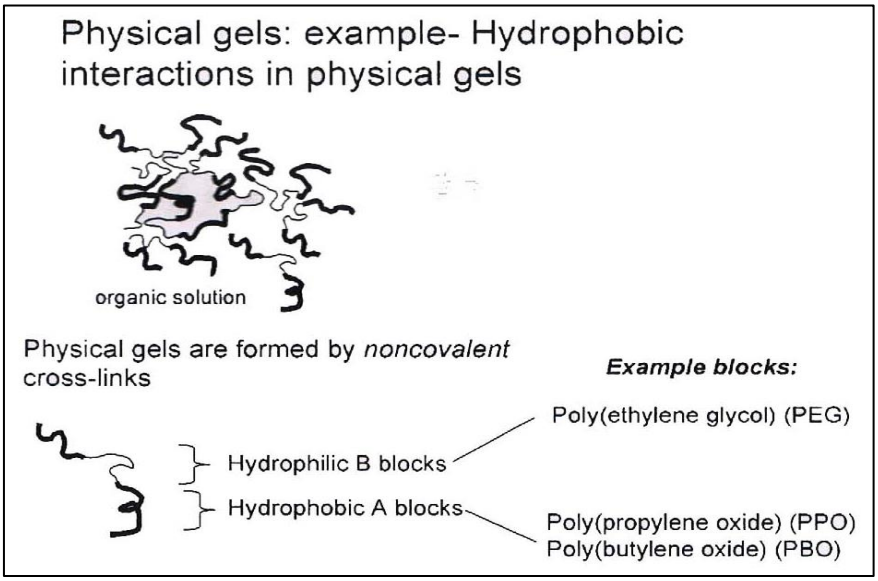


Fig. 2: Hydrophobic Interaction of Hydrogels

CHARACTERISTIC OF HYDROGEL

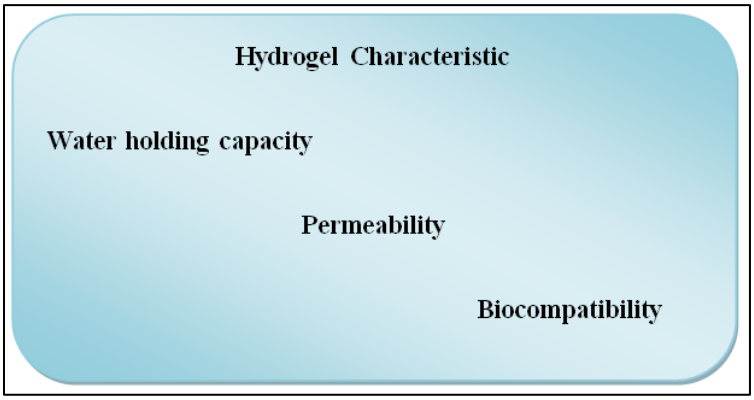


Fig. 3: Characteristic of Hydrogel

The salient features of a hydrogel are illustrated as:

The network expands and reveals the hydrophobic groups, which are also capable of interacting with the water molecules. Hydrations of the polar hydrophilic groups take place as they associate with water, which promotes the development of primary bonded water. This led to the production of "secondary bound water," also known as hydrophobically bound water. Total bound water is a term that typically refers to combined primary and secondary bound water. Due to the network chains' osmotic drive towards infinite dilution, the cross-linked network will absorb auxiliary water. The covalent or physical cross-links, required for an elastic network retraction force, make this additional swelling incompatible. The hydrogel will achieve an equilibrium swelling condition as a result. The additional water absorbed is referred to as "free water." Hence, labile bond-containing biodegradable hydrogels are advantageous in applications including tissue engineering, drug delivery systems, and wound healing. Both the polymer backbone and the cross-links utilised to create the hydrogel can have these linkages. Under physiological circumstances, the labile bonds can rupture through chemical or enzymatic hydrolysis [9]. The hydrogel's third-most crucial conspicuous need is biocompatibility. The term "biocompatibility" refers to the hydrogel's immune system compatibility. Its degradation products are likewise non-toxic. In a perfect world, they would be converted into harmless compounds or would be removed by the renal filtering process. Because their hydrophilic surface has a low interfacial free energy when in contact with human fluids, hydrogels typically acquire a good biocompatibility [10-13].

SUMMARY AND CONCLUSION

The ability of hydrogels to deliver therapeutic molecules to a desired region by initiating the release by an external stimulus like temperature, pH, glucose, or light has received sufficient scientific validation. Due to their biocompatibility and biodegradability, these hydrogels have been used to create products for nanobiotechnology and have amazing uses in the field of controlled drug delivery.

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