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A REVIEW ON HYDROGEL DRUG DELIVERY SYSTEM

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ABSTRACT

Conventional drug administration often requires high dosages or repeated administration to stimulate a therapeutic effect, which can lower overall efficacy and patient compliance, and result in severe side effects and even toxicity. Hydrogels can provide spatial and temporal control over the release of various therapeutic agents, including small-molecule drugs, macromolecular drugs and cells. Hydrogels as a drug delivery system have been used in many branches of medicine, including cardiology, oncology, immunology, wound healing, and pain management. Due to their high water content, these gels resemble natural living tissue more than any other type of synthetic biomaterial. Chemical initiator initiates the polymerization reaction. Some applications are used of hydrogels in human body. Some environmental variables, such as low pH and elevated temperatures, are found in the body. For this reason, either pH-sensitive and/or temperature sensitive hydrogels can be used for site-specific controlled drug delivery. Hydrogels that are responsive to specific molecules, such as glucose or antigens, can be used as biosensors as well as drug delivery systems.

KEYWORDS: Drug Delivery, Controlled Release, Polymerization.

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.[1,2] Hydrogels also possess a degree of flexibility very similar to natural tissue, due to their significant water content.[3] Thus, hydrogels can imbibe water nearly 10-20 times its molecular weight and hence become swollen.[4] Some examples of Hydrogels include contact lenses[5], wound dressing[6,7] superabsorbents. the hydrogel technologies may be applied to food additives, pharmaceuticals, Biosensor and BioMEMs devices and drugcarriers.[8]

ADVANTAGES OF HYDROGEL[9]

- ✓ Can be injected in vivo (in a whole, living organism) as a liquid that then gels at body temperature.
- ✓ Hydrogels have good transport properties and it can be injected.
- ✓ Entrapment of microbial cells with in hydrogel beads has the advantage of low toxicity.
- ✓ Protect cells.
- ✓ Good transport properties (such as nutrients to cells or cell products from cells).
- ✓ Timed release of medicines or nutrients.
- ✓ Easy to modify.
- ✓ Can be biodegradable or bio absorbable.

FORMULATION METHOD OF HYDROGEL

(A) Use of crosslinkers[10]

- ➢ Copolymerization of monomers using multifunctional co-monomer, which acts as cross linking agent, chemical initiator initiates the polymerization reaction which can be carried out in bulk, solution or suspension.
- ➢ Cross linking of linear polymers by irradiation or by chemical compounds. Monomers used here contain an ionizable group that can be ionized or can undergo a substitution reaction after the polymerization is completed.
- ➢ Thus, the hydrogels synthesized may contain weakly acidic groups like carboxylic acids or weakly basic groups like substituted amines or a strong acidic and basic group like sulfonic acid and quaternary ammonium compounds.
- ➢ Cross linkers incorporated are glutaraldehyde, calcium chloride and oxidized konjac glucomannan (DAK). They impart sufficient mechanical strength to the polymers and thus prevent burst release of the medicaments.

(B) Isostatic ultra high pressure (IUHP)
Suspension of natural biopolymers (eg.starch) are subjected to ultra high pressure of 300-700 MPa for 5 or 20 minutes in a chamber which brings about changes in the morphology of the polymer (i.e. gelatinization of starch molecules occur).Temperature in the chamber varies from 40 to 52^{O}C.[11]

(C) Use of nucleophilic substitution reaction
A pH and temperature sensitive hydrogel viz. hydrogel of N-2-dimethylamino ethylmethacrylamide (DMAEMA) has been prepared using nucleophilic substitution reaction between methacyloyl chloride and 2-dimethylamino ethylamine.[12]

(D) Use of gelling agent
Gelling agents like glycophosphate1-2propanediol, glycerol, trehalose, mannitol etc have been used in the preparation of hydrogels. However, presence of negative charged moieties and turbidity are the problems associated with the method.[13]

(E) Use of irradiation and freeze thawing
Irradiation method is suitable as well as convenient but the processing is costly along with the poor mechanical strength of the product .Freeze thawing method imparts sufficient mechanical strength and stability to the hydrogels except that they are opaque in appearance with little swelling capacity. However, hydrogels prepared from microwave irradiation are more porous than conventional methods.[14]

(F) Synthesis of hydrogel in industry
Formulation of monomer along with initiators and additives lead to polymerization which forms the gel. The gel is dried, sieved and mixed with other additives and post treatment is done if needed. The final formulation is packed and dispatched.

(G) General methods to produce physical & chemical gels[15,16]

Physical cross-linking
1. Heating (or) cooling a polymer solution.
2. Ionic interaction.
3. Complex coacervation.
4. Hydrogen bonding.
5. Heat-induced aggregation.
6. Freeze-thawing.

Chemical cross-linking
1. Chemical cross-linkers.
2. Grafting.
3. Chemical grafting.
4. Radiation grafting.

❖ DESIGN CRITERIA FOR HYDROGELS

Table 1: Design criteria for hydrogels.

Design criteria	Design variable
Polymer transport properties Molecular diffusion	Molecular weight of polymer Molecular weight and size of properties Cross linking density Hydrogen degradation rate
Physical properties Gelling mechanism Structural properties	Temperature, ph., ionic strength Molecular properties of polymer Mechanical strength
Biological properties Biocompatibility	Cytotoxicity of hydrogel Capsule formation

APPLICATIONS OF HYDROGELS[17,18]

- **Wound Healing**

Modified polysaccharide found in cartilage is used in formation of hydrogels to treat cartilage defects. Forexample, the hydrogel of gelatin and polyvinyl alcohol (PVA) together with blood coagulants are formulated.

- **Soft Contact Lenses (silicon hydrogels and polyacrylamides)**

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

- **Industrial Applicability**

Hydrogels are used as absorbents for industrial effluents like methylene blue dye. Another example is adsorption of dioxins by hydrogel beads.

- **Tissue Engineering**

Micronized hydrogels are used to deliver macromolecules (phagosomes) into cytoplasm of antigen-presenting cells. This property is also utilized in cartilage repairing. Natural hydrogel materials used for tissue engineering include agarose, methylcellulose and other naturally derived products.

- **Drug Delivery in GI Tract**

Hydrogel deliver drugs to specific sites in the GIT. Drugs loaded with colon specific hydrogels show tissue specificity and change in the pH or enzymatic actionscause liberation of drugs. They are designed to be highly swollen or degraded in the presence of micro flora.

- **Rectal Delivery**

Hydrogels showing bio adhesive properties are used for rectal drug delivery. Miyazaki et al. explored the

xyloglucan gel with a thermal gelling property as matrices for drug delivery.

- **Ocular Delivery**

Chiton et al. reported silicon rubber hydrogel composite ophthalmic inserts. Cohen et al. developed in-situ forming gelling system of alginate with high gluconic acid contents for the ophthalmic delivery of pilocarpine.

- **Transdermal Delivery**

Swollen hydrogels can be used as controlled release devices in the field of wound dressing. Hydrogel based formulations are being explored for transdermal iontophoresis to obtain enhanced permeation of products viz. hormones and nicotine.

- **Subcutaneous Delivery**

Hydrogel formulations for subcutaneous delivery of anticancer drugs are being prepared viz. cross-linked PHEMA was applied to cytarabine (Arc-c). Implantable hydrogels are now leading towards the development of biodegradable systems which don't require surgical removal once the drug has been administered.

- **Novel Hydrogel for Controlled Drug Delivery**

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

- **Hydrogel for Gene Delivery**

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

- **Cosmetology**

Hydrogels when implanted into breast accentuate them for aesthetic reasons. These implants have silicon elastomer shell and are filled with hydroxyl propyl cellulose polysaccharide gel.

- **Tropical Drug Delivery**

Instead of conventional creams, hydrogel formulation is employed to deliver active components like Desonide, a synthetic corticosteroid used as an anti – inflammatory for better patient compliance.

- **Protein Drug Delivery**

Interleukins conventionally administered as injection are now given as hydrogels which show better compliance and form in-situ polymeric network and release proteins slowly.

CONCLUSION

Hydrogels cover play a significant role in biomedical applications. Significant progress has been made in improving the properties of hydrogels used for drug delivery and expanding the range of drugs and kinetics which can be achieved using a hydrogel based delivery vehicle. Reduced release efficiency, burst effects, complex geometries and unknown correlation between in vitro andin vivo release complicates our understanding of these devices.

There is need for continued improvement in the delivery of not only hydrophobic molecules, but also the delivery of more sensitive molecules viz. proteins, antibodies or nucleic acids which gets deactivated by interactions with the hydrogel delivery vehicle. Solution of such problems would greatly expand the potential of hydrogel based drug delivery to successfully deliver the next generation drugs at the desired rate and location in the body.

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