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Superporous Hydrogel (SPH): An Innovative Approach of Gastro retention

Leena P Deore[1]*, and Devidas G Bachhav[2]

[1]KBHSS Trust's Institute of Pharmacy, Bhygaon Road, Malegaon Camp, Malegaon, Nashik (MS), India.
[2]MGVM'S SPH College of Pharmacy, LVH Marg, Malegaon Camp, Malegaon, Nashik (MS), India.

ABSTRACT

Gastroretentive drug delivery is an approach to prolong gastric residence time, thereby targeting site specific drug release in the upper part of GIT for local or systemic effect. Gastroretentive drug delivery system involves various approaches like : High–density system, bioadhesive or mucoadhesive system, swelling and expanding system, magnetic system, superporous hydrogel, incorporation of passage delaying food agents, ion exchange resins, bioadhesive liposomal system, floating systems: raft forming system, gas generating system, low density system, hydrodynamically balanced system, hot-melt extrusion etc. Superporous hydrogel developed as novel drug delivery system for those drugs having absorption window in stomach and upper part of gastrointestinal tract (GIT). Superporous hydrogel accommodate a large amount of water within short period through interconnected capillary channels. In order to overcome the problems associated with convetional superporous hydrogels related to mechanical strength modified by developing second generation of superporous hydrogel composite (SPHCs) and third generation of superporous hydrogel hybrids (SPHHs) and superporous hydrogel interpenetrating network (SPHs-IPN). This review includes various generations, methods of preparation, techniques of drug loading, method for synthesis of superporous hydrogels, list of various reagent used in synthesis of superporous hydrogel and their role, applications, evaluation of superporous hydrogel.

Keywords: Gastroretentive drug delivery system, Superporous hydrogel, Superporous hydrogel composite, Superporous hydrogel hybrids.

Corresponding author

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INTRODUCTION

Drug delivery technologies are as important as new chemical entities entering into the pharmaceutical industries, allowing more effective use of existing drugs and successful development of new drug candidate [1]. The scientific and technological advances in recent years enables in development of controlled oral drug delivery system by overcoming physiological adversities, such as short residence time (SRT) and unpredictable gastric emptying time (GET) [2]. The most recent advancement in the gastroretentive drug delivery is the development of various types of superporous hydrogel.

Superporous Hydrogels (SPH)

A hydrogel is three dimentional network of crosslinked polymers which are physically or chemically bonded. Hydrogels with effective pore sizes in the range of 10 - 100 nm are termed as microporous hydrogels and pore sizes in the range 100 nm - 10 µm are termed as macroporous hydrogel. Absorption of water in dried hydrogel by diffusion process and relaxation of the polymer chains in the rubbery region. Here rate limiting factor is slow swelling property of dried hydrogels, it take at least several hours to attain equilibrium swelling. To overcome this slow swelling property of dried hydrogels, current inventors developed a superporous hydrogels that can swell within time limit [3]. SPHs are a new type of hydrogel that have numerous supersize pores inside them. Superporous hydrogels developed as novel drug delivery system for those drugs having absorption window in stomach and upper part of GIT [4]. Hydrogels having ability to create effective pore size larger than 10 micrometer are known as superporous hydrogels [5]. SPH is 3 dimensional network of hydrophilic polymer that are not soluble and absorb large amount of water in short period due to it contain numerous inter connected microscopic pores. It differ from other types of porous hydrogel like macroporous hydrogel. [6,7,8]. These systems swell rapidly and maintain integrity in the harsh stomach environment. They are not soluble and accommodate a large amount of water in a very short period of time due to presence of interconnected microscopic pores [9]. Because of porous structure SPHs posses more surface area and shorter diffusion distance. Due to this they swell very rapidly on contact with water. Superporous hydrogel does not have only fast swelling but also have properties like slipperiness, biodegradability, biocompatibility, high mechanical strength, high swelling capacity and stability in acidic condition of stomach [10]. Swollen hydrogel strong enough to withstand with shear force, abrasion, pressure generated in stomach by gastric fluid. The swollen hydrogel capable of bearing pressure more than 50-70 cm water pressure. Because of this property these devices are proposed for extending gastric residence time of drug [11]. Superporous hydrogels have a porous structure that acts as a capillary network. The capillary properties of superporous hydrogels are a result of an oriented pore structure that is produced during the production. High interconnectivity is present in the majority of the superporous hydrogel, but at the surface, little interconnectivity is present. The high interconnectivity and pore structure is maintained when the superporous hydrogel is compressed radially, but the interconnection is disrupted when compression is axial. A reduction in dry volume is possible, allowing the superporous hydrogel to be small enough to be taken as an oral dosage form. The swelling of the compressed superporous hydrogels is

slightly slower than the uncompressed superporous hydrogels but still much faster than a similar nonporous hydrogel. The swelling of superporous hydrogels is responsive to the environment in which the swelling takes place. In acidic conditions, superporous hydrogels swell to a much lower degree than in basic solutions because of the ionization of the acrylic acid on the polymer chains. The swollen size of the superporous hydrogel is large enough to be maintained in the stomach after ingestion. The density of the superporous hydrogel causes it to float in simulated gastric fluid, which will aid in the retention in the stomach prior to swelling. Swelling of superporous hydrogels in blood is very slow due to the poor wetting of the dry hydrogel and the viscous property of blood [12].

Principle of the gastric retention of superporous hydrogels [13-15]

The gastric retention of superporous hydrogels is based on their fast swelling property. This approach is described in figure 1. Superporous hydrogel is filled in a capsule so that the initial volume is small which is easy to swallow (Fig.1-A). After oral administration, it swells rapidly in the gastric fluid to a large size. So that its emptying into the intestine is prevented (Fig.1- B).When the gastric contraction reaches the hydrogel, the gastric tissues slide over the hydrogel (Fig.1- C). As it is elastic, slippery and high mechanical strength it able to withstand gastric contraction and also due to low density of superporous hydrogel than gastric content it floats and releases drug in upper part of GIT (Fig.1- D). When a drug is released from this dosage form, it slowly undergoes degradation in the stomach by either mechanical force or chemical/enzymatic hydrolysis of the polymer chains constituting the hydrogel (Fig.1- E). Eventually, the degraded superporous hydrogel dosage form is eliminated from the stomach (Fig.1- F). The sequence shown in figure 1 is based on animal studies performed on gastric retention of hydrogels.

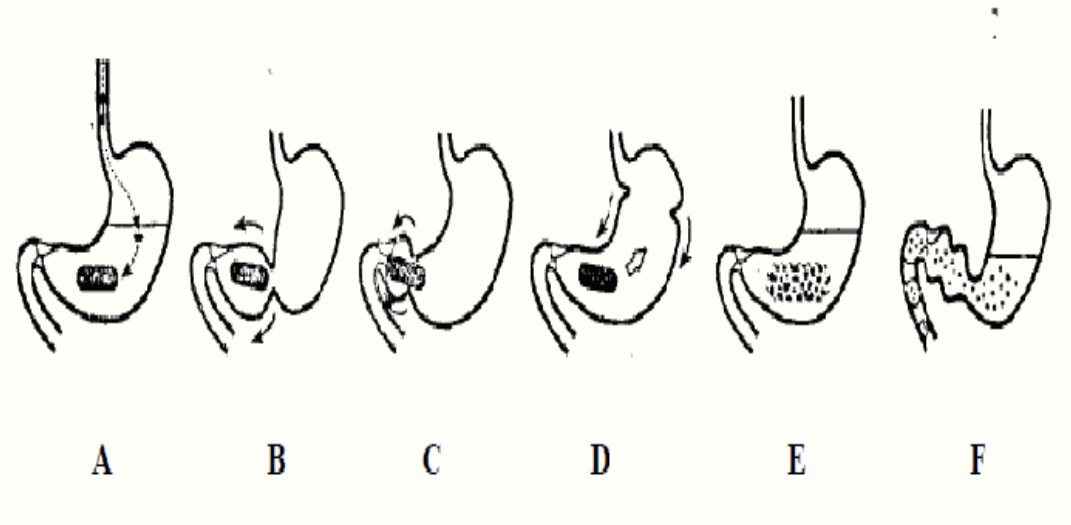

Fig 1: Schematic representation of gastric retention and subsequent emptying of superporous hydrogel

Basic requirements for gastric retention of superporous hydrogel [16]

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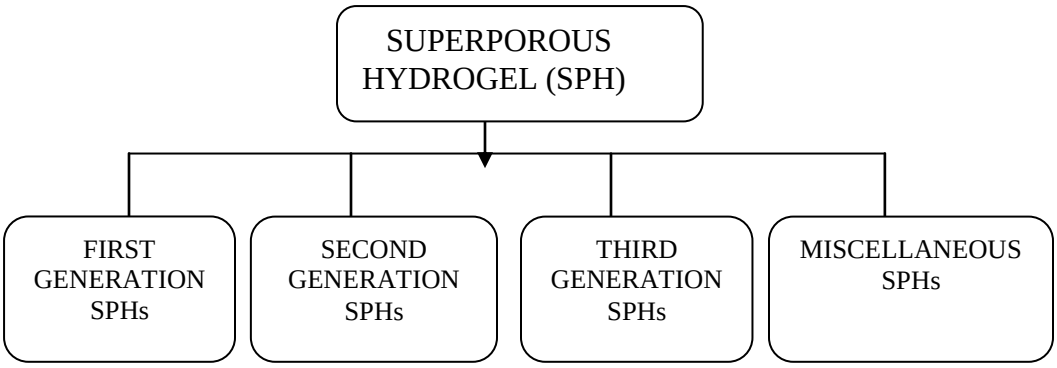
Superporous hydrogels must possess following properties in order to act as gastric retention device:

- Initial size should be small enough for easy swallowing. Swelling should be fast enough to overcome gastric emptying by intragastic migrating motor complex (IMMC).
- Size of swollen hydrogel should be large enough to be retained in the stomach.
- Swollen hydrogel should be strong enough to withstand contraction pressure, abrasion and shear forces in stomach (i.e. more than 50-70 cm water pressure).
- A superporous hydrogel dosage form should be eliminated from the stomach after drugs are released. This can be obtained by either mechanical degradation to break the dosage form into small pieces or by chemical or enzymatic degradation by including biodegradable crosslinkers like glycidyl acrylate, modified albumin.

Advantages of SPH [**17**]

- The swelling rate is very fast. The Superporous hydrogel swell completely within a minute regardless of the size of the dried superporous hydrogel.
- Superporous hydrogels swell to such an extent that the weight of fully swollen superporous hydrogel is higher than the weights of dried superporous hydrogels.
- Though the superporous hydrogels contain small percentage of solid content of the total weight, it can exert significant expansion force during swelling.
- Superporous hydrogels can also be made elastic, which minimizes their rupture.
- The unique properties of superporous hydrogels can also be used for non-pharmaceutical and non-biomedical applications.

Classification of superporous hydrogel:



First Generation: Conventional SPH (CSPH) was first discovered by *Chen et al* with fast swelling kinetics and super absorbent properties in 1999 [6].

It involves vinyl monomers like acrylamide, ionic monomer like salt of sulfopropylacrylate potassium, acrylic acid etc. In order to preserve porous structure of SPH alcohol is used. Dried SPH hard and brittle, but the hydrophilic nature of the polymer results in moisture-induced plasticization of the rigid structures into soft and flexible structures. The swollen SPHs are sometimes difficult to handle without breaking. When the SPHs are dried, the porous structure become collapsed or shrunken due to the surface tension of water pulling the polymer chains together during the drying process. To avoid this problem, water inside SPHs is replaced with alcohol (e.g., ethanol) [3]. The low surface tension of alcohol prevents the porous structure from collapsing during drying. Their structures are easily broken apart even under very low pressures due to lack of desirable mechanical properties of the conventional SPHs. The CSPH are fragile against bending or tensile stresses. By incorporating wetting agent the rate of water uptake is also enhanced [1,13,18,19].

Second Generation: These higher modulus hydrogel were introduced by *Chen et al* in 2000 as an improvement over CSPH in terms of high mechanical strength. These are also known as superporous hydrogels composites (SPHC) [10]. For making SPH composites, a matrix-swelling additive or a composite agent is utilized. A composite agent used in SPH composites is a cross-linked water-absorbent hydrophilic polymer that can absorb the solution of monomer, cross-linker, initiator and remaining components of the SPH synthesis. Since similar reactions will happen at the interface, the swollen particles would then be connected to each other through the extended polymeric chains. 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 proceeds entire the solution [20]. The presence of composite agent in SPH composites results in improved mechanical properties over conventional (e.g. the first generation) SPH, but the SPH composites are still brittle and thus break into pieces upon application of stresses. This modification over conventional SPHs resembles modification of superabsorbent polymers through surface cross-linking. Overall, this type of modification results in a higher modulus polymer network in the swollen state, which is susceptible to failure under the brittle fracture mechanism [21,22]. The most widely used composite agents are crosslinked sodium carboxymethylcellulose (ac-di-sol), crosslinked sodium starch glycolate (primojel) and crosslinked polyvinylpyrrolidone (crosspovidone). Polyvinyl alcohol, carbopol are also used to improve the mechanical strength of SPHs. Though, this modification leads to polymeric networks with improved mechanical strength in swollen state but still these are prone to breakdown under high tensile stress [23].

Third Generation- Further advancement in mechanical strength leads to third generation SPHs which includes superporous hydrogels interpenetrating networks (SPH-IPNs) and superporous hydrogel hybrid (SPHH). A second polymeric network is incorporated into SPH frame to form interpenetrating network structure in case of SPH-IPNs. A water soluble hybrid agent is involved. The hybrid agent evenly diffuses and dissolves into polymer solution leading to formation of integrated semi interpenetrating network which upon treatment of hybrid agent yields integrated IPNs structure. They are able to withstand various types of stresses like compression, bending and twisting etc [24]. Various hybrid agents have been used and specific treatment has been applied to get integrated IPNs hydrogels, e.g.

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Natural hydrocolloid: Sodium alginate, chitosan, sodium carboxymethylcellulose, and pectin etc. Natural hydrocolloids show ionotropic gelation via treatment with metal ion like calcium, iron etc. (e.g. sodium alginate with Ca^{+2} ions, chitosan with phosphates).
Synthetic: Water soluble polyvinyl alcohol.
Ethylenebisacrylamide: A thermally resistant chemical crosslinker.
Cerium ammonium nitrate is used to prepare grafted SPHHs: Stronger SPHHs can be prepared by replacing the diacrylate crosslinker with a trifunctional acrylate. The SPHHs having lower salt sensitivity can be prepared using a quaternary ammonium salt (diallyldimethyl ammonium chloride) as a secondary monomer [24]. The unique properties of SPHHs are their elasticity and spongy nature. Each hybrid agent must required specific treatment. Various third generation SPHs can be prepared ranging from high modulus to highly elastic and rubbery (in their water-swollen states) depending on the type hybrid agent and its associated treatment.
Miscellaneous SPHs: Development of SPHs with mechanical properties identical to that of SPHCs has been attempted applying different approaches, including acidification (using HCl), impregnation (using diallyldimethyl ammonium chloride or cationic polyethyleneimine or cationic resin of polyamidoamineepichlorohydrin), rubberization (adding rubber emulsions), surface crosslinking (using glycerin), ionotropic gelation (using synthetic polymers other than hydrocolloids; like polyvinyl acetate), bulk crosslinking (using higher concentration of a chemical crosslinker), thermogelation (using ovalbumine protein, egg white) and ionotropic gelation (using ion-complexable co-monomers; e.g. acrylic acid) [25]. General features of various generations of superporous hydrogel are given in Table 1.

Table 1: General features of SPH generations [1]

Formulation	CSPH	SPHC	SPHH
Property modifier: a material used to enhance mechanical properties; these include croslinked and non-crosslinked hydrophilic natural and synthetic polymers	None	Superdisintegrants including crosslinked CMC; polyvinyl pyrilidone and starch glycolate	Water–soluble CMC, alginate,chitosan, polyvinyl alcohol
Swelling capacity	100-300 g g^{-1}	100-300 g g^{-1}	Up to about 50 g g^{-1}
Swelling rate	5-30 s	5-30 s	5s to a few min
Mechanical properties	No mechanical strength	Resists up to 2 N cm^{-2}	Resists up to 20-100Ncm^{-2}
Treating agent	No	No	Ion, calcium, aluminium, iron, phosphate ,copper
Water washing ability	Impractical because of high swelling in water	Very difficult, because of high swelling in water	Readily possible because of high strength and low swelling
Drying	Forced and vacuum	Forced/vacuum and freeze drying	Forced/vacuum and freeze drying

Physical appearance in dried state	Rigid brittle	Rigid brittle	Rigid brittle
Characterization	Fast swelling and weak mechanical properties; moisture induced plasticization, fragile against bending, compression and tensile stresses	Fast swelling, and improved mechanical properties, moisture induced plasticization, higher modulus networks fail under brittle fracture mechanism	Fast swelling and improved mechanical properties, moisture induced plasticization, highly elastic in swollen state very resistant against different stresses, ductile fracture mechanism

Methods For Preparation Of Superporous Hydrogels [17,19]

Following methods are useful in the preparation of superporous hydrogel.

- Porosigen technique
- Cross linking technique
- Phase separation technique
- Gas blowing or foaming agent

Porosigen technique: Porous hydrogels can be made by preparing the hydrogels in the presence of dispersed water-soluble porosigen. These porosigen are hydrophilic in nature. So, they solubilize as they come in contact with water and generate the porous structure in the hydrogel.

e.g. - Micronized sucrose, micronized lactose, micronized dextrin, micronized cellulose, sodium chloride, poly ethylene glycol (PEG), poly ethylene oxides etc. which form meshwork that can be removed by washing with water. The pore size generates in the hydrogel depends on the size of porosigens [26].

Cross linking technique: Cross linking of individual hydrogel particles lead to aggregates of particles. The pores in such structures are present between hydrogel particles. The size of pores is much smaller than the size of particlesIndividual hydrogel particles can be crosslinked to form crosslinked aggregates. Pores are formed between the hydrogel particles. Such aggregate macrostructures were prepared by initially mixing the hydrogel particles (in the range of a few hundred micrometers) with a solution of a crosslinking agent, water, and hydrophilic organic solvent such as isopropanol. This technique is limited to absorbent particles with chemically active functional groups on the surface [27,16].

Phase separation technique: In solution polymerization, monomers are usually mixed in diluent that is good for both monomers and polymers. If, however, the diluent is a nonsolvent for the polymer formed (e.g. Polyhydroxy ethyl methyl acrylate in water), the solubility of the polymers dramatically decreases as the polymerization proceeds. This results in phase separation of the polymer rich monomer phase into droplets, which then join together to form a network paralled with large spaces (e.g. heterogeneous, porous hydrogels) by the end of the

polymerization process. This process is called heterogeneous solution polymerization. The pore sizes of macroporous hydrogels prepared by phase separation are typically only a few micrometers. In addition, the overall porosity is very low, and this implies that the pores are not well interconnected. The major limitation of the phase separation method is that only very limited types of porous hydrogels can be prepared. In addition, there is not much control over the porosity of the gels when prepared by phase separation [16,28].

Gas blowing (or foaming) technique: Hydrogels can be prepared in the presence of gas bubbles. In this technique the monomers are polymerized or water-soluble polymer chains are crosslinked around gas bubbles generated by a blowing agent. The gas blowing technology has been widely used in the preparation of plastic foams from materials such as polyurethanes, rubber, and poly (vinyl chloride). The key ingredient in the foaming process is a blowing agent (or foaming agent), which is defined as any substance or combination of substances capable of producing cellular structure within a polymer matrix. Foaming agents are classified as:

(a) Physical foaming agents that expand when pressure is released (e.g., nitrogen and carbon dioxide) and
(b) Chemical foaming agents that decompose or react to form a gas (e.g., sodium bicarbonate in the presence of acid). Recently, the gas blowing technique was used in laboratory to prepare SPHs. Because this technique used is for the preparation of SPHs, they were also called “hydrogel foams.” In the synthesis of SPHs by the gas blowing technique, foaming and polymerization have to occur simultaneously. They are safe, cheap and easy to use. For this reason, it is important to control the timing for foaming and polymerization. In the study mentioned above, inorganic carbonates, such as sodium carbonate and sodium bicarbonate were used as the foaming agent. These inorganic carbonates have long been used safely as a gas-forming ingredient in effervescent tablets for antacids [11,29].

Drug Loading Into Superporous Hydrogel [17,22]

There are two methods for drug incorporation into superporous hydrogel:

I. Drug loading into superporous hydrogel reservoir devices
II. Drug loading into superporous hydrogel polymers

Drug loading into superporous hydrogel reservoir device: Two types of drug delivery systems has been designed as follow:

1. Core inside shuttle system
2. Core attached to surface of shuttle system

These systems involve two components: a core and a conveyor system. Core is the part which contains drug blend with appropriate excipients and conveyor is made up of SPH and SPHC [23,30].

Core inside the shuttle system: In this system, core is prepared in two different forms viz. micro particles and gross mass.

Micro particles: These are prepared by dispersing the drug in melted polymers like PEG 6000 and cooling of the mixture to get gross mass. This gross mass is crushed in mortar and sieved through mesh size 400 µm, which is used as core material. SPHC is used as the body of the conveyor system because of its greater mechanical strength and SPH is used as the cap of the conveyor system because of its high swelling ratio. A hole is made inside SPHC in its swollen state by use of borer, as the core has to be incorporated inside SPHC. The SPHC is then dried by either at ambient temperature or by reduced pressure at 60°C. This is called as the body of conveyor which is capped by piece of SPH.

Core attached to surface of shuttle system: In this system, core is in the form of small tablets which are prepared by dispersing the drug in melted polymer like PEG 6000 and sieving the mass through mesh size 400 µm, which were mixed with magnesium stearate and compressed into tablets using single punch machine (40 N hardness). The second component is conveyor made up of only SPHC in which two holes were made on counter side instead of one as in previous approach. The core material in the form of small tablets was placed inside the holes by using bio-adhesive (cyanoacrylate) glue. The polymer swells when it comes in contact with gastric fluids and the size of holes is enlarged. The glue helps to keep the dosage forms at the site of drug absorption. The same assembly is placed into gelatin capsule shells of size 000.

Drug loading into superporous hydrogel polymers

The amount of water required for complete swelling of specific weights of SPH and SPHC is determined. Then, aqueous solutions of given drug is prepared in previously determined amount of water and weighed amount of polymer is placed in drug solution to suck up the drug solution. After 20 min, completely swollen polymers loaded with drug are placed in oven at 30°C for drying overnight [31].

Drug loading by using wide opening syringe: Wide opening syringe is used to load drug into superporous hydrogel. Drug is loaded at centre of SPH carrier in certain depth this avoids the use of biodegradable glue.

Drug is directly dispersed or dissolves into mixture of monomers or initiators this avoids drug loss during loading [32].

Ingredients Required For Preparing Superporous Hydrogel:
The ingredients required for preparing superporous hydrogel are as shown in Table 2.

Table 2: Role of ingredients with their examples [2]

Sr. No.	Role of Ingredients	Examples
1	Monomers	Acrylic Acid(AA),Acrylamide(AM), 3-Sulphopropyl acrylate

		potassium(SPAK),Hydroxy ethylmetyl acrylate (HEMA),N-isopropyl acrylamide (NIPAM), Acrlonitrile (AN), Polyvinyl alcohol(PVA)
2	Cross linking agents	**Chemical cross linker:** Glutaraldehyde,N,N-methylenebisacrylamide(BIS) **Ionotrpic cross linker:** Metal ions like calcium iron and phosphorus
3	Foam Stabilizers	Pluronic F127,Pluronic P105,Silwet L7605,Span,Tween
4	Polymerization initiator pairs	APS/TEMED(Ammonium persulfate /N,N,N,N-tetramethylenediamine, KPS/Sodium metabisulfite, APS/ Sodium metabisulfite, Azo-initiator(V545)
5	Foaming agents	Sodium bicarbonate, Sodium carbonate, Potassium bicarbonate
6	Composite agents	Crosslinked sodium carboxy methylcellulose(Ac-Di-Sol), Crosslinked sodium starch glycolate(Primojel), and Crosslinked polvinylpyrrolidone (crospovidone), Carbopol, Polyvinyl alcohol(PVA)
7	Hybrid agents	**Natural polymers:** Sodium alginate, Sodium carboxy methylcellulose (Na CMC), Chitosan based on ionotropic gelation,Pectin **Synthetic polymers:** Poly vinyl alcohol(PVA) based on cryogelation

SPHs Synthesis [29]**:**

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. Figure 2 explains the foaming process for the preparation of superporous hydrogels. The important step of this process is to use acid to control the polymerization kinetics. Addition of $NaHCO_3$ leads to foam formation as well as rise in pH, which accelerates the polymerization process. After the addition of $NaHCO_3$, 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 $NaHCO_3$ results in foaming and at the same time the pH of the solution rises (B). As pH increases it accelerates the polymerization process, which is completed before the foam subsides. This results in formation of superporous hydrogel (C).

Drying of Superporous Hydrogel [17]

Drying of superporous hydrogel is one by two way:

I. First way, swollen superporous hydrogel are placed in food dehydrator by blowing in warm air (60°C).
II. Swollen superporous hydrogel are dehydrated first by applying about 5–10 ml of absolute ethanol. During the dehydration process, the soft and flexible superporous hydrogel become hard and brittle. After the dehydration is completed, the excess ethanol in dehydrated superporous hydrogel is removed by draining using paper towel. Then the superporous hydrogel are dried in a oven at 55°C for a day [6].

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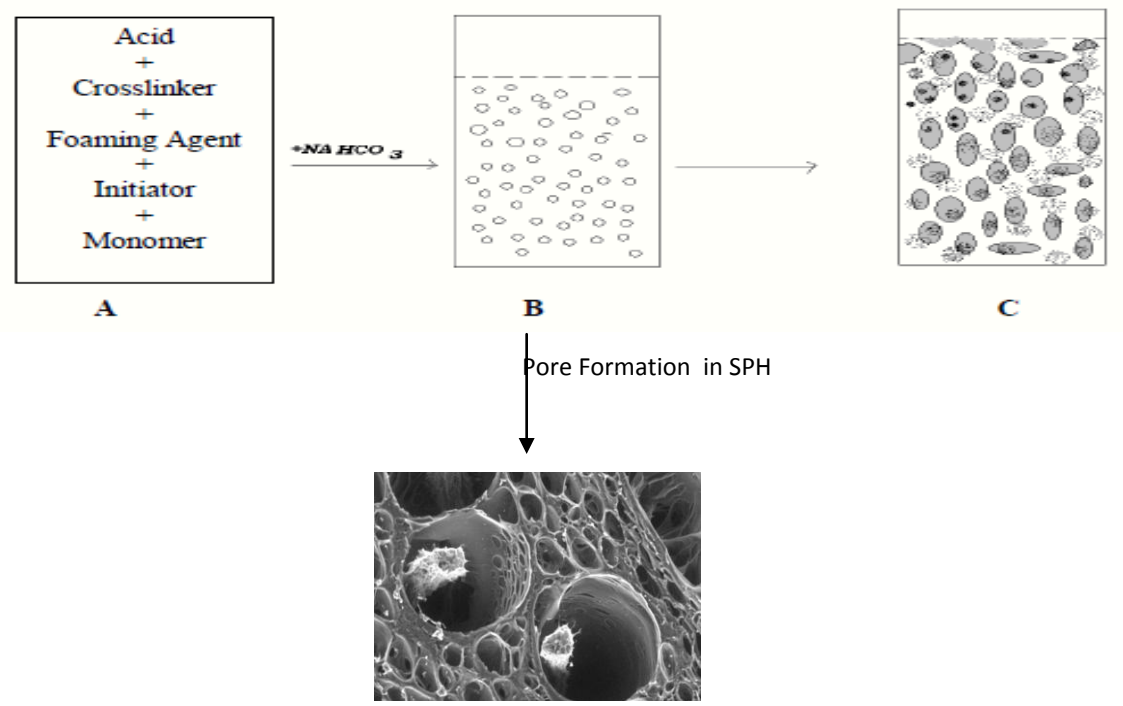

Fig 2: Schematic representation of the superporous hydrogel preparation[16].

APPLICATIONS OF SPHS:

Peroral Peptide Delivery Systems: Conventional SPHs and SPHCs for peroral peptide delivery have been investigated. These systems are designed to swell in the intestine with the SPH physically adhering to the gut wall and delivering the incorporated peptide directly to the site. The carboxyl-carrying SPHs can potentially induce calcium extraction, presumably causing the tight junctions of the gut wall to open and deactivating the harmful gut enzymes. After peptide delivery and absorption across the gut wall, the SPH becomes over-hydrated and is broken apart by the peristaltic forces of the gut. The proper selection of the type and thickness of enteric coating will potentially help to target this dosage form to any specific site in the small intestine or to the colon **[**23].

Site-Specific Drug Delivery: These systems are particularly useful for drugs that are specifically absorbed from stomach or the proximal part of the small intestine e.g. riboflavin and furosemide. A bilayer-floating capsule was developed for local delivery of misoprostol, which is a synthetic analog of prostaglandin E1 used in gastric ulcers caused by use of NSAIDs. By targeting slow delivery of misoprostol to the stomach, desired therapeutic levels could be achieved and drug waste could be reduced **[**34].

Fast-Dissolving Tablets: Fast-dissolving tablets are orally administered without the need for water and swallowing which is beneficial especially to children and the elderly. The methods used to prepare fast-melting tablets are freeze-drying, sublimation and direct compression. The

first two methods make tablets that dissolve within 5–15 sec, but the technology is expensive and tablets prepared are not strong mechanically. Another method of preparation of fast-dissolving tablets by the direct compression method is the addition of fine particles of SPH to the granulation or powder formulation. The SPH microparticles within the tablet core accelerate water absorption by an increased wicking mechanism. Tablets prepared by direct compression with the use of SPH microparticles disintegrate in less than 10 sec[35].

Development of Diet Aid: Diet soft drinks, meal replacement shakes, diet 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 [35].

Chemoembolization and Occlusion Devices: Chemoembolization is a combined method of embolization and chemotherapy. Embolization has been used for the treatment of cancer by restricting the oxygen supply to the growing tumours. This method can be combined with chemotherapeutic agents to achieve local delivery and low systemic toxicity. A chemotherapeutic agent and an anti-angiogenic agent can be loaded into SPHs for chemoembolization therapy. The strong SPHs are better candidates for this application because they fit better in the blood vessels and provide better blocking [36,37].

Development of Occlusion Devices for Aneurysum Treatment: SPHs can also be used to produce biomedical devices for the treatment of aneurysms. An equivalent SPH is prepared in smaller size after determining the size and shape of an aneurysm site. When a superporous hydrogel is positioned at the aneurysm site, it swells quickly to occupy the space and make the blood clot. Deposition of superporous hydrogels can result in up to 95% aneurysm occlusion without any evidence of parent artery compromise and inflammatory response. A new occlusion device prepared by combination of superporous hydrogel and platinum coils, called as Hydrocoil, is currently under development by Micro-Vention, Inc, in Aliso Viejo, California [38].

Gastroretentive Tablets: Dry blending and direct compression is used to make gastroretentive tablets. The SPH particles of acrylic acid/sulfopropyl acrylate copolymers are mixed with gelatin and tannic acid, and then tableted by direct compression. Formation of hydrogen bond between gelatin and tannic acid, as well as the carboxyl groups on the polymeric carrier, produce an integrated matrix, which is shown to be stable after swelling. The gastroretentive tablet can swell up to 22 times its own volume within a 40 min. period maintaining its original shape [39].

Other Applications: SPHs can also be used in industries other than pharmaceutical and biomedical, where rapid and extensive swelling in an aqueous medium is required. The use of SPHs is beneficial to hygiene, agriculture, horticulture, pet, toy and many other industries in their products. The immediate swelling of SPHs can be enjoyed by the children and they can

learn the associated science and knowledge as it is shown with the super absorbent polymers. The SPHs can be coloured and may have decorative applications. SPHs may be a suitable substitute for silica gel as they quickly absorb moisture from the surrounding environment. The high swelling pressure of SPHs can potentially be used to trigger an alarm system upon the penetration of water [40].

Evaluation Of Superporous Hydrogel:

1) Measurement of Density [2,40]**:** It was difficult to measure the density of superporous hydrogel directly. Density of superporous hydrogel determined by solvent displacement method. Actually it was a apparent density. Mass of SPH was measured then this SPH placed in graduated cylinder containing measured volume of absolute hexane. Density calculated as follows:

$$\text{Density} = M_{SPH} / V_{SPH}$$

Where, M_{SPH} : Mass of SPH

V_{SPH} : Volume of SPH

2) Swelling studies [3]**:** Swelling time was calculated by placing SPH in deionised water until it attained equilibrium swelling. Time required for equilibration is noticed. The dried SPH was allowed to hydrate in excess of deionised water at room temperature. The weight of fully swollen hydrogel is measured at different time interval, remove excess of water from surface by gental bloting. The swelling ratio was determined by following equation:

$$Qs = (Ms-Md/Md) \text{ X } 100$$

Where, Ms=Mass of fully swollen SPH

Md= Mass of dried SPH

3) Water Retention [16,41]**:** Water retention capacity as a function of time determined from the following equation:

$$Wrt = (Wp – Wd) / (Ws – Wd) X100$$

Where,

Wd = weight of the dried hydrogel,

Ws = weight of the fully swollen hydrogel, and

Wp = weight of the hydrogel at various exposure times.

For determination of the water-retention capacity of the hydrogels as a function of time and exposure at 37ºC, the water loss of fully swollen polymer at time intervals was determined by gravimetry.

4) *In vitro* Buoyancy studies [2]**:** Buoyancy studies were performed by placing piece of superporous hydrogel in a beaker containing 100 ml of 0.1N HCl and at 37°C ± 0.5°C. Time taken by piece of hydrogel to rise on surface and float was taken as a floating lag time. The time for which it remains float is called total floating time.

5) Porosity measurement [2]**:** The porosity of superporous hydrogel measured by immersing dried SPH in absolute ethanol over night and weighed after excess of ethanol on the surfacewais blotted. The porosity was measured as follows:

$$\text{Porosity} = (M_2 - M_1 / V \rho) \times 100$$

Where,

M_2: Mass of SPH in swollen state

M_1: Mass of SPH in dried state

ρ: Density of ethanol

Volume (V) was measured from its displacement volume.

6) Scanning Electron Microscopy [41,42]**:** The morphology or texture of superporous hydrogel was examined with scanning electron microscopy (SEM). In order to ensure that porous structure generated during SPH synthesis. Dried Superporous hydrogel composit cut into pieces to expose their inner structure and imaged in a SEM.

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