

HYDROGEL NEW TREND IN DRUG DELIVERY SYSTEM: REVIEW

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ABSTRACT

From the past few decades, the pharmaceutical industry has knowledgeable impressive growth year after year. Constant introduction of life-saving drugs has propelled this growth. Controlled-release technologies allow for effective use of existing drugs and successful development of new drug candidates. Developing new drug delivery technologies and utilizing them in product development is critical for pharmaceutical companies to survive. Hydrogels are three-dimensional hydrated network formed by crosslinking polymers through either covalent bonds or noncovalent bond interactions. The high water content of hydrogels renders them biocompatible to living systems and their soft nature can minimize damages to the surrounding tissues. Due to these reasons, hydrogels have received significant attentions in recent years for biomedical applications, such as drug delivery and tissue engineering.

KEYWORDS: Hydrogels, crosslinking polymers, biomedical applications, drug delivery.

INTRODUCTION**Hydrogel Drug Delivery System**

Focus on hydrogel that are known to reduce the problems of not only conventional dosage forms but also of delivery systems which requires a biocompatible, convenient and stable drug delivery system for molecules.

Hydrogel is three dimensional hydrophilic polymer networks capable of swelling in water or biological fluids and retaining large amount of fluids in a swollen state. Their ability to absorb water is due to the presence of hydrophilic group such as -OH, -CONH, -CONH₂, COOH and SO₃H. These structures imbibe water or biological fluids in large amount atleast 10-20 times their molecular weight, thus become swollen. Cross linked hydrogels have sufficient mechanical strength and physical integrity.

If water is removed from these swollen biomaterials, they are called xerogels, which are then dried hydrogels. In a chemical hydrogel, all polymer chain is cross-linked to each other by covalent bonds, and thus, the hydrogel is one molecule regardless of its size. For this reason there is no concept of molecular weight of hydrogels, and

hydrogels are sometimes called infinitely large molecules or super macromolecules.

One of the unique properties of hydrogel is their ability to maintain original shape during and after swelling due to isotropic swelling. Swelling only changes the size of the original shape. Water content in hydrogels affect different properties like permeability, mechanical properties, surface properties, and biocompatibility. Hydrogels have similar physical properties as that of living tissues, and this similarly is due to the high water content, soft and rubbery consistency, and low interfacial tension with water or biological fluids.^[1-5]

Advantages of Hydrogel^[1, 2, 4-6]

1. Environment protects cells and other substances (drug, protein, and peptides).
2. Good transport properties.
3. Biocompatible
4. Biodegradable
5. It has versatile route of administration like injection, topical, oral, rectal, and nasal.
6. Easy to modified.
7. Timed release of growth factors and other nutrients to ensure proper tissue growth.

8. Entrapment of microbial cells within hydrogel with the advantages of low toxicity.
9. Environmentally sensitive hydrogels have the ability to sense changes of pH, temperature.

Disadvantages of Hydrogel

1. Low mechanical strengths
2. Hard to handle
3. Difficult to load
4. Sterilization
5. High cost
6. In contact lenses –lens deposition, hypoxia, dehydration and red eye reaction.

Classification of Hydrogel^[1-5, 7-11]

Hydrogels are classified according to their origin, Physical, chemical properties and Preparation Method. They can also be classified according to the release mechanism they are follows

Origin

- a. Natural- Dextran, Chitosan, Collagen.
- b. Synthetic - Poly (vinyl alcohol), acrylamide.

Ionic Charge (based on the nature of the dependent groups)

- a. Neutral - dextran.
- b. Anionic - (-ve charge) carrageenan
- c. Cationic - (+ ve charge) chitosan
- d. Ampholytic -collagen

Water Content or Degree Of Swelling

- a. Low swelling
- b. Medium Swelling
- c. High Swelling
- d. Suparable Swelling

Network Structure

- a. Non-porous
- b. Micro-porous -10-100nm
- c. Macro-porous-100nm-10 μ m
- d. Super-porous -200 μ m porous size.

Network Morphology

- a. Amorphous-random and non crystalline
- b. Semicrystalline-structure
- c. Hydrogen Bonded-hydrogen bond
- d. Hydrocolloids

Component (based on method of preparation)

- a. Homopolymer –from one type of monomer
- b. Copolymer-from more than one type of monomer
- c. Multipolymer- more than one type of polymer
- d. interpenetrating- network of two polymers.

Cross-Linking Method

- a. Chemical-hydrogen bonding
- b. Physical-covalent bonding

Function

- a. Biodegradable or Non- Biodegradable
- b. Stimuli Responsive- temp, pH.
- c. Superabsorbent-

Mechanism Controlling Drug Release

- a. Diffusion control release-1.Reservoir 2. Matrix
- b. Swelling control release.

Structure of Hydrogel^[1,2,4,8,11]

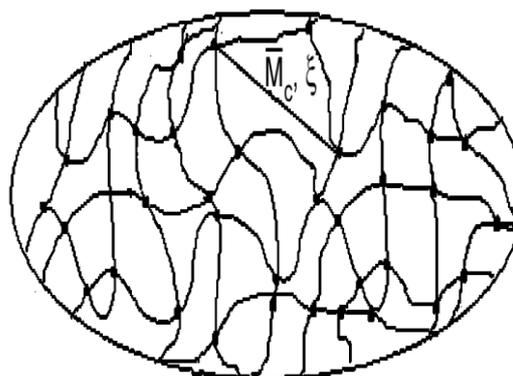


Figure No.1.1.Schimatic representation of the cross-linked structure of a hydrogel. M_c is the molecular weight of the polymer chains between cross-links and ξ is the molecular mesh size.^[8]

Network Structure of Hydrogels

The structure of an idealized hydrogel is shown in figure 1.the most important parameters that define the structure and properties of swollen hydrogels are the polymer volume fraction in the swollen state, v_2, s , and the effective molecular weight of the polymer chain between cross-linking points, M_c , and the correlation distance between two adjacent cross-links, ξ . Rubber-elasticity theory and equilibrium-swelling theory are extensively applied to describe these three dependant parameter.

The polymer volume fraction in the swollen state (v_2, s) describes the amount of liquid that can be imbibed in hydrogels and is defined as a ratio of the polymer volume (V_p) to the swollen gel volume (V_g).It is also a reciprocal of the volumetric swollen ratio (Q) which can be related to the densities o the solvents (ρ_1), polymer (ρ_2) and the mass swollen ratio (Q_m).

$$v_{2,s} = \frac{V_p}{V_g} = Q^{-1} = \frac{1}{\frac{Q_m}{\rho_1} + \frac{1}{\rho_2}}$$

The effective molecular weight of the polymer chain between cross-inking points is commonly related to the degree of cross-linking in the gel(X) as

$$X = \frac{M_0}{2M_c}$$

Where, M_0 is an estimate of the molecular weight of the repeating units.

ξ is the distance between sequential cross-linking points, which represents an estimate of the available space between the macromolecular chains accessible for the drug diffusion and can be calculated from the following equation:

$$\xi = v_{2,s}^{-1/3} \cdot l \cdot \left(\frac{C_n \cdot 2M_c}{M_r} \right)^{1/2}$$

Where C_n is Flory characteristic ratio which is a constant for a given polymer-solvent system, l is the carbon-carbon bond length and M_r is the weight of the repeating units from which the polymer chain is composed.

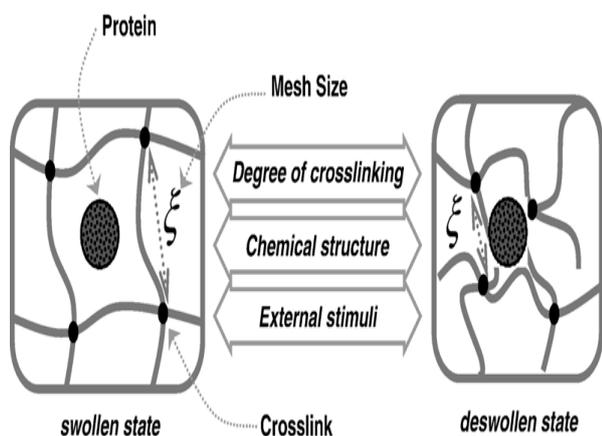


Figure No.1. 2. Mesh size in hydrogels at swollen or shrunk states.^[1,11]

Properties of Hydrogel^[1, 4,6-8,10,11-13]

Swelling

Hydrogel are characterized, first by their, capacity to absorb water or aqueous solution. Hydrogel containing hydrophilic groups swell to a higher degree compared to those containing hydrophobic groups. Hydrophobic groups collapse in the presence of water, thus minimizing their exposure to the water molecule and show retarded release .where hydrophilic groups easily swell in water and thus maximizes exposures to the water molecule and thereby maximum drug entrapment and release observed .the amount of the aqueous medium incorporated in a hydrogel is determined .generally gravimetrically and can be expressed in several ways. The fractional hydration (W) can be obtained as follows:

$$W = (w_1 - w_0) / w_1$$

Where w_1 and w_0 are the weights of swollen and dry gels respectively.

The swelling ratio(r) is expressed as:

$$R = (w_1 - w_0) / w_0$$

At the particular temperature the volume fraction of polymer (f_2) within a hydrogel at swelling equilibrium is given by:

$$\phi_2 = (D_0/D)^3$$

Factors Affecting Swelling of Hydrogel

Cross-Linking Ratio

It is defined as the ratio of moles of cross- linking agent to the moles of polymer repeating units. The higher the cross-linking ratio, the more cross-linking agent is incorporated in the hydrogel structure. Highly cross-linked hydrogels have a tighter structure, and will swell less compared to the same hydrogels with lower cross-linking ratios .cross-linking hinder the mobility of the polymer chain, hence lowering the swelling ratio.

The Chemical Structure of the Polymer

Hydrogel containing hydrophilic groups swell to a higher degree compared to those containing hydrophobic groups. Hydrophobic groups collapse in the presence of water, thus minimizing their exposure to the water molecule. As a result, the hydrogels will swell much less compared to hydrogels containing hydrophilic groups.

Temperature

Swelling of temperature-sensitive hydrogels can be affected by changes in the temperature of the swelling media.

Ionic Strength and P^H

Ionic strength and P^H affect the swelling of ionic strength and P^H -sensitive hydrogels, respectively. There are many other specific stimuli that can affect the swelling of other environmentally-responsive hydrogels.

Mechanical Properties

- Drug and other biomolecules must be protected from the harmful environments in the body such as, extreme P^H environment before it is released at the required site.
- The strength of the material can be increased by incorporating cross linking agents, co- monomers, and increasing degree of cross linking.
- Elasticity of the gel is important to give flexibility to the cross linked chains, to facilitate movement of incorporated bioactive agent.
- The carrier gel must be able to maintain its physical integrity and mechanical strength in order to prove an effective biomaterial.

Biological Properties

Most toxicity problem associated with hydrogel arise due to unreacted monomers, oligomers and initiators that leach out during application. Thus an assessment of the potential toxicity of all material used for fabrication of gel is an integral part of determining suitability of the gel for biological applications. Steps are also taken to eliminate contaminants from hydrogels, by repeating washing and treatment.

Rheological Properties

Hydrogel can also be described in a rheological way. Aqueous solution of hydrophilic polymer at low concentration, where no entanglement of chains occurs, normally shows Newtonian behavior. Once cross linking between the different polymers chains are introduced, thus obtained networks shows visco-elastic and sometimes pure elastic behavior.

Molecule Release Mechanisms for Hydrogel Formulation^[2,14]

The physiochemical properties of the hydrogel network as well as the selection of drug-loading method will be determined the mechanisms by which the loaded drug is released from the crosslinked matrix. The incorporation of the drugs into hydrogel delivery matrices can be performed via one of the following method.

Post-Loading

Absorption of drugs is achieved after hydrogel networks are formed. If an inert hydrogel system is used, diffusion is the major driving force for drug uptake and release will be determined by diffusion and/or gel swelling. In the presence of hydrogels containing drug binding ligands, term accounting for drug-polymer interaction and drug diffusion must both be included in any model description of release.

In-situ Loading

Drugs or drug-polymer conjugation are mixed with polymer precursor solution and hydrogel network formation and drug encapsulation are accomplished simultaneously. In these systems, the release of the drugs can be controlled by diffusion, hydrogel swelling, reversible drug-polymer interaction, or degradation of labile covalent bonds.

Drug Release Mechanism from Hydrogel^[1,2,8,10,11,13-16]

Due to hydrophilicity of hydrogels they can imbibe large amounts of water. Therefore the molecule release mechanisms from hydrogels are not as like hydrophobic polymers. Due to their hydrophilicity, hydrogels can imbibe large amounts of water (>90 wt. %). For hydrogels, both simple and sophisticated models have been previously developed to predict the release of an active agent from a hydrogel device as a function of time. These models are based on the rate-limiting step for controlled release and are therefore categorized as follows:

Diffusion-Control of Hydrogel

Most commonly applicable mechanism for describing drug release from hydrogels is Diffusion-controlled. Fick's law of diffusion with either constant or variable diffusion coefficients is commonly used in modeling diffusion-controlled release. Drug diffusivities are generally determined empirically or estimated a priori using free volume, hydrodynamic, or obstruction-based theories. Types of diffusion –controlled hydrogel delivery system are as follows.

- Reservoir system
- Matrix system

Swelling-Control of Hydrogel

Swelling-controlled release occurs when diffusion of drug is faster than hydrogel swelling. The modeling of this mechanism usually involves moving boundary conditions where molecules are released at the interface of rubbery and glassy phases of swollen hydrogels. The release of many small molecule drugs from hydroxypropyl methylcellulose (HPMC) hydrogel tablets is commonly modeled using this mechanism.

Chemically-Control of Hydrogel

Chemically-controlled release is used to describe molecule release determined by reactions occurring within a delivery matrix. The most common reactions that occur within hydrogel delivery systems are cleavage of polymer chains via hydrolytic or enzymatic degradation or reversible or irreversible reactions occurring between the polymer network and releasable drug. Under certain conditions the surface or bulk erosion of hydrogels will control the rate of drug release. Alternatively, if drug-binding moieties are incorporated in the hydrogels, the binding equilibrium may determine the drug release rate. Chemically-controlled release can be further categorized according to the type of chemical reaction occurring during drug release. Generally, the liberation of encapsulated or tethered drugs can occur through the degradation of pendant chains or during surface erosion or bulk-degradation of the polymer backbone

Types of Hydrogel^[3,4,12-14,17-20]

Stimuli Sensitive Hydrogels

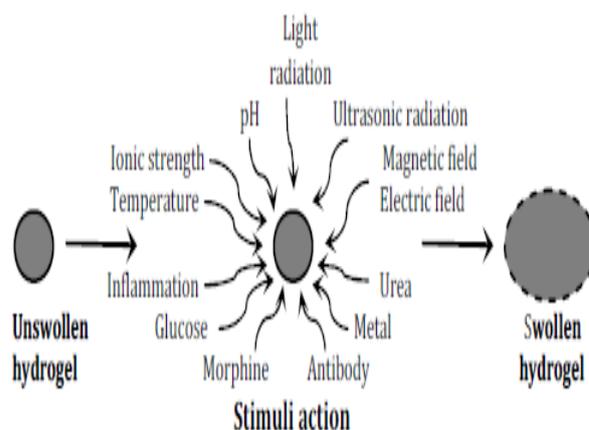


Figure No.1.3. Stimuli responsive swelling hydrogels.^[19]

P^H – Sensitive Hydrogels

These hydrogels respond to changes in the P^H of the external environment. These gels have ionic group (which readily ionisable side groups) attached to impart peculiar characteristic. Some of the P^H sensitive polymer used in hydrogel preparation.

Temperature Sensitive Hydrogels

The hydrogel being cross linked polymers are temperature sensitive. These hydrogels are pharmaceutically well accepted owing to large number of temperature sensitive drugs being delivered in these dosage forms. These temperature sensitive hydrogels is particularly targeted for the formulation of temperature sensitive hydrogels.

Electrical Signal –Sensitive Hydrogel

Hydrogels sensitive to electric current are usually made of polyelectrolyte such as the pH sensitive hydrogels. Electro-sensitive hydrogel undergo shrinking or swelling in the presence of an applied electrical field.

Light Sensitive Hydrogel

Light sensitive hydrogels can be used in the development of photo-responsive artificial muscles or as the in situ forming gels for cartilage tissue engineering. In the study gels may undergo transdermal photopolymerisation after subcutaneous injections were found to be applicable for drug release devices.

Ion –Sensitive Hydrogel

Polymers may undergo phase transition in presence of various ions. Some of the polysaccharides fall into the class of ion-sensitive ones. While k-carrageenan forms rigid, brittle gels in reply of small amount of K^+ , i-carrageenan forms elastic gels mainly in the presence of Ca^{2+} .

Glucose Sensitive Hydrogel

These hydrogels are sugar sensitive and show variability in response depending upon the presence of glucose. Glucose sensitive phase reversible hydrogel is formulated by the interaction between polymer-bound glucose and concanavalin A. One of such pharmaceutical hydrogel system is the cross linked poly-coacylamide hydrogel which liberates the drug in controlled manner only when the concentration of glucose is high in the surrounding environment causing swelling of the hydrogel. Glucose sensitive hydrogels has been characterized by the release of model proteins by insulin and lysozymes through the hydrogel membrane as the free glucose concentration in the environment has been changed. Glucose sensitive hydrogels particularly useful for the determination of the viability of compound that is particularly useful for the presence of glucose and fructose.

Nanohydrogels

Nanohydrogels are the hydrogels which are prepared in water by self aggregation of polymers of natural origin like dextrane. these type of hydrogels are prepared from natural polysaccharides. The hydrogels are prepared by the aggregation of particles called micelles. The cholesterol containing polysaccharide is stirred at 50 °C for 12h in aqueous buffer which leads to swelling of the cholesterol containing polysaccharide. After sonication at 25 °C for 10 min, nanoparticles of hydrogels is formed.

size and density of hydrogel nanoparticles can be controlled by changing the degree of substitution of cholesterol group of such polysaccharides. these hydrogels are of nano dimensions usually of 20-30 nm and are used for cell targeting as they release the entrapped drug by swelling caused by change in the pH of surrounding environment.

Preparation of Hydrogel^[1-3,6,7,9,10,12,13,18,20,21]

As these hydrogels are polymeric network, implies that crosslinks have to be present in order to avoid dissolution of the hydrophilic polymer chain in aqueous solution. Hydrogels are most frequently used for controlled release of bioactive agents and for encapsulation of cells and biomolecules. The nature of the degradation products can be tailored by a proper selection of the hydrogel building blocks. Keeping this consideration in mind, various physical and chemical crosslinking methods are used today for the design of biocompatible hydrogels.

Physical Crosslinking

In physical crosslinking, polysaccharide forms crosslinked network with counter ion at the surface. High counter ion concentration would require longer exposure times to achieve complete crosslinking of the polysaccharide. For physical crosslinking different methods have been investigated.

- Crosslinking by ionic interaction
- Crosslinking by crystallization
- Hydrophobised polysaccharides
- Crosslinking by hydrogen Bonds
- By protein interaction

Crosslinking by Ionic Interaction

Ionic polymers can be crosslinked by the addition of di- or-trivalent counterions. This method underlines the principle of gelling a polyelectrolyte solution with a multivalent ion of opposite charges. Alginate is a polysaccharide with mannuronic and glucuronic acid residue can be crosslinked by calcium ions. Crosslinking can be carried out at room temperature and physiological pH. Therefore alginates gels can be frequently used as matrix for the encapsulation of living cells and for the release of proteins.

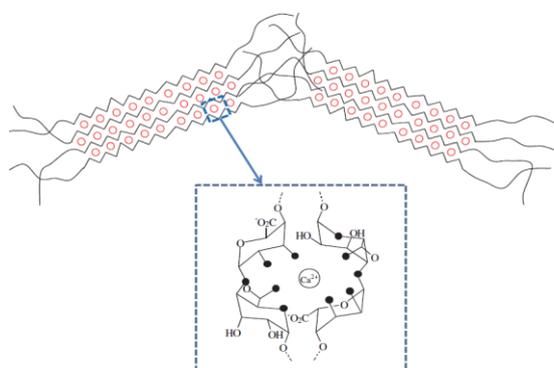


Figure No.1.4. Ionotropic gelatin by interaction between anionic groups on alginate (COO^-) with divalent metal ions (Ca^{2+}).^[7,9]

Cross Linking by Crystallization (Freeze Thawing Method)

When aqueous solution of PVA are stored at room temperature they gradually from a gel with, however, a low mechanical strength. Interestingly, once aqueous solution of this polymer undergoes freeze-thawing process a strong and highly elastic gel is formed. Addition of alginate to the PVA solution before freeze thawing, the gel properties could be modulated. With increasing in concentration of alginate, the mechanical strength of gel increased which was associated with a decreased in release of model drug.

Hydrophobised Polysaccharides

Examples of polysaccharides reported in literature used for preparation of physically crosslinked hydrogels by hydrophobic modification are chitosan, dextran, and pullulan and carboxy methyl curdlan. As example, the hydrophobic antitumor drug adriamycin (ADR) was taken up inside the particles by simply mixing the pullulan suspension with ADR. Slow release was observed at P^H 7.4, which increases at lower P^H of the medium due to increased solubility of drug.

Crosslinking by Hydrogen Bonds

Poly(acrylic acid) and poly(methacrylic acid) from complexes with poly(ethylene glycol) by hydrogen bonding between the oxygen of the poly(ethylene glycol) and the carboxylic acid group of poly(meth)acrylic acid). Also hydrogen bonding has been observed in poly(methacrylic acid-g-ethylene glycol). the hydrogen bonds are only formed when the carboxylic acid groups are protonated. This also implies that the swelling of gels is P^H dependent. Recently a hydrogel system was developed using the principle of DNA hybridization via hydrogen bonding.

By Protein Interaction

Genetic engineering has also been used for the preparation of hydrogels. The major advantages is that the sequence of peptides and, therefore its physical and chemical properties can be precisely controlled by the proper design of the genetic code in synthetic DNA sequences. These hydrogel can also be used for drug delivery with drug release influenced by concentration, polymer composition, and temperature. Crosslinking by antigen-antibody interaction was also performed.

Chemical Crosslinking

Chemical cross linking of the polysaccharide is highly versatile method with good mechanical stability. During cross linking counter ions diffused in to the polymeric and cross linking agent reacts with polysaccharide forming either intermolecular or intermolecular linkages. Factors which affects the cross linking are concentration of the cross linking agent and cross linking time. The high concentration of cross linking like physical cross linking high counter ion concentration would require longer exposure time to achieve complete cross linking of the polysaccharide However the addition of the cross

linking agent leads to adverse effect if the compound is toxic, which on liberation in the body becomes harmful. The various methods for chemical cross linking are as follows

- Cross linking by radical polymerization
- Cross linking by aldehyde
- Cross linking by addition reaction
- Cross linking by condensation reaction.

Cross Linking by Radical Polymerization

Chemical Cross linking can be carried out by radical polymerization in presence of Cross linking agent. In particular dextran is used as building block for (degradable) hydro gel. Dextran is a bacterial polysaccharide consist essentially of-1, 6 linked D-glucopyranose residues the low molecular weight have been used as plasma expander which has resulted in the good documentation of the pharmacological activities and side effect of dextran. Dextran has therefore been investigated for the delivery of drug, protein and imaging agent. Moreover, due to presence of dextran in colon delivery system research on polymerizable dextran was pioneered by Edman et al. have reacted dextran dissolved in water with glycidylacrylate.

Chitosan cross linking leads to formation of permanently covalent network, which may allow the free diffusion of water/bioactive and also enhance the mechanical properties. Chemical Crosslinking is formed by irreversible covalent links as in covalently cross linked Chitosan. Thus allow drug delivery to be efficiently controlled.

Crosslinking by Aldehyde

In order to establish cross linking, rather drastic condition have to be applied (low pH, high temperature etc.) this has especially been investigated for the preparation of cross linked amine containing polysaccharide. Because glutaraldehyde is a toxic compound even at low concentration shows cell growth inhibition alternatives has been developed. Cross linking of gelatin using polysaccharide obtained by partial oxidation of dextran has been reported. The swelling and the degradation of the gel could be controlled by the amount of adipic acid dihydrazide. These hydro gel films have therefore potential to act as a delivery matrix for sustained release of drug at wound sites.

Crosslinking by Addition Reaction

Polysaccharide can be Cross linking with 1, 6-hexamethylenediisocyanate and many other reagents. The network properties can be easily tailored by the concentration of the dissolved polysaccharide and the amount of Cross linking agent. The Cross linking reaction are preferable carried out in organic solvent, because water can react with the Cross linking agent. Further, since the Cross linking agent is generally very toxic, the gels have to be extracted extensively to remove traces of unreacted agent. Once these matrices are aimed for the release of pharmaceutically active agent, they

have to be loaded after the gel formation and extraction processes. This means that protein molecule can be loaded in meshes of the gel which are larger than the protein and these systems therefore show typically first-order release. This often results in limited duration of the release. Finally, between the polymer chain, linkages are established which are stable. This means that degradation only occurs once the polymer backbone is degraded by enzyme.

Cross Linking by Condensation Reaction

A very efficient reagent to cross link polysaccharides with amide bond is NN-(3-dimethylaminopropyl)-N-ethyl carbodiimide. In order to obtain the alginate gel with better mechanical properties than the ionically cross linked gel, Mooney *et al.* developed a method to cross link covalently using N-ethyl carbodiimide. The mechanical properties could be controlled by the amount of PEG-diamine in the gel and molecular weight of PEG.

Characterization of Hydrogel^[3,7,9,17,20,22-26]

Generally hydrogels are characterized for their morphology, swelling property and elasticity. Morphology is indicative of their porous structure. Swelling determines the release mechanism of strength of the network and determines the stability of these drug carriers. Some of the important features for characterization of hydrogels are as follows.

Morphological Characterization

Hydrogels are characterized for morphology which is analyzed by equipment like stereomicroscope. Also the texture of these biomaterials is analyzed by scanning electron microscope to ensure that hydrogels, especially of starch, retain their granular structure. The scanning electron microscope is an instrument that produces a largely magnified image by using electron instead of light to form an image. A beam of electron produced at the top of the microscope by an electron gun. The electron beam follows vertical path through the microscope which is held within a vacuum. The beam travels through electromagnetic field and lenses, which focus the beam down toward the sample. Once the beam hits the sample, electrons X-ray are ejected from the sample. Detectors collect X-rays, backscattered electron, and secondary electron and convert them into a signal that is sent to screen similar to a TV screen.

X-Ray Diffraction

It is also used to understand whether the polymer retains their crystalline structure or they get deformed during the processing pressurization process. The diffraction analysis is quite a popular study for the morphological characterization of the hydrogel. The retention of the crystalline structure or their deformation during pressurization has played a vital role. Deffraction analysis is the estimation of crystalline or amorphous characteristics. The appearance of new peaks in powder pattern is characteristic of drug-exipient interaction-ray diffraction is particularly used for the determination of

the halos that is a characteristic of impurities in powder that determines the pattern of the arrangement in the hydrogel.

In vitro Diffraction

Since hydrogel are the swollen polymeric network interior of which is occupied by drug molecules therefore release studies are carried out to understand the mechanism of release over a period of application. The in-vitro diffractions study is quite popular for studying the release profile of hydrogel. One that basis the bioequivalence study is carried out to estimate to release of the dosage form. The parameters are matched with the standard plot so that the equivalence between the drug solutions is carried out. In -vitro diffraction of type-I collagen hydro gel containing bioactive glass and silica solgel micromeritics particles are formulated and their in-vitro apatite forming ability have been simulated by the body fluids that is assessed.

FTIR (Fourier Transform Infrared Spectroscopy)

Any change in the morphology of the hydro gel change their IR absorption spectra due to stretching and O-H vibration. Formation of coil or helix which is indicative of the cross linking is evident by appearance of bond near 1648cm⁻¹. the stretching or bonding vibration are basically responsible for the change in IR absorption spectra. FTIR is an important technique in organic chemistry. It is an easy way to identify the presence of the certain functional group in a molecule. Also one can use the unique collection of absorption bonds to confirm the identity of a pure compound or to detect the presence of certain impurities.

Swelling Behavior

The hydrogel is allowed to increase in aqueous medium or medium of specific pH to know the swell ability of this polymeric network. These polymers show increase in dimensions related to swelling. The hydro gel swells in the water to form the polymeric network. The formation of this polymeric network is responsible for the morphological characterization of drug .Polymers is characterized by viscosity method, osmometry, light scattering and size exclusion chromatography.

Rheology

Hydrogels are evaluated for viscosity under constant temperature of usually 4c by using cone plate type viscometer. This viscometer is highly specific for the evaluation of the viscosity. The viscosity is determined by the simple equation of determining the angle of repose through that height and length is determined.

Application of Hydrogel^[1-3,6,7,8,10,14,18,23]

Drug Delivery in the GIT

The ease of administration of drug and the large surface for administration makes the GI tract most popular route for drug delivery. Patel and Amiji proposed stomach specific antibiotic drug delivery system for the treatment of Helicobacter pylori infection in peptic ulceration

diseases. They developed cationic hydrogel with pH sensitive swelling and drug release properties for antibiotic delivery in the acidic environment of the stomach. Akiyam reported novel peroral dosage form of hydro gel formulations with protease inhibitor activities. Recently oral insulin delivery using pH responsive Complexation hydro gel was reported. The hydro gel used was cross linked copolymers of PMMA with graft chain of polyethylene glycol. These hydro gel protect the insulin in the harsh, acidic environment of the stomach.

Rectal Delivery

Hydrogel offers a way in which to overcome limitations of this route, provided that the hydro gel shows bioadhesive properties. It was reported that increased bioavailability of propanol subject to extensive first-pass metabolism was observed by adding certain mucoadhesive polymeric compound to polyhexamer based thermally gelling suppositories. The polymeric compound tested was polycarboxiphil and sodium alginate. Miyazaki et al. investigated the potential application of xyloglucan gel with the thermal gelling property as matrices for drug delivery. Another important issue in rectal drug delivery is to avoid rectal irritation. The product discussed above, indicated no such mucosal irritation after drug administration.

Ocular Delivery

Hydrogel because of their elastic properties can represent an ocular drainage-resistant device. In-situ forming hydro gel is attractive as an ocular drug delivery system because of their facility in dosing as a liquid, and long term retention property as a gel after dosing.

Transdermal Delivery

In recent years however a Transdermal route for the delivery of the drug has been investigated. Swollen hydro gel can be delivered for long duration and can be easily removed. These hydro gels can also bypass hepatic first class metabolism making comfortable for the patient. Current research in this field is now focused on electrically assisted delivery using iontophoresis and electroporation. Hydrogel based formulation are being looked at for Transdermal iontophoresis to obtain enhanced permeation of products in question such as, hormones and nicotine.

Subcutaneous Delivery

Implantable device that are subcutaneously inserted tend to illicit immune response of the body leading to inflammation, carcinogenicity and immunogenicity. Thus biocompatibility becomes a major issue, and all implantable material must be compatible with the body. Hydro gels are an ideal candidate for implantable material. They have water content, environment similar to biological tissue, making relatively biocompatible.

Protein and Peptide Drug Delivery

Hydrogel formulation for subcutaneous delivery of anticancer drug has been proposed. For example cross

linked PHEMA was applied to cyratatine (Ars-C). Current studies on implantable hydrogel are leading toward the development of biodegradable system which do not require surgical removal once the drug has been administered

Wound Healing

Modified polysaccharide found in the cartilage is used in formation of hydrogel to treat cartilage defect. For example, the hydro gel of gelatin and polyvinyl alcohol (PVA) together with blood coagulants are formulated.

Soft Contact Lenses

The first commercially available silicon hydro gel adopted two different approaches. First approach by Bausch and Lomb was a logical extension of its development of silicon monomers with enhanced compatibility in hydro gel forming monomers. The second by Ciba vision was the development of siloxy monomers containing hydrophilic polyethylene oxide segments and oxygen permeable polysiloxane unit.

Cosmetology

Hydrogel when implanted in to the breast accentuates them for aesthetics reason. These implants have silicon elastomers shell and are filled with hydroxyl propyl cellulose polysaccharide gel.

Industrial Applicability

Hydrogel is used as absorbent for industrial effluents like ethylene blue dye. Another example is adsorption of dioxins by hydrogel beads.

Tissue Engineering

Micronized hydrogels are used to deliver macromolecule into cytoplasm of antigen-presenting cell this property is also utilized in cartilage repairing. Natural hydro gel material are used for tissue engineering include agarose, methylcellulose and other naturally derived product.

Hydrogel for Gene Delivery

Modification of hydrogel composition leads to effective targeting and delivery of nucleic acid to specific cells for gene therapy. Hydrogel versatility has potential application in the treatment of many genetic and/or acquired diseases and condition.

Novel Hydrogel for Controlled Drug Delivery

HYPAN is the novel hydro gel having properties useful controlled drug delivery. Physical network of crystalline clusters distinguishes HYPAN hydro gel from others.

Hydrogels as Scaffold Materials

Hydrogels are an attractive Scaffolding material because their mechanical properties can be tailored to mimic those of natural tissues. As Scaffolds, hydrogels are used to provide bulk & mechanical constitution to a tissue construct whether cells are adhered to or suspended within the 3D gel framework. The fundamental obligation of a tissue scaffold is to maintain cellular proliferation

and desired cellular distribution throughout the expected servicelife of the construct.

Role of Hydrogels in Drug Delivery System^[10,12]

Localizes drug delivery can be achieved by introducing the drug directly at the target site. The major class of biomaterial considered as implantable drug delivery system is hydro gels. These hydrophilic networks are capable of absorbing great amount of water while maintaining structural integrity. Their structural similarity to the extracellular matrix makes it biocompatible. These synthetic polymers have generated wide interests and are now at the forefront of drug delivery research.

In order to incorporate gel into the body, an opening must be created, with at least the same dimensions as that of the gel. This leads to potential risk and discomfort to the patient. Thus focus has shifted to developing injectables materials with ability to form three dimensional matrices under physiological matrices. This in situ formation can be achieved through specific chemical cross linking reaction. Gel structuring is triggered by environmental stimuli (P^H , temp. solvent, exchange etc.). Synthetic hydrogel, with their ability to imbibe water, flexibility, and biocompatibility, are ideal carriers for the development for novel pharmaceutical formulations and for the delivery of drugs, protein and as targeting agent for drug delivery.

The network structure and the nature of component play a key role in the diffusion behavior; molecules mesh size changes and stability of the incorporated bioactive agent. The use of hydrogel allows not only delivery of drug, but also controlled release, in the manner required by the pharmaceutical scientists. For example drugs can be delivered only when needed, may be directed to specific site and can be delivered formulations have been examined in great detail. Review related to the various applications of hydrogels in drug delivery various sites available in the body such are readily available.

CONCLUSION

With ongoing research in advanced drug delivery formulations to provide stable and economical drug delivery systems, the focus is on hydrogels which are known to reduce the problems of not only conventional dosage forms but also of novel drug delivery systems which require a biocompatible, convenient and stable drug delivery system. Hydrogels, the swellable polymeric materials, have been widely investigated as the carrier for drug delivery systems.

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