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Research Article

A REVIEW ON HYDROGEL PHARMACEUTICAL PREPARATIONS

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A B S T R A C T

Hydrogels are very important formulations in the pharmacy. They were having the swelling property and varying degree of flexibility similar to the natural tissue. They are trapping large quantities of water in their net like structure and can shrink when they were dried.Hydrogels are having good transport properties when they are given in parenteral route. Hydrogel are expensive and non- adherent. They are employed in developing transdermal drug delivery systems, tissue engineering's, and regenerative medicines. Hence hydrogels are having very important role in pharmacy. Many drugs are formulated by using this technique.

INTRODUCTION

Hydrogels are three dimensional network of hydrophilic cross linked polymer that do not dissolve but can swell in water or can respond to the fluctuations of the environment stimuli. Hydrogels are highly absorbent natural or synthetic polymer networks. Hydrogels also possess a degree of flexibility very similar to natural tissue,due to their significant water content. They have both solid, liquid like properties and they are highly biocompatible.They can trap large quantities of water in the network structure and can shrink when dried.

Classification

Hydrogels are classified on the basis of preparation and on the basis of cross linking .On the basis of preparation they are classified in to homo polymer, copolymer, semi inter penetratingnetwork, interpenetratingnetwork and basing on cross linking they are classified in to chemical hydrogels, physical hydrogel.

METHODS OF PREPARATION

Homo polymeric hydrogel:These are polymeric networks derived from a single species of monomer. Thismonomer is a basic structural unit comprising of any polymer network.Photopolymers may have structural cross linked skeletal structure depending upon the polymerisation technique and the nature of the monomer.

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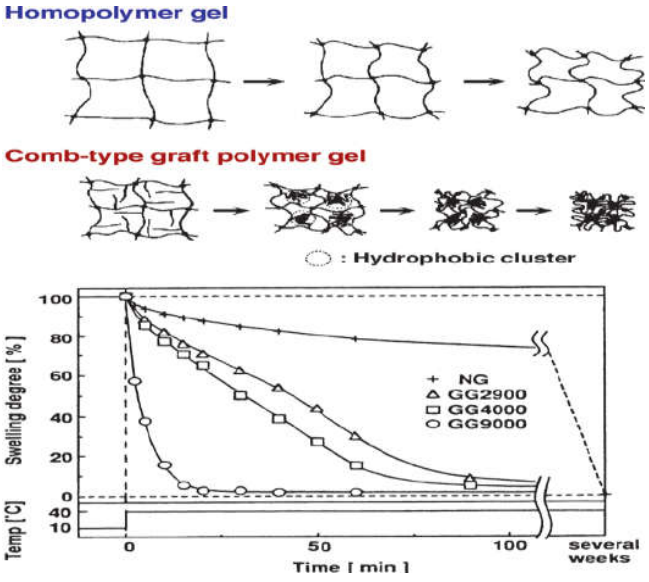


Fig 1 structure of photopolymer gel

Co polymeric hydrogel

Copolymerisehydrogels are composed of two types of monomers in which at least one is hydrophilic in nature. E.g.: the biodegradable tri block poly (ethylene glycol)-poly (caprolactone)-poly ethylene glycol (PEG) co polymeric hydrogel .This co polymeric hydrogel is used for the development of drug delivery system. The mechanism involved here is ring opening copolymerisation of caprolactone.

Semi inter Penetrating Network

One polymer is linear and penetrates another cross linked network without any other chemical bonds between them; it is called a semi interpenetrating network. It can more effectively preserve rapid kinetic response.Rates to PH or temperature due to the absence of restricting interpenetrating elastic network. This PH sensitive semi IPN was synthesised by copolymerisation in the presence of N, N-methylene bis acrylamideas a cross linking agent. The network contains both covalent and ionic bonds .The covalent bonds retained the three dimensional structure of hydrogel and the ionic bonds imparted the hydrogel with higher mechanical strength and PH responsive reversibility.

Inter Penetrating Network (IPN)

IPNsare conventionally defined as intimate combination of two polymers, at least one of which is synthesised or cross linked in the immediate presence of other. This is typically done by immersing a pre polymerised hydrogel into a solution of monomers and a polymerisation initiator.IPN can overcome thermodynamic incompatibility occurs due to the permanent interlocking of network segments and limited phase separation can be obtained.The main advantage of IPNs are relatively dense hydrogel matrices can be produced which feature stiffer and tougher mechanical properties controllable physical properties and more efficient drug loading compared to other hydrogels.

Advantages of Hydrogels

- Hydrogels possess a degree of flexibility very similar to natural tissue, due to their significant water content.
- Entrapment of microbial cells with in hydrogel beads has the advantage of low toxicity.
- Timed release of growth factors and other nutrients to ensure proper tissue growth.
- Hydrogels have good transport properties and it can be injected.
- Hydrogels are biocompatible and they are easy to modify.

Disadvantages of Hydrogels

- Hydrogels are expensive, they are non -adherent, and they may need to be secured by a secondary dressing.
- Hydrogels used as contact lenses causes lens deposition, hypoxia, dehydration and red eye reactions.

Applications

- It can influence cell behaviour by mimicking the extracellular matrix.
- Hydrogels will provide new and improved methods of regenerative medicine, biotechnology, pharmacology and biosensors in the future.
- Hydrogels used in transdermal drug delivery systems, wounddressing, tissueengineering.

Mechanism of Drug Release

The Drug Release Depends on the Following Factors

1. Composition of hydrogel (it includes type of polymer, type of drug and additives.
2. Geometry (size and shape)
3. Preparation techniques.
4. Environmental conditions during drug release.

The following Physical and Chemical Phenomena will Affect the Drug Release Kinetics. Viz.

- wetting of the drug delivery device surface with release medium.(ex :water)
- Release medium penetration into the drug delivery device.
- Creation of pores filled with the water.
- Degradation of drug or polymer.
- Diffusion of drug and or products of polymer degradation inside the hydrogel matrix.
- Diffusion of drug and or products of polymer degradation in the fluid.
- Autocatalytic effects during hydrogel matrix degradation.
- Swelling of polymer, closing of pores caused by polymer swelling.
- Chemical reactions between the drugs and products of polymer degradation and or water.
- Adsorption and desorption process.

More over these phenomena are concerned only during drug transport in the model system , not in the living system.To describe the mechanism of drug transport in the living body the following phenomena must be taken in to account

- Enzymatic degradation
- Protein binding
- Active and passive drug uptake into cells.

From the Process Engineering Point of view the Mechanism Consist of the Following Phenomena

- Exterior diffusion
- Interior diffusion
- Desorption
- Chemical reaction

Exterior Diffusion

It takes place when drug molecule diffuses from surface of the hydrogel .The rate of mass transport can be described by the following expressions.

$$NA = KL(C^{*}_{AL}-C^{\$}_{AL})$$
$$GA = (AC^{*}_{AL}-C^{\$}_{AL})$$

Where:

NA =flux of drug.
GA = mass transfer rate.
KL = mass transfer coefficient.
C^{*}_{AL} = surface concentration of drug.
$C^{\$}_{AL}$= bulk concentration of the drug.
A = area of mass transfer.

Interior Diffusion

In general, the rate of drug release is controlled by interior diffusion. Theories based on ficks law of diffusion distinguish two types of systems.

1. Reservoir 2. Monolithic devices.

1. Reservoir:

Here the drug release is described by ficks first law of diffusion.

$N_A = -D\ dc_A/d_x$
Where NA = Flux of the drug
D = Drug diffusion coefficient
CA = Drug concentration.

Monolithic Devices

Here the drug release is described by ficks second law of diffusion.Where

c = Concentration
t = Time
x = Distance
D =Diffusion coefficient

Desorption

The drug is absorbed from the hydrogel pore surface and then diffuses with in the pore.

Here the movement of molecule is described by ficks first law of diffusion.

The drug release can be described by the following equation
$Dv\ dc/dt = [(N_A+dN_A) - N_A]\ 1a\text{-}r_A\ dv$

This equation describes the differential volume of the medium. That is in the pore between X and X+Dx.

Chemical Reaction

In this ,drug and/or products of polymer degradation can react with the release medium inside its pores. The released medium molecule diffuses to hydrogel medium pores during the contact with the drugs /products of polymer degradation they undergo a chemical reaction. Thisis either reversible /irreversible.

Principle and Requirements for the Gastric Retention of Super Porous Hydrogels

Principle

The gastric retention of super porous hydrogel is based on their fast swelling property. A super porous hydrogel is enclosed in a capsule so that the initial volume is small for easy swallowing. After oral administration, it swells quickly in in the gastric juice to a large size, so that its emptying into the intestine is prevented. When the gastric contraction reaches the hydrogel, the gastric tissues slide over the hydrogel, since it is elastic and slippery .while a drug is released from this dosage form, it slowly undergoes degradation in the stomach by either mechanical force or chemical or enzymatic hydrolysis of the polymer chains constituting the hydrogel. Eventually ,the degraded super porous hydrogel form is eliminated from the stomach.

Requirements for Gastric Retention of Super Porous Hydrogels for Drug Delivery

1. The size is small enough for easy swallowing. In this study hard gelatine capsules with size 000 were used to house the super porous hydrogel dosage form.
2. Swelling is fast enough to overcome the gastric emptying.
3. The size of the swollen gel is large enough to be retained in the stomach.
4. The swollen gel should be strong enough to withstand the peristaltic contraction.

Synthesis and Characterisation of Superporous Hydrogels

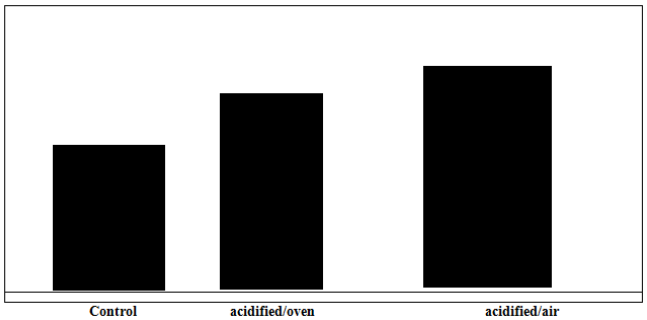
Synthesis

It is similar to the synthesis of ordinary hydrogels except that a foaming agent is added to make super porous hydrogels. The timing of polymerisation has to be matched with the timing of foam formation. If the kinetics of the two process are different, then super porous hydrogels with inter connected pores will not be formed. The key to this process is to use acid to control the polymerization kinetics .addition of $NaHCO_3$ results in foam formation as well as increase in pH, which accelerates the polymerization process with in few minutes after the addition of $NaHCO_3$, polymerisationbecomes complete.

Any vinyl polymer can be used to make superporous hydrogel .but it significantly affects the overall properties of the super porous hydrogels. When Acrylamide was used as the only monomer, the super porous hydrogels show neither large swelling volume nor good mechanical strength. When sulfopropyl acrylamide potassium salt (SPAK) was used alone the superporous hydrogels swelled to a large size in the simulated gastric fluid but were not strong .when AM and SPAK were copolymerised, however, super porous hydrogels showed good swelling and also good mechanical properties.
The mechanical strength of super porous hydrogels can be improved by introducing a composite material .of the many composite materials tested, Ac-Di-Sol was found to be superior to others in increasing the mechanical strength of super poroushydrogels. Ac-Di-Sol particles can be added to the monomer solution before polymerization and foaming.The possible reason for the improved structural integrity is that the addition of Ac-Di-Sol increases the cross linking density of the super porous hydrogel. If toomuch Ac-Di-Sol is incorporated,a good mixing of all the ingredients becomes difficult due to the increase of solution viscosity.

Acidification of the SPAK Super Porous Hydrogels

Post treatment of synthesized super porous hydrogels were attempted to further improve the mechanical strength of the super porous hydrogels. After the preparation they were washed in the SGF (PH 1.2) for 24 hrs. then they were dried in 60^0c oven or air dried at room temperature. The dried super porous hydrogels were allowed to swell in SGF and their mechanical properties were tested using a bench comparator. The ultimate compression pressure (UCP) was used to measure the mechanical strength of superporous hydrogels.UCP was determined by applying increasing amounts of weights until a point when the super porous hydrogel started cracking. The pressure at that point was defined as UCP.



The Above Figure Shows Three Types of Super Porous Hydrogels

1. Super porous hydrogel without any treatment after synthesis
2. Super porous hydrogel that were washed in simulated gastric fluid aftersynthesis and then oven dried at 60^0c for 24 hrs.
3. Super porous hydrogels that were washed in SGF after synthesis and then air dried at room temperature for 5 days.
4. The washing step partially acidified the anionic SO_3^- group into SO_3H group and substantially changed the properties of the super porous hydrogel s. the acidification of the super porous hydrogels made them much stronger than the super porous hydrogel withoutacidification. And after acidification of super poroushydrogel that is dried at room temperature is even stronger than those dried in a60^0c oven.

CONCLUSION

Hydrogels are three dimensional network of the hydrophilic crosslinking polymers that are dissolving and swelling when they are placed in the large quantities of water. They were classified into various types basing on the mode of preparation, crosslinkings. There are various methods of preparation basing on the type of hydrogels. They are having vast applications in the preparation of medicines. They will entrap microbial cells with hydrogel beads. They were also having good transport properties when they are given in the form of injection preparations. The drug release was depended on the type of formulation. Hence this technique was employed for the preparation of pharmaceutical formulations**.**

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