Hydrogels as potential drug delivery systems

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Hydrogels, the swellable polymeric materials, have been widely investigated as the carrier for drug delivery systems. These biomaterials have gained attention owing to their peculiar characteristics like swelling in aqueous medium, pH and temperature sensitivity or sensitivity towards other stimuli. Hydrogels being biocompatible materials have been recognized to function as drug protectors, especially for peptides and proteins, from in vivo environment. Also these swollen polymers are helpful as targetable carriers for bioactive drugs with tissue specificity. This article presents an overview to the advances in hydrogel based drug delivery that have become the interest of most researchers.

Key words: Hydrogels, pH sensitivity, temperature sensitivity, glucose sensitivity, biodegradable.

INTRODUCTION

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 for molecules as small as NSAIDs (Non-steroidal anti-inflammatory drugs) or as large as proteins and peptides (Graham and Mc-Neil, 1984; Bajpai and Sonkusley, 2002). There are a number of evidences when such drug delivery devices are imperative such as delivery of insulin at elevated blood sugar levels where it is required to constantly provide the drug in the system. These controlled drug delivery systems are designed for zero order release kinetics which ensure constant drug release over a prolonged period of time. Drug targeting is achieved by using biocompatible polymers along with drug in micronized form and then attaching certain “homing devices” like antibodies. It leads to exposure of drug to diseased cells while the normal cells are protected (Stasny et al., 2002; Lowman and Peppas, 1991). All these approaches of dosage form designs require a carrier which should be biocompatible and biosensitive like hydrogels which are hydrophobic polymeric network of three dimensional structures consisting of single chain of polymers (monomers) being cross-linked or chains of co-polymers being cross-linked. The cross linking renders these structures insoluble in water due to ionic interaction and hydrogen bonding (Peppas et al., 2000). These structures imbibe water or biological fluids in large amount at least 10-20 times their molecular weight thus become swollen (Kim et al., 1992). Cross-linked hydrogels have sufficient mechanical strength and physical integrity. If water is removed from these swollen biomaterials they are called xerogels, which are the dried hydrogels. When these dried hydrogels absorb 10-20 times weight of water they become super absorbent. Dehydrated hydrogels are called aerogels as their water is removed without causing structural deformation. Microgels are, however, those having small particles with a diameter of 100 nm and also swell in water.

The network structure of hydrogels can be macro-porous, microporous or nonporous. Macroporous hydrogels are having large pores of dimension 0.1 to 1 μm. These hydrogels release the drug entrapped inside the pores through mechanism dependent on drug diffusion coefficient. Porosity and tortuosity of the gel network (Rowley et al., 1999; Aroca et al., 2007; Liu et al., 2000). Microporous hydrogels are having small pore size of the gel network, usually in the range of 100-1000 Å. The drug releases by molecular diffusion and convection. However, when drugs and polymers are thermodynamically-cally compatible, partitioning of drug through the hydrogel walls is predominant. Nonporous hydrogels are the mesh-like structures of macromolecular dimension (10–100 Å) and are formed due to cross linking of monomer chains. The release of drug is only by diffusion mecha-

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CHARACTERIZATION OF HYDROGELS

Generally hydrogels are characterized for their morphology, swelling property and elasticity. Morphology is indicative of their porous structure. Swelling determines the release mechanism of the drug from the swollen polymeric mass while elasticity affects the mechanical strength of the network and determines the stability of these drug carriers (Khare and Peppas, 1995). 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 SEM to ensure that hydrogels, especially of starch, retain their granular structures (Szepes et al., 2008).

X-ray diffraction

It is also used to understand whether the polymers retain their crystalline structure or they get deformed during the processing pressurization process (Szepes et al., 2008; Yu and Xiao, 2008; Pal et al., 2008).

In-vitro release study for drugs

Since hydrogels are the swollen polymeric networks, 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 (Szepes et al., 2008; Yu and Xiao, 2008).

FTIR (Fourier Transform Infrared Spectroscopy)

Any change in the morphology of hydrogels changes their IR absorption spectra due to stretching and O-H vibration. Formation of coil or helix which is indicative of cross linking is evident by appearance of bands near 1648 cm\(^{-1}\) (Yu and Xiao, 2008; Pal et al., 2008).

Swelling behavior

The hydrogels are allowed to immerse in aqueous medium or medium of specific pH to know the swellability of these polymeric networks. These polymers show increase in dimensions related to swelling (Yu and Xiao, 2008; Yin et al., 2008; Kim et al., 1992).

Rheology

Hydrogels are evaluated for viscosity under constant temperature of usually 4 °C by using Cone Plate type viscometer (Schuetz et al., 2008).

PREPARATION OF HYDROGELS

Hydrogels are prepared by various methods. Some of the important methods are discussed below:

Isostatic ultra high pressure (IUHP)

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 (Szepes et al., 2008).

Use of cross linkers

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 photocrosslinkable chitosan (Az-Ch-LA) is formed which has desired integrity (Ta et al., 2008; Pal et al., 2008; Singh et al., 2007; Tokuyama et al., 2007; Chen et al., 2007b).

Use of water and critical conditions of drying

Aerogels of carbon have been prepared by super critically controlling the drying conditions. Aerogels of resorcinol formaldehyde hydrogels have also been prepared by using water as solvent and sodium carbonate as pH regulator. The final texture of hydrogel is governed by molar ratio of resorcinol to sodium carbonate. This method of preparation leads to porous hydrogels with no shrinkage during drying process. The method is expensive but leads to formation of xerogels with suffi-
cient mechanical strength (Leonard et al., 2008).

**Use of nucleophilic substitution reaction**

Hydrogels of N-2-dimethylamino ethyl-methacrylamide (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 (Wang et al., 2007).

**Use of gelling agents**

Gelling agents like glycolophosphate, 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 (Schuetz et al., 2008; Guo and Gao, 2007).

**Use of irradiation and freeze thawing**

Hydrogels prepared by chemical methods (i.e., use of crosslinkers, gelling agents or reaction initiators) are having problems of removal of residue or unnecessary charged moieties present. Irradiation method is suitable and convenient but the processing is costly. The mechanical strength of such hydrogels is less. However with freeze thawing method, the hydrogels so formed have sufficient mechanical strength and stability but are opaque in appearance with a little swelling capacity. However, hydrogels prepared by microwave irradiation are more porous than conventional methods (Yang et al., 2008; Zhao et al., 2008; Wang et al., 2007; Chen et al., 2007a; Mohdy and Safrany, 2008).

**TYPES OF HYDROGELS**

**pH sensitive or ion sensitive hydrogels**

These hydrogels respond to changes in pH of the external environment. These gels have ionic groups (which are readily ionizable side groups) attached to impart peculiar characteristics. Some of the pH sensitive polymers used in hydrogels’ preparations are polymethyl methacrylate (PMMA), polyacrylamide (PAAm), polyacrylic acid (PAA), poly dimethylaminoethylmethacrylate (PDEAEMA) and polyethylene glycol. These polymers though in nature are hydrophobic but swells in water depending upon the pH prevalent in the external environment. Any change in pH of the biological environment causes changes in the swelling behaviour, for example, the hydrogel of caffeine is prepared with polymer PDEAEMA at pH below 6.6. As the polymer shows high swellability but when pH changes to higher side, the polymer showed shrinkage leading to drug release. The other pH sensitive hydrogels are copolymer of PMMA and polyhydroxyethyl methyl acrylate (PHEMA) which are anionic copolymers, swell high in neutral or high pH but do not swell in acidic medium. It was also observed that pH and ionic strength determines kinetics of swelling of PHEMA and guar gum (Peppas and Peppas, 1990; Das et al., 2006). Other drugs that have been delivered through pH sensitive hydrogels are listed in Table 1.

pH sensitive hydrogels have also been used to encapsulate proteins in acrylamide polymer cross-linked with bisacrylamide acetal cross linkers. At pH of around 5, the pore size of the acetal cross-linked hydrogels increases leading to release of protein. However at neutral pH, the acetal groups remain intact as cross linkers and protein do not diffuse out easily (Murthy et al., 2002; Gupta et al., 2002).

**Temperature sensitive hydrogels**

The hydrogels 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. The release as well as mechanical characteristics of drug and hydrogels are altered with the change in the temperature of external environment (Prabaharan and Mano, 2006). Negative thermo-sensitive hydrogels contract upon heating above their low critical solution temperature. Positive thermo-sensitive hydrogels contract upon heating above their upper critical solution temperature (Soppimath et al., 2002). In general, these hydrogels are hydrophobic polymers which show variable network in response to temperature thus modulate the drug release. These thermo-sensitive gels are specific, controllable and biocompatible drug delivery devices. They could be biodegradable also. The drugs which are widely been explored for such devices are usually from category of anticancer, anti diabetic, hormones or proteins and peptides. Sometimes these gels are formed within the system and are particularly beneficial for tissue targeting to inflamed or diseased areas (Ramanan et al., 2006; Ruel and Leroux, 2004; Bae et al., 1991). Drugs like insulin, heparin and indomethacin have been delivered using these types of hydrogels. Tanaka (1978) developed the thermo-sensitive hydrogels of PNIPAAm (polyisopropylacrylamide). The cross-linked polymers containing 75% NIPAAm (N-isopropyl acrylamide) and rest of MAA (methacrylic acid) showed temperature dependent swelling. However, the combined effect of temperature and pH controls the drug release only when hydrogel gets swollen (Peppas et al., 2000; Kim and Park, 2002).

Thermo-sensitive macrocapsules of nanoparticles have been developed recently where the matrix consists of
Table 1. Various drugs delivered through pH responsive hydrogels for drug delivery.

<table>
<thead>
<tr>
<th>Therapeutic moieties</th>
<th>Polymers</th>
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<tr>
<td>Calcitonin</td>
<td>Copolymer of polymethacrylic acid and polyethylene glycol.</td>
<td>Serres et al. (1996); Torres and</td>
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温度敏感的乙烯基纤维素聚合物被包覆在 thermo-sensitive 膜层中，准备通过交联方式与 poly NIPAAm 交联。这种交联方式在低温时会导致聚合物交联而产生高交联密度，从而导致聚合物的溶胀。在高温度下，聚合物的溶胀会被降低，这样可以控制药物的释放。

Glucose sensitive hydrogels

这些凝胶是糖敏感的，并具有在不同温度和pH值下可溶胀性。一种典型的药物凝胶系统是聚乙烯醇-甲基丙烯酸甲酯（MAA）-N-乙酰胺的凝胶，它在高浓度的葡萄糖存在下会溶胀，而在低浓度下会收缩。这种凝胶在血糖水平较高时会溶胀，从而释放药物。
causing decrease in swelling behaviour. This enzyme can be present in bound form or it could be attached to the polymer chain (Yoshioka and Calvert, 2002). The conducting behavior of gels which gives the idea of swelling vary with the ions liberated due to formation of gluconic acid or by ionization of amine present in the polymer (usually acrylates) used for preparation of hydrogels. Therefore, these smart biomaterials show controlled delivery of solute usually proteins like insulin, lysozyme or BSA (Bovine serum albumin) in response to external environment (Tang et al., 2003).

Apart from temperature, pH, glucose sensitive hydrogels, other stimuli like light, electric field, chemicals and ions have been utilized for formulation of responsive hydrogels (Suzuki and Tanaka, 1990; Lam et al., 2006; Zhang et al., 2005; He et al., 2008b). But these have not gained considerable attention in the field of drug delivery.

**Nanohydrogels**

Nanohydrogels are the hydrogels which are prepared in water by self aggregation of polymers of natural origin like dextran. These types of hydrogels are formed from natural polysaccharides like dextran, pullulan, or cholesterol-containing polysaccharide. The cholesterol-containing polysaccharide is stirred at 50°C for 12 h in aqueous buffer which leads to swelling of the cholesterol containing polysaccharide. After sonication at 25°C for 10 min, nanoparticles of hydrogels are formed. The size and density of hydrogel nanoparticles can be controlled by changing the degree of substitution of cholesterol groups of such polysaccharides (Akiyoshi et al., 1998; Kim et al., 2000). 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 the surrounding environment. Drugs like adriamycin has been delivered to tumor cells and the drug showed pH dependent release and the highest release was when pH was below 6.8 (Na and Bae, 2004). These nanoparticles of hydrogels have been used for controlled release of proteins like lysozyme, albumin, immunoglobulin. The amount of protein released is dependent on the square root of time. Hydrogels especially of dextran are made biodegradable by encapsulation of enzyme dextranase (Hennink et al., 1997). The hydrogels of pullulan nanoparticles have been used for cell targeting by encapsulating active drug in aqueous core of Aerosol OT/ n-hexane (Gupta and Gupta, 2004).

Similar hydrogels have been made by self-assembling nanoparticles of linoleic acid modified chitosan. 1.8% linoleic acid substituted chitosan has structural integrity and shows loading capacity of 19.85 to 37.57% of bovine serum albumin. These nanoparticles hydrogels are biocompatible and biodegradable and are ideal for tissue targeting (Chenguang et al., 2007). The nanohydrogel of polysaccharide-mannose from *Saccharomyces cerevisiae* have been prepared or encapsulating insulin or BSA. The incorporation of calcium phosphate prevents the initial burst release thus these hydrogels are used for controlled drug delivery (Yamane and Akiyoshi, 2007).

**Pharmaceutical applications of hydrogels**

To provide sustained or controlled drug delivery into systems, the hydrogels are designed, modulated and characterized for the expected *in-vivo* results. These hydrogels have gained existence in drug delivery through parenteral, ocular, rectal, vaginal, dermal and nasal routes (Matsuda, 2002; Obaidat and Park, 1997; Kim and Park, 2002). Some of the important pharmaceutical applications of hydrogels are discussed below.

**Wound healing**

A modified polysaccharide that occurs in cartilage has been used in formation of hydrogels to treat cartilage defects has been developed (Fenglan et al., 2004). The polysaccharide is functionalized with methacrylate and aldehyde group which react with proteins of skin tissues, while the methacrylate cross links with back bone of disaccharide chondroitin; thus, a network is formed from where the chondrocytes cells are released (Baroli, 2007; Netti et al., 1993). Honey hydrogels have been used for

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<td>Adrenochrome (Blood coagulating agent)</td>
<td>Co-polymer of poly-PNIPA and poly-PNIPA-Co-AA</td>
<td>Chen et al. (2007); Li et al. (2008).</td>
</tr>
<tr>
<td>5-Flurouracil</td>
<td>NIPAAm-Co.AAm</td>
<td>Bikram et al, (2007); Wanf et al. (2008).</td>
</tr>
<tr>
<td>Insulin</td>
<td>NIPAAm-Co.AAm</td>
<td>Gupta et al. (2007).</td>
</tr>
<tr>
<td>Vaginal Microbicide</td>
<td>Polypepsion caprolactone-co-lactide-polyethylene glycol; Chitosan</td>
<td>Shim et al. (2007); Lee et al. (2004); Klouda and Mikas, (2008); Sun et al. (2007).</td>
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PNIPA is poly N-isopropyl acrylamide; PNIPA-Co-AA is poly N-isopropyl acrylamide-co-acrylic acid; NIPAAm is N-isopropylacrylamide.

**Table 2. Temperature sensitive hydrogels for drug delivery.**

causing decrease in swelling behaviour. This enzyme can be present in bound form or it could be attached to the polymer chain (Yoshioka and Calvert, 2002). The conducting behavior of gels which gives the idea of swelling vary with the ions liberated due to formation of gluconic acid or by ionization of amine present in the polymer (usually acrylates) used for preparation of hydrogels. Therefore, these smart biomaterials show controlled delivery of solute usually proteins like insulin, lysozyme or BSA (Bovine serum albumin) in response to external environment (Tang et al., 2003).

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prompt wound healing. These hydrogels have matrix in which honey is cross-linked and most acceptable, easily peeled, and transparent system (Yusof et al., 2007). The hydrogel of gelatin and PVA (polyvinyl alcohol) along with blood coagulant have been formulated. The cell adhesive hydrogel ensured better effect than corresponding gel or ointment in controlling blood coagulation (Mukherjee and Banthia, 2006).

Colon specific drug delivery

Colon specific hydrogels of polysaccharides have been specifically designed because of presence of high concentration of polysaccharidase enzymes in the colon region of GI (gastrointestinal) tract. Drugs loaded in such hydrogels show tissue specificity and change in the pH or enzymatic actions that cause liberation of drug (Singh et al., 2007). Controlled delivery of Ibuprofen to colon has been achieved through hydrogel of guar gum cross linked with glutaraldehyde as cross linker (Das et al., 2006).

Cosmetology

For aesthetic purpose, hydrogels have been implanted into breast to accentuate them. These hydrogels swell in-vivo in aqueous environment and retain water. These breast implants have silicone elastomer shell and are filled with hydroxyl propyl cellulose polysaccharide gel (Adam et al., 2007).

Topical drug delivery

Hydrogels have been used to deliver active component like Desonide which is a synthetic corticosteroid usually used as an anti-inflammatory. Instead of conventional creams, the hydrogels have been formulated for better patient compliance. These hydrogels have moisturizing properties therefore scaling and dryness is not expected with this drug delivery system (Trookman et al., 2007; Rowley et al., 1999; Wyhne et al., 2002). Antifungal formulations like cotrimazole has been developed as hydrogel formulation for vaginitis. It has shown better absorption than conventional cream formulations (Chang et al., 2002). For ocular drug delivery of pilocarpine and timolol, the polymers which form gel such as xyloglucan have been used for sustained drug delivery. Hydrogels of poly hydroxyethyl methacrylamide (pHEMA), N, N-dimethyl acrylamide (DMAAm) and 2-(N-ethyl per fluoroctane sulphonamide) ethylacrylate (FOSA) have been used for ocular delivery to have complete absorption through cornea. Drugs like diclofenac and phenaramine maleate have been successfully delivered through hydrogels (Miyazaki et al., 2001; Bugalassi et al., 2000; Xinmeng et al., 2007; Nanjawade et al., 2007).

Industrial applicability

Hydrogels have been used as absorbents for industrial effluents like methylene blue dye (Paulino et al., 2006). The other example is the adsorption of dioxins by hydrogel beads. The DNA of Salmon milt adsorbs dioxins which produce health hazards like carcinogenicity, immunotoxicity or endocrine disruption.

Modified dosage forms

An interesting research in this field of drug delivery is of bio-macromolecules like insulin delivered to the site of absorption with hydrogels of poly (methacrylamide –co- N- vinyl- 2- Pyrrolidone co- itaconic acid). The insulin entrapped in this matrix showed release at the desired interval. The swelling behaviour was analyzed in medium containing pepsin which degrades insulin. Thus when an optimized concentration of cross linkers like N, N’ – methylene bisacrylamide are used then maximum entrapment efficiency is observed. Thus the release and unwanted degradation of drugs like insulin can be prevented by hydrogel based drug delivery devices (Bajpai and Saggu, 2007; Sato, 1984).

Tissue engineering

The micronized hydrogels (microgels) have been used to deliver macromolecules like phagosomes into cytoplasm of antigen-presenting cells. The release is because of acidic conditions (Murty et al., 2002; Jain et al., 2007). Such hydrogels mold themselves to the pattern of membranes of the tissues and have sufficient mechanical strength. This property of hydrogels is also used in cartilage repairing (Park et al., 2007; Gyenes et al., 2007).

Protein drug delivery

Interleukins which are conventionally given as injection are now given as hydrogels. These hydrogels have shown better patient compliance. The hydrogels form in-situ polymeric network and release proteins slowly. These are biodegradable and biocompatible also (Hiemstra et al., 2007; Klouda and Mikos, 2008; Patil et al., 1996; Sutter et al., 2007). For ocular drug delivery of pilocarpine and timolol, the polymers which form gel such as xyloglucan have been used for sustained drug delivery. Hydrogels of poly hydroxyethyl methacrylamide (pHEMA), N, N-dimethyl acrylamide (DMAAm) and 2-(N-ethyl per fluoroctane sulphonamide) ethylacrylate (FOSA) have been used for ocular delivery to have complete absorption through cornea. Drugs like diclofenac and phenaramine maleate have been successfully delivered through hydrogels (Miyazaki et al., 2001; Bugalassi et al., 2000; Xinmeng et al., 2007; Nanjawade et al., 2007).

Miscellaneous applications

Hydrogels are also used in other forms of drug delivery
like pulsatile drug delivery or oral drug delivery (He et al., 2008a; Guo and Gao, 2007; Gazzaniga et al., 2008). Injectable hydrogels are also been investigated for cancer drug delivery. In situ gel-forming hydrogels for prolonged duration have also been reported (Ta et al., 2008; Fang et al., 2008).

Conclusion

There are enough scientific evidences for the potentiality of hydrogels in delivery of drug molecules to a desired site by triggering the release through an external stimulus such as temperature, pH, glucose or light. These hydrogels being biocompatible and biodegradable in nature have been used in the development of nano biotechnology products and have marvelous applications in the field of controlled drug delivery as well. That is why these turn-able biomedical drug delivery devices are gaining attention as intelligent drug carriers.

REFERENCES


Kim JJ (1999). Phase- reversible glucose sensitive hydrogels for modulated insulin delivery. PhD dissertations, Purdue University, Indiana, USA.


Kim MR, Park TG (2002). Temperature- responsive and degradable...


