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Hydrogels: A review

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Abstract

Hydrogels are hydrophilic, three dimensional and polymers network that hold the large quantity of water of biological fluids. Water is the large constituents of human body which applied for the biomedical purposes. Polymers are playing significance role in the pharmaceutical field. Hydrogels are biomaterials due to their important quantities such as biocompatibility, biodegradability and non toxic properties and these properties makes hydrogel acceptable for medical and pharmaceutical field. This article concerning the general knowledge about hydrogels i.e. significance, method of preparation, synthesis of hydrogels, chemical and physical properties, feature, advantage and disadvantage.

Keyword: Hydrogel, Feature, Classification, Application.

Introduction

Hydrogels are hydrophilic, three dimensional network that hold the large quantity fluid water is the large constituents of human body which applied for the biomedical purposes. Generally it based on the chemical composition which is responsive to the various stimuli such as heating, pH, light, and chemicals **[1].** Hydrogels can also be prospect by rheological manners and swollen polymer network which flatter hydrated in the liquid media that are referred to as the hydrogel structure **[2].** Many theories are involved in the swelling mechanism such as Equilibrium swelling theory, Rubber elastic theory, Mechanism of Gelation and Calculation of mesh size. Hydrogels can be prepared from natural polymers are polysaccharides, polypeptide **[1, 3].** Hydrogels formulation applied on the skin surfaces which categories into two groups such as topical and transdermal route. Topical formulations provide the drug at the particular site of the skin surfaces without systemic exhibition while transdermal formulations applied to the local area of the skin surfaces which maintain and deliver the effective concentration of drug in the systemic circulations. Aerosol, spray, semi solid and patches are the examples of the transdermal formulations **[4].** Hydrogel have different method for the in vivo administration of drug, which are based on the localization and pathological condition. Most available topical subcutaneous, orthotopic, intraperitoneal, oral, ocular and rectal. Topical or transdermal plays a vital role for the skin infection, subcutaneous for toxicological effect, orthotopic and intraperitoneal injections for therapy while oral administration have some disadvantage due to the presence of some digestive enzymes **[5].** According to Witchterls and Lim in 1960, cross-linked hydroxyl ethyl methaacrylate has excellent water holding capacity, high water retention, good biocompatibility and biodegradability, limited or minimal toxicity and simplified synthetic method. Hydrogels are formed by physical and chemical cross- linking network. Conductive hydrogel, Injective hydrogel, Double network hydrogel, Responsive hydrogel, Nanocomposite hydrogel, sliding hydrogel and other Novel hydrogel **[6].**

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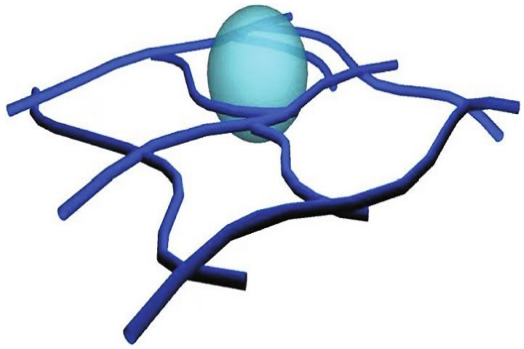

Fig. 1: Hydrogel Network [6]

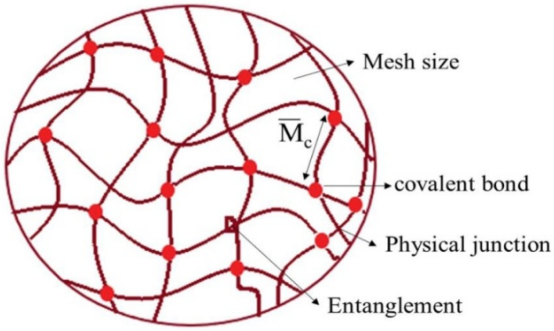

Fig. 2: Structure of hydrogel [7]

Advanced hydrogel materials have unique properties to swell under particular sympathetic circumstances and response to available of stimuli that are referred to as the environmental or stimuli sensitive. Some synthetic polymer hydrogels are included cross- linking hydrogel, water in hydrogel, poly (vinyl alcohol), poly (hydroxyethyl methaacrylate), polyvinyl pyrrolidone, polymidine, polyacrylate, polyurethane, polyethylene glycol and derivatives **[8]**

Feature of hydrogel [9, 10]

- It should have rewetting capacity and highest absorbancy under load (AUC).
- They exhibit little residual manners and soluble content.
- During storage condition it has good stability and durability in the swelling environment.
- It is colorless, odorless, non toxic and also exhibit highest photo stability in nature.
- Hydrogel must be pH neutrality after in swelling media and highest biodegradability.
- Drug should have adapted hydrophilicity and molecular weight of less than 500 Daltons.
- PH value of drug between 5 and 9.

- Drug must be high acidic or alkaline in solution which are not suitable for topical drug delivery system.

Advantage and disadvantage of hydrogel [11, 12]

Advantage	Disadvantage
Hydrogels are homogeneous to the natural tissue due to high water holding capacity and it contain the degree of flexibility.	Limitation of hydrogels in contact lenses is hypoxia, dehydration, lenses deposition and red eye reactions.
It should be biodegradable, biocompatible and good transport properties.	It should be non adherent, hard to sterilized and hard to load with drugs or nutrients.
It may be low toxicity	High cost
Hydrogels can be injected and easily to modify.	It has low mechanical strength.
It have capability to change of pH, temperature and concentration.	It can be hard to handle.

Classification of hydrogel [13, 14, 15]

➢ **Classification based on source**

- Hydrogel can be divided into two group i.e. Natural origin and synthetic origin.

➢ **Classification based on the polymeric composition/ Method of preparation**

- Homopolymeric hydrogels- It is known as the polymeric network which acquire from a single species of the monomer. These hydrogels have cross linked skeletal structure which depend on the nature of the polymerization technique and monomers.
- Copolymeric hydrogels- Copolymeric hydrogels are referred to as different monomers unit in which included one hydrophilic component.
- Multipolymer Interpenetrating polymeric hydrogels (IPN) - It is two independent natural polymer or synthetic polymers component. In this type of classification one polymer is noncross linked polymer network.

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Classification based on the configuration/ physical structure of the network

According to the physical structure and chemical composition, these hydrogels can be classified into Amorphous (non- crystalline), semi crystalline, hydrogen bonded, super molecular structure or hydro colloidal aggregation.

Classifications based on the physical appearance

Hydrogels are film, matrix and microsphere which depend on the polymerization techniques.

Classifications based on the type of the cross linking

Hydrogels are divided into two categories i.e. physical and chemical nature of the cross linking. Physical linking is the transient junction while chemical linking is the permanent junctions in whom both junctions are ionic interactions, hydrogen bonds, or hydrophobic interaction.

Classifications based on the network electrical charges/ ionic charges

On the basis of presence or absence of electrical charges hydrogels are divided into four categories i.e. Ionic (anionic or cationic), Non ionic (neutral), amphoteric electrolytes (ampholytic), zwitterionic.

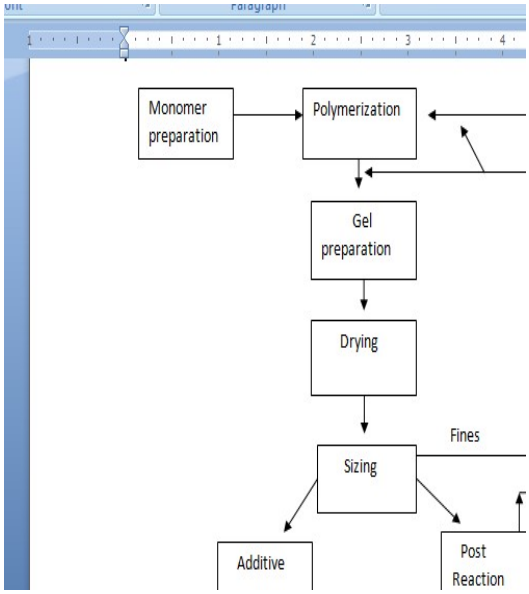
Based on the mechanical controlling the drug release

It involves the diffusion controlled, swelling controlled, chemically controlled, and environmentally responsive release system, diffusion controlled, chemically controlled, environment responsive system.

Preparation method of hydrogel [16]

Hydrogels can be prepared from the different method i.e. cold method, fusion method and dispersion method.

Dispersion method is widely used for the preparation of gel. In these process polymers was dispersed in distilled water with constant stirring and heat the colloidal viscous dispersion get clear gel solution. Drugs were dissolving in solvent media and added to the dispersion. Using TEA (Triethanolamine) until it reaches desired pH value ex. methylcellulose gels are prepare from dispersion method than in cold water. **Fusion method** are depends on the gelling agent such tragacanth gels are prepared at low temperature and Carbopol gels have unique procedure. **Cold method** is used for the heat labile drugs.



Synthesis of hydrogel

Physical cross linking [18]

Physical or reversible gels have stable by proportionately weak interaction established polymers chain such as hydrogen bond, ionic interaction or hydrophobic. It incorporated cooling or heating polymers solution, ionic interaction, hydrogel bonding, freeze thaw cycles, maturation or aggregation

Chemical method [18]

These processes are synthesis of hydrogels incorpoted the chemical cross linking, grafting of monomers. Chemical cross linking are established the bonds in the middle of polymer chain. Cross linking of natural and synthetic polymers contain hydroxyl, carboxylic and amine groups and grafting process included the polymerization of monomer

Use of gelling agent [19]

Some substances with their suitable concentration (wt %) are used for the gelling agent such as collagen (0.2- 0.4), gelatin (2-15), agar (0.1-1), alginate (0.5-1), gellum gum (0.5-1), pectins (0.8-2), starch (6), carboxymethylecellulose (4-6), hydroxypropylmethylcellulose (2-10), hydroxypropylcellulose (8-10), methylcellulose (2-4), Polaxomer (15-50), carbomer (0.5-2) etc.

Isostatic ulta high pressure (IUHP) [20]

Some natural biopolymers like starch are come in contact with IUHP of 300-700 MPa for 5 or 20

minutes, which accompany the changes in the morphological structure of the polymers (i.e. formation of the gelatinization of the starch molecules). Temprature of Isostatic ulta high pressure are varies from 40-52°C.

Nucleophilic substitution reaction [20]

N-2-dimethylamino ethylmethacrylamine (DMAEMA) is pH and temperature sensitive hydrogels. Nucleophilic substitution reaction occurs between chloride and 2- diemethilamino ethylamine.

Natural and synthetic polymers [21]

Natural polymers and their derivatives are of many types such as Cationic polymers (plylysine, chitosane), Anionic polymers (pectin and alginic acid), and Neutral polymers (agrose) and Amphoteric polymers (gelatin and fibrin). Synthetic polymers are polyesters which included PEG-PLA-PEG, PEG-PLGA-PEG while combination of both natural as well as synthetic polymers is P (PEG-CO-Peptides), Alginate-g (PEO-PPO-PEO).

Semi interpenetrating network and inter penetrating network [22]

Semi interpenetrating the linear polymers, it penetrate cross linked network without involving the chemical bond between them while interpenetrating network are inter connected of two molecules which synthesized other and by this process dense hydrogels are formed.

Significance of hydrogel [23, 24]

Physical and chemical properties: - Hydrogel depend on the two major effect i.e. particles size and molecules attraction or repulsion. It is realistic design to know the solute molecules interact with the gel particularly they partition between the gel phase and liquid phase.

Swelling: - Hydrogel is the hydrophilic, cross linked (physically or chemically) polymer chain are able to absorb the large quantity of the water holding capacity. Generally dry hydrogel start to soak water range from 10-20%. Temprature, pH, ionic species, and electric signal can be changes the appearance of hydrogel and this variation may take place at microscope level.

Mechanical properties: - Mechanical properties can be depending on the nature of the material. It required a gel with stiffness by increasing the cross linking chain. The evaluation parameters of biomedical applications are ligament, wound dressing, tendon repairs, and matrix for drug delivery, tissue engineering, and cartilage replacement materials.

Cross linking: - It is the important properties of the hydrogel. Physical cross linking and chemical bound gel are the category of cross linking hydrogels. Many collaborative reactions are involve for the cross linking process such as Michael's reaction, Michaelis-Arbuzov reaction, and nucleophilic addition reactions.

Biocompatible properties: - Hydrogels are the non toxic and biocompatibity in behavior. Most polymers used for cytotoxity and in vitro toxic test. Biocompatibity consist of two polymer i.e. biosafty and Biofunctionality.

Porosity and permeation:- Pores size could be created in hydrogel by the phase separation process and it depends on the three factor i.e. concentration of the chemical cross- links of the polymer strand, net charge of polyelectrolytes and concentration of the physical entanglement of the polymer strands .

Drug release mechanism from hyrdogel devices [20, 25, 26]

Many factor affected in drug delivery mechanism such as arrangement of hydrogel (type of polymer, drug and additives), configurations (shape and size), preparation method, environmental circumstances, physical and chemical phenomena. Sophisticated and simple models are depending on the rate limiting steps for controlled release which are divided into the following ways i.e.

Diffusion controlled model follow the flick's law of diffusion which play an effective for drug release from hydrogels. Controlled release drug diffusivities are calculated from the volume, hydrodynamics or obstruction based theories. Types of diffusion are divided into reservoir system and polymer hydrogel membrane.

Swelling controlled release is slower than the diffusion controlled model. Mechanism of this model includes moving boundary conditions. Examples are drug with HPMC, combination of methyl/ cellulose with HPMC, Methacel matrices.

Chemical controlled release model are determined by the reaction take place within drug matrix. Cleavage of polymer chain i.e. enzymatic degradation or hydrolytic or reversible or irreversible reaction take place between the

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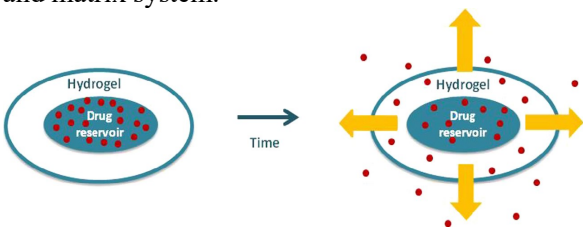
polymer chain and releasable drug are example of the chemically control release.

Biomedical application of hydrogel

Drug delivery [27, 28, 29]

If drug conduct hydrogel, brought near the liquid media then water make a holes into the apparatus or arrangement and dismiss the drug into the solution. According to the Brownian motion diffusion play a vital role for the dissolution of drug into a liquid media. Hydrogels are important for the enlargement the control drug delivery system for a long duration and these system can be categories into two system i.e. reservoir system and matrix system.



(drug diffusion from the core through the hydrogel membrane)

Fig. 4: Reservoir system

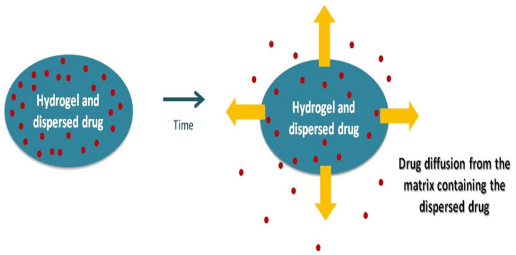


Fig. 5: Matrix system

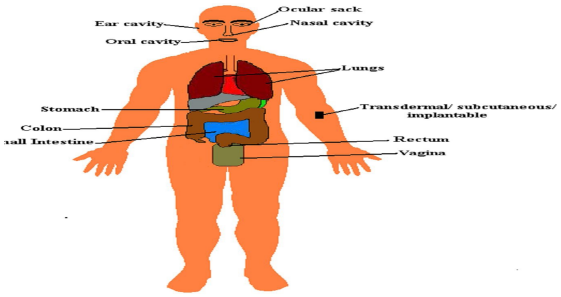
Various model and equations are useful for the mechanism of drug release such as Zero order kinetics, First order kinetic, Baker- Lonsdale model, Kerseymeres peppas model and Hopfenberg model.

Oral, topical, transdermal, vaginal, ophthalmic, intranasal, rectal, injectable, micro/ nanogel delivery vehicles, hydrogel mediated drug delivery vehicles are the different administration of drug delivery system.

The anatomy and physiological applications for stabilized drug delivery system [15]

Tissue engineering [30]

Tissue engineering (TE) play an important role in the regenerative medicine. It is categories into three part i.e. cell/ tissue, scaffold and implantation and or grafting. Pore size of scaffold are >80um and combined with polymer or ceramics. It is responsible for the cell migration into the core of scaffold, angiogenesis and provides of supplements to the cell. Sterilization of hydrogel is an alter characteristics of scaffold.



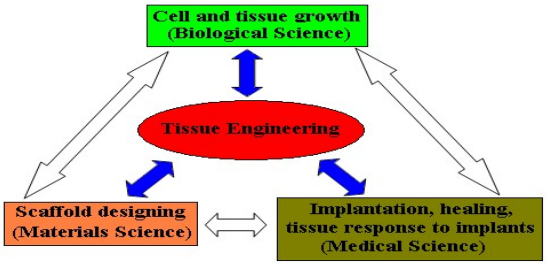


Fig. 6: Multidisciplinary approach of tissue engineering

Wound dressing [30]

Hydrogels have capability of stimulation the regeneration of skin. It can be loaded with drug which is responsible for the treatment of wound.

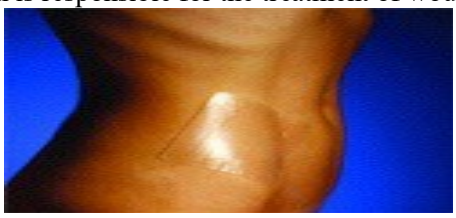


Fig.7: Diagram of wound dressing

Environment and Bacterial culture [31]

Matrix have the capability to hold the purifying the microorganism. Chlorella and spirulina these microorganisms are used to remove the pollutants chemical from water resources. While in bacterial culture agar is very popular substrate in application of biotechnology. Various type of agar like Columbi agar, Brucella agar, Schaedler agar or Trypicasesoy agar are gives a suitable environment for their culture on a solid.

Hydrogel to fix bone replacement [32]

During the replacement of heep and knee are laminar with hydrogel which swell or enlarge in

the aquous media. Coating material are hyaluronic acid esters, methaacrylate and replacement prepare from stainless steel, titanium, metal alloys etc.

Conclusion

Several studies indicated the usefulness of gels special hydrogels balance the drug concentration in body within therapeutic limitation for long duration. Topical drug delivery system and dosage form are conscious to be applied to the dermatological disease. In semi solid formulation ointment, lotion, gels, and topical solution are frequently used and hydrogels have various physical and chemical properties, swelling, mechanical properties, cross linking, biocompatible properties, porosity and permeation. Hydrogels have played a significance role in biomedical field i.e. drug delivery, tissue engineering, wound dressing, environmental, bacterial culture, hydrogel to fix for bone replacement therapy.

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