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Review Article

SUPERPOROUS HYDROGEL: A REVIEW

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Abstract

Superporous hydrogels (SPHs) were originally developed as a novel drug delivery system to retain drugs in the gastric medium. These systems should instantly swell in the stomach and maintain their integrity in the harsh stomach environment, while releasing the pharmaceutical active ingredient Moreover, an instant swelling of hydrogel has too revealed potential application for peroral intestinal peptide and protein absorption. The fast swelling property is based on water absorption through open porous structure by capillary force. The poor mechanical strength of SPHs was overcome by developing generations. This review discusses the preparation, characterization and application of SPHs.

Keywords: Hydrogels, swelling, SPHs

INTRODUCTION

Hydrogels having ability to create effective pore size larger than 10 micrometer are known as Superporous hydrogels. SPHs possess an average pore size of greater than 100 microns and swell to equivalent size within a minute because of rapid intake of water by capillary wetting through number of interconnected open pores. SHPs have tendency to swell to a large size with a swelling ratio about 100 or more and must have mechanical strength high enough to withstand pressure by gastric contraction. This can be achieved by incorporating hydrophilic particulate material Ac- Di- Sol (Cross carmellose Sodium). A superporous hydrogel is a 3-dimensional net-work of a hydrophilic polymer which absorbs a large amount of water in a very short period of time because of the presence of interconnected microscopic pores. Due to porous structure, SPHs has hundreds of times greater surface area and shorter diffusion distance than conventional hydrogels do. These structures allow dried SPHs to swell very fast to a very large size on contact with water. Because of these unique properties, SPHs were initially used to develop gastric retention device that increases the gastric very residence time of drugs to get long-term, oral controlled drug delivery. Gastric retention devices would be most beneficial for local action of drugs in the stomach, e.g. antacids and antibiotics for bacteria based ulcers or drugs that are required to be absorbed primarily in the stomach. Many drugs having narrow absorption window, i.e. mainly absorbed from the proximal small intestine, bioavailability of those drugs would be increased by gastric retention. For drugs which are absorbed rapidly from the gastrointestinal tract (GIT), should have slow release from the stomach to improve the bioavailability. Gastric retention devices can also be used for those drugs that are poorly soluble at an alkaline pH or drugs that are degraded in the colon (eg, metoprolol). Several important properties of SPHs, like fast swelling capacity, large swelling ratio, and surface slipperiness, make them an excellent candidate to develop gastric retention devices. The weak mechanical property of fully swollen SPHs limits their practical application which can be overcome by making SPHs composites. To overcome this slow swelling property of dried hydrogels, the current inventors have synthesized a super SPHs

porous hydrogel that can swell within minutes despite the consequences of the size of the matrix. SPHs swell very fast regardless of their size, and this is due to the interconnected porous structure. The interconnected structural pores provide water absorption into the centre of the SPHs by capillary force. Even though these super porous hydrogels provided drastically fast swelling kinetics and high swelling degree, the mechanical strength of the fully swollen super porous hydrogels was besides poor to be useful. In some cases, the abundant swollen super porous hydrogels could not be picked up and broke easily due to their very poor mechanical properties. Usually, mechanically strong super porous hydrogels can be made by increasing the cross linking density, but this would result in a very small extent of swelling with a loss of the superabsorbent property. Therefore, it is preferred to make super porous hydrogels having fast swelling and high absorbency uniqueness as well as high mechanical strength. [1]

ADVANTAGES OF SPHs -

Superporous hydrogels has three unique properties that conventional hydrogels do not have.

a. The swelling rate is very fast. The Superporous hydrogels swell completely within a minute regardless of the size of the dried superporous hydrogel.

b. Superporous hydrogels swell to such an extent that the weight of fully swollen superporous hydrogel is higher than the weights of dried superporous hydrogels.

c. Though the superporous hydrogels contain small percentage of solid content of the total weight, it can exert significant expansion force during swelling.

d. Superporous hydrogels can also be made elastic, which minimizes their rupture.

e. The unique properties of superporous hydrogels can also be used for non-pharmaceutical and non-biomedical applications. [2]

GENERATIONS OF SUPERPOROUS HYDROGELS

Superporous hydrogels are porous hydrophilic crosslinked structures with the capability of absorbing aqueous fluids up to a few hundred times their own weight. Highest swelling is generally reached in a fraction of a minute with having average pores of 200 mm in size. There are three generations of super porous hydrogels were developed:

- First generation SPHs- Conventional SPHs.
- Second generation SPHs- SPHs composite.
- Third generation of SPHs- SPH hybrid.

FIRST GENERATION SPHs (CSPHs)-

These first generation SPHs are prepared by Chen et al, in the year 1999. First time he prepared SPHs with fast swelling kineticks and superabsorbent properties. These are polymerized and cross linked with different vinyl monomers and they require a foaming agent, foam stabilizer and a foaming aid, along with these different wetting agents are also added to increase the water absorption rate to less than a minute. Highly hydrophilic acrylamide, salts of acrylic acid, and sulfopropyl acrylate are mostly used for preparation of CSPHs. Generally dried SPHs are brittle and hard in nature, but when they are dissolved in aqueous fluids, the moisture-induced plasticization of these polymers results into soft and flexible structures. When these polymers are in dry state, handling is very difficult, because during drying process the porous structure becomes collapsed due to the surface tension of water, which pulls the polymer chains together. This problem can be overcome by replacing the water with alcohol, since it has low surface tension, which prevents the porous structure from collapsing during drying

SECOND-GENERATION SPHs - SPH Composites

In the year 2001 Park et al was first time introduced these SPH composites. In second generation SPHs are developed to overcome the lack of desirable mechanical properties in CSPHs, by modifying the conventional SPHs with the addition of superdisintegrants into the formulation. In SPH composites, composite is a matrix, which contains both dispersed phase and continuous phase. The preparation of SPH composites also includes the same monomer, cross linker, and initiating system in CSPHs, but along with these we also use swellable filler, i.e composite agent (which is cross-linked water-absorbent hydrophilic polymer). While this filler dispersed into the reacting mixture, it would swells and absorbs a mixed solution of monomer, cross linker, initiator and the water-soluble foaming additives. Upon polymerization, the at the same time the pH of the solution rises (B).

polymer chains are formed, since the filler serves as the local point of physical cross-linking. Each composite agent or swollen filler serves as an isolated individual reactor, throughout the polymerization process, in which cross-linking polymerization occurs. As the cross-linking polymerization precedes entire the solution, individual composite agent particles are connected together by connecting the polymer chains.

THIRD-GENERATION SPHs- SPH Hybrids

The third generation of SPHs is improved versions of the second generation, and developed based on SPH hybrids for synthesizing SPHs which are having high mechanical and elastic properties. In second generation SPHs, pre-cross-linked matrix-swelling additive is added, where as SPH hybrids are prepared by adding a hybrid agent that can be cross-linked after SPH is formed. The hybrid agent is a water-soluble or water-dispersible polymer that can form crosslinked structure (in a manner similar to forming interpenetrating network) through chemical or physical cross-linking. Examples of hybrid agents are polysaccharides including sodium alginate, pectin, chitosan or synthetic water-soluble hydrophilic polymers such as poly (vinyl alcohol). Once the second network is formed, the whole system becomes similar to interpenetrating polymer networks. [3]

PREPARATION OF SPHs:-

Synthesis of Superporous Hydrogels:

Synthesis of superporous hydrogels is same to the synthesis of ordinary hydrogels but the only difference is that a foaming agent is added to prepare superporous hydrogels. The timing of the polymerization has to be matched with the timing of foam formation. If the kinetics of the two processes are not matched, then superporous hydrogels with interconnected pores will not be formed. The important step of this process is to use acid to control the polymerization kinetics. Addition of NaHCO3 leads to foam formation as well as rise in pH, which accelerates the polymerization process. After the addition of NaHCO3, polymerization becomes complete within a few minutes. The pH of the monomer mixture is low because of the addition of acid (A), and this makes polymerization very slow. The addition of NaHCO3 results in foaming and The pH increase accelerates the polymerization process, which is completed before the foam subsides. This results in formation of superporous hydrogel (C).

Superporous Hydrogels for Gastric retention:

Any vinyl monomer can be used to prepare superporous hydrogels using the process described in Fig.3. The type of monomer included in the superporous hydrogel preparation significantly affects the overall properties of the superporous hydrogels. Mechanical property is the important property of SPHs. The superporous hydrogels has neither large swelling volume nor good mechanical strength, when acrylamide (AM) is used as the only monomer. When sulfopropylacrylamide potassium salt (SPAK) is used alone, the superporous hydrogels swells to a large size in the simulated gastric fluid (SGF) but are not strong. When AM and SPAK are copolymerized, however, superporous hydrogels shows good swelling as well as good mechanical properties.

Superporous Hydrogel Composites:-

The mechanical strength of superporous hydrogels can be improved greatly by incorporating a composite material. Among the many composite materials, Ac-Di-Sol is superior to others in improving the mechanical strength of superporous hydrogels. Ac-Di-Sol can be added to the monomer solution before polymerization and foaming. Addition of Ac-Di-Sol increases structural integrity by increasing the (physical) crosslinking density of the superporous hydrogel. If Ac-Di-Sol is incorporated in very large proportion however, a good mixing of all the ingredients becomes difficult because of increase in the viscosity of the solution.

Acidification of the SPAK Superporous hydrogels: -

Pretreatment of SPHs by acidification increase the mechanical strength of the superporous hydrogels. The ultimate compression pressure (UCP) is used to measure the mechanical strength of superporous hydrogels. UCP value is determined by applying increasing amounts of weights until a point when the superporous hydrogel started cracking.

The pressure at this point is defined as penetration pressure (PP) and calculated by the following equation:

PP = *F*u/*S*

are commonly used to evaluate SPH mechanical

Where *F*u is the ultimate compressive force at complete breakage of polymer and *S* is the contact area of the lower touch. [4]

CHARACTERIZATION OF SPHs-

1. Swelling:

The SPHs in general are mostly characterized by their swelling and mechanical properties in different media. The swelling properties are measured by weight, volume and dimension at different time intervals to obtain swelling rate or at equilibrium to obtain swelling capacity. The swelling and mechanical properties of SPHs are generally sensitive to the type and nature of the swelling medium because SPHs are mostly based on hydrophilic and ionic monomers. The most important factors are ionic strength, pH, salts, organic solvents and pressure. The SPH swelling properties (measured by volume (VSR) or weight (WSR)) generally increase with an rise in pH, and a decrease in ionic strength, salt concentration, cation valency and pressure. Although swelling is mostly measured gravimetrically and volumetrically, a texture analyzer is used to obtain the SPH swelling properties under load. The swelling medium can be tap water, distilled water, aqueous media of different ionic strengths and pHs, combined aqueous/organic media, simulated gastric fluid (gastric retention application), simulated intestinal fluid (intestinal application) and so on. Moreover, swelling parameters can be evaluated at low (room temperature) or medium/high temperatures (body fluid temperature of 37^0C). Another swelling parameter exclusive to the SPHs is the Tcore. The SPHs are opaque in their dry state and become transparent in their hydrated, swollen state. The Tcore measures the opaque/transparent transition in SPHs.

The swelling ratio is calculated by following equation: $Q = (Ms - Md) / Md$

Where, *Q* is the swelling ratio, Ms the mass in the swollen state and Md the mass in the dried state.

2. Mechanical Properties:

Although the measurement of SPH swelling properties is simple, quantifying the SPH mechanical properties is challenging. The SPHs in their swollen state are generally weak, containing pores of different sizes and their overall microstructure is much more complex. Regular mechanical testers and texture analyzers properties.

3. Gastric Simulator:

Generally the pores inside the SPH vary from 100 to 1000 *m*m in size. Under homogeneous loading, pores of different sizes resist deformation differently. The SPH mass will break apart from its weakest point, which cannot be monitored by using regular mechanical testers. A gastric simulator, based on the water-hammer theory, utilizes a controlled amount of different types of stresses on objects immersed in the testing fluid to simulate the forces that a sample might receive upon ingestion in the body. The stress concentrated on the weakest part of the SPH body will lead to the formation of craze, crack and finally rupturing of the whole platform. The simulator measures the amount of energy absorbed by the sample until it fails under certain stresses. The gastric simulator is valuable in screening formulations and in designing SPH-based gastro-retentive platforms. [5]

4. Measurement of Gelation Kinetics:

As the polymerization reaction proceeds, the viscosity continuously increases until the full network structure (gel structure) is formed. The gelation time is defined as a time period for gel formation followed by addition of glyoxal. It is measured by a simple tilting method after adjustment of pH to 5.0 with acetic acid. It is determined by the duration of time taken by the reactant mixture to become viscous and henceforth the viscous solution no longer falls down in the tilted tube position.

5. Determination of Void Fraction:

The void fraction can be calculated by the following equation:

Void Fraction = Dimensional volume of the hydrogel / Total volume of pores

The void fraction inside superporous hydrogels is determined by immersing the hydrogels in HCl solution (pH 1.2) up to equilibrium swelling. The dimensions of the swollen hydrogels are measured and by using these data, sample volumes are determined as the dimensional volume. In the meantime, the amount of absorbed buffer into the hydrogels is determined by subtracting the weight of dried hydrogel from the weight of swollen hydrogel and the resulting values are assigned as the total volume of pores in the hydrogels.

there have been a large number of approaches

6. Water Retention:

The following equation is used to determine the water retention capacity (WRt) as a function of time:

WRt = (Wp - Wd) / (Ws - Wd)

Where,Wd is the weight of the dried hydrogel, Ws is the weight of the fully swollen hydrogel, and Wp is the weight of the hydrogel at various exposure times.

For determination of the water-retention capacity of the hydrogels as a function of the time of exposure at 37^{o}C, the water loss of the fully swollen polymer at timed intervals was determined by gravimetry. [6]

7. Porosity Measurement:

For porosity measurement, the solvent replacement method is used. Dried hydrogels are dipped overnight in absolute ethanol and weighed after excess ethanol on the surface is blotted. The porosity is calculated from the following equation:

Porosity = (M2 – M1) / ρV

Where, M1 and M2 are the mass of the hydrogel before and after immersion in absolute ethanol, respectively; ρ is the density of absolute ethanol and V is the volume of the hydrogel. [7]

8. Drug Loading:

The method of soaking or equilibration is used for drug loading. In this method the amount of buffer necessary for complete swelling of superporous hydrogel is determined. Thereafter the drug solution in the determined amount of buffer which is required for complete swelling is prepared. Subsequently, superporous hydrogel is placed in the drug solution and left until all the drug solution is sucked up. Then the completely swollen superporous hydrogel loaded with the drug is placed in an oven at 30^{o}C for drying overnight

9. Safety/Toxicity:

The safety and non-toxicity of synthetic superporous hydrogels must be demonstrated before these delivery systems can be pharmaceutically acceptable. Swine emesis model study has been used to investigate the safety of novel gastroretentive SPH platforms.[8]

PHARMACEUTICAL APPLICATIONS OF SPHs:

1. Development of Gastric Retention Devices-

Gastric retention devices are mostly useful in delivery of many drugs. From the last 2 decades using well-established principles to prevent the dosage form from exiting the pylorus during gastric emptying. The main aim to develop gastric retention devices is to make an oral formulation, which doesn't pass through the pylorus by fast swelling to a large size. They are most beneficial in the delivery of drugs, which acts locally in stomach (e.g., antacids and antibiotics for bacteria-based ulcers etc), or primarily absorbed in the stomach. These gastric retention devices are also useful for drugs which are or degraded in the colon (eg: Metaprolol) and which are poorly soluble in alkaline pH medium. However prolonged gastric retention devices are not necessary in cases like, the drugs which are primarily absorbed in the colon (since it sustain the blood levels up to 24hours), and also for drugs which are unstable in the presence of acidic pH. This gastric retention is also not desirable for drugs like asprin, and non-steroidal anti inflammatory drugs. [9]

2. Development of Fast-Dissolving Tablets-

The major benefit of the fast-dissolving tablet technologies is that the dosage forms can be administered easily in the absence of water and without the need of swallowing. This feature is especially useful to children and the elderly. There are basically three different technologies were developed from the initial success of first fast-dissolving tablets: They are freeze-drying, sublimation or heat molding, and direct compression. By using freeze-drying technology the tablets which are dissolved within 5 seconds can be prepared, whereas by using sublimation or molding technology, tablets which are dissolved within 15 seconds can be prepared. But these two methods are having the disadvantage that they are expensive and the produced tablets are mechanically weak. Therefore direct compression technology was developed, which is less expensive and prepared tablets are having good physical resistance. By this method the prepared tablets are disintegrate within 10 seconds due to the fast uptake of water into the core of tablet. This direct compression method involves the addition of fine particles of superporous Hydrogels to the drug and other excipient.

3. Development of Diet Aid:

Diet soft drinks, meal replacement shakes, diet • biomedical device for treating aneurysms. When

drugs and even surgical methods have been used to lose weight. The SPHs can theoretically occupy a significant portion of the stomach space due to their rapid and extensive swelling, leaving less space for food, and thereby suppressing appetite. This type of system can help to lose weight in obese people. Maintaining the integrity and volume of the swollen SPH for a substantial period of time is the major challenge in the use of SPHs as a weight loss aid.

Developing new drug delivery technologies and utilizing them in product development is critical for pharmaceutical companies to survive. Superporous hydrogels are a new class of hydrogel materials that, regardless of their original size, rapidly swell to a large size. Different generations of SPHs evolved to address the needs for certain pharmaceutical applications, including gastric retention. Studies have shown that some SPH formulations are potentially exploitable for heavy duty applications in which superb swelling and mechanical properties are required in harsh swelling media. The feasibility of using these SPHs in oral solid and semi-solid dose formulations have also been studied. Preliminary safety and efficacy of certain SPH formulations have been evaluated in-vivo, paving the way for further development of these materials for pharmaceutical, food and biomedical applications. Superporous hydrogels can be made elastic, and this property can minimize their rupture. Various pharmaceutical and biomedical applications of superporous hydrogels have been made, and several products are under development. The unique properties of superporous hydrogels can also be used for non-pharmaceutical and non-biomedical applications. [10]

4. **Development of Occlusion Devices for Treatment of Chemoembolization-** Chemoembolization is a combined method of embolization and chemotherapy. Embolization has been used for cancer treatment by restricting the oxygen supply to the growing tumours. This method could be combined with chemotherapeutic agents to achieve local delivery and low systemic toxicity. A chemotherapeutic agent and an anti-angiogenic agent could be loaded into SPHs for chemoembolization therapy. The property of fast swelling to a large size of superporous hydrogels has been useful in the development of a new the size and shape of an aneurysm site is predetermined by a non-invasive imaging method, a superporous hydrogel of the same shape (but smaller size) can be made. When a superporous hydrogel is deployed at the aneurysm site, it swells quickly to occupy the space and make the blood clot. Deposition of superporous hydrogels resulted in up to 95% aneurysm occlusion without any evidence of parent artery compromise and inflammatory response. A new occlusion device made of a combination of superporous hydrogel and platinum coils, known as Hydrocoil, is currently under development. A bioactive can be released from the superporous hydrogels either to enhance or to delay blood clotting. [11]

5.**Biomedical applications-** In the biomedical area, SPHs and SPH composites can be used to make various biomedical devices, such as artificial pancreas, artificial cornea, and artificial skin, articular cartilage, soft tissue substitutes, cell growth substrates in tissue engineering, burn dressings, surgical augmentation of the female breast, or hemoperfusion in blood detoxification and in the treatment of uremia. Vascular ingrowth into superporous hydrogels are useful for cell transplantation, tissue engineering and in combination with cell therapies. Hydroxyapatite containing super porous hydrogel composites 35 and novel scaffolds of poly (2-hydroxyethyl methacrylate) super porous hydrogels are useful for bone tissue engineering.(12)

CONCLUSIONS -Superporous hydrogels are a new class of hydrogel materials that, regardless of their original size, rapidly swells to a large size. Different generations of SPHs evolved to address the needs for certain pharmaceutical applications, including gastric retention. Superporous hydrogels can be made elastic, and this property can minimize their rupture. Various harmaceutical and biomedical applications of superporous hydrogels have been made, and several products are under development. The unique properties of superporous hydrogels can also be used for non-pharmaceutical and non-biomedical applications.

REFERENCES

1. Palak K. Patel**,** Sanket N. Mistry, Gunjan J. Patel, Dr. P. D. Bharadia, V. M. Pandya, D.A. Modi, *Recent in Controlled Drug Delivery System: Superporous Hydrogels,* IJPI's Journal of Pharmaceutics and Cosmetology Vol 1: 5 (2011) page no.54-65.

2. Drug Delivery Technology, Superporous Hydrogels for Pharmaceutical & Other Applications Issue Date: Vol. 2 No. 5 July/August 2002. Page no. 46-55

3. D.harika , R. sunitha, P.srivallikumari and D.varun, *SUPERPOROUS HYDROGELS-VERSATILE DRUG RELEASE RETARDENT*, Vol.2 (4) July – August -2011 page no.329-341.

4. Dergunov SA, Nam IK, Doldina MK, Nurkeeva ZS, Shaikhutdinov EM. Swelling behavior of chitosan-polyHEA hydrogels in anionic surfactant solutions and their thermosensitivity. Colloids Surf. A. 2004; 238: 13-18.

5. Omidian H, Park K, Rocca JG. Recent developments in superporous hydrogels JPP 2007, 59: 317–327.

6. Tang C, Yin L, Pei Y, Zhang M, Wu L. New superporous hydrogels composites based on aqueous carbopol Solution (SPHCcs): synthesis, characterization and in vitro bioadhesive force studies. Eur. Polym. J. 2005; 41: 557-562.

7. Gemeinhart RA, Chen J, Park H, Park K. pH-sensitivity of fast responsive superporous hydrogels. J. Biomater. Sci. Polymer Edn. 2000; 11: 1371-1380.

8. Bajpai SK, Bajpai M, Sharma L. Prolonged gastric delivery of vitamin B2 from a floating drug delivery System: an in vitro study. Iran. Polym. J. 2007; 16: 521-527.

9. Khalid, M.N., Agnely, F., Yagoubi, N., Grossiord, J.L. and Couarraze, G. (2002). Water state characterization, swelling behaviour, thermal and mechanical properties of chitosan based networks. Eur. J. Pharm. Sci. 15: 425-432.

10. Kim, D. and Park, K. (2004). Swelling and mechanical properties of superporous hydrogels of poly (acrylamide-coacrylic acid)/ polyethylenimine interpenetrating polymer networks. Polymer 45: 189-196.

11. Klumb, L.A. and Horbett, T.A. (1992). Design of insulin delivery devices based on glucose sensitive membranes. J. Controlled Release 18: 59-80.

12. Shailendra Kumar Singhet al., Superporous hydrogels as gastroretentive devices, acta pharmaceutica scienica, 53: 7-24(2004).

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