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Super Porous Hydrogels: A Review

P. V. Kamala Kumari[1*], M. Sharmila[1] and Y. Srinivasa Rao[1]

[1]Department of Pharmaceutics, Vignan Institute of Pharmaceutical Technology, Duvvada, Visakhapatnam - 530049, India.

Authors' contributions

This review was carried out in collaboration among all authors. Author PVKK gathered details of manuscript and contributed in writing the manuscript regarding this review topic. Author MS contributed in collecting the information from various books. Author YSR analyzed these data and necessary inputs were given towards the designing of the manuscript. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Super porous hydrogels (SPHs) basically developed initially create as a novel drug delivery system to absorb and continue to hold the drugs in the gastric medium which allows absorption in stomach and upper part of the gastrointestinal tract. These systems get swollen in the stomach instantly and in the harsh stomach environment they maintain their integrity, while the pharmaceutical active ingredient is being released. Instant and fast swelling property of hydrogel is based on water absorption through open porous structure by capillary force. SPHs have the poor mechanical strength which has got over by developing the second-generation SPH composites (SPHCs) and the third-generation SPH hybrids (SPHHs). The present review has been focused on the preparation, characterization and application of SPHs.

Keywords: Super porous hydrogels; gastric retention; absorption window; second and third generation SPH.

1. INTRODUCTION

Drug delivery technologies are very important in the pharmaceutical industries as new chemical establishments are entering, allowing successful development of a new drug as well as effectual usage of existing drugs [1]. The delivery system represents best compliance and also industrial

**Corresponding author: E-mail: kamalaparavastu@gmail.com;*

applications. Reason for the establishment of hydrogels is to control the release of a drug from a conventional solid dose formulation. Hydrophilic polymers are cross-linked to form a continuous network to form hydrogels. These are capable of absorbing water and other aqueous fluids. Recent trend to develop novel drug delivery systems has improved the bioavailability and therapeutic response of currently approved drugs [2].

2. HYDROGEL DRUG DELIVERY

Hydrogel drug delivery is most commonly used in the US market despite of more than 100 prescription drugs. Although this is a water soluble polymer, it shows gel properties when wide open to an aqueous environment. HPMC is used in tablet form to resist the release of drug over a longer time with different degrees of substitutions. HPMC is enabled to function as a controlled delivery system in two features. First, it is hydrophilic due to its hydroxyl propyl contents. Second, the HPMC chains are in a compressed form in a tablet, which prevents them from a fast dissolution in the aqueous environment. These two features provide gelling properties such as those found in a chemically cross-linked hydrogel. Even though there isn't no chemical cross-linking in the HPMC structure; the pressure applied during tablet preparation supplies enough entanglement and barrier for the retarded polymer dissolution.

3. GASTRO RETENTIVE DRUG DELIVERY SYSTEM

The most easy and preferred means of any drug delivery to the system is oral administration. Recent inclining interest in pharmaceutical field about controlled release of drug delivery through oral route have been an achievement in improving curing advantages, such as ease of dosing administration, patient compliance and formulation flexibility [3]. Drugs which are removed immediately from the systemic circulation and are easily absorbed from gastrointestinal tract (GIT) also have short lives. Suitable curing activity can be achieved by periodic dosing of drugs. Releasing the drug slowly into the gastrointestinal tract (GIT) by oral sustained-controlled release and these formulations are an attempt to avoid this limitation and maintain drug in the systemic circulation for a long time. Such a drug would be remained and release it in the stomach controlled manner so that drug could be continuously supplying to the absorption sites in the gastrointestinal tract (GIT). There are mainly two adversities that drug delivery system suffers: the short gastric retention time (GRT) and unpredictable short gastric emptying time (GET), which can also result to incomplete drug release from the dosage in the absorption zone (stomach or upper part of small intestine) which leads to diminished efficacy of administered dose [4]. It is desirable to achieve a prolong gastric residence time by the drug delivery to formulate a site-specific orally administered controlled release dosage. Prolonged gastric retention increases bioavailability and improves the solubility of the drug in a high pH environment [5]. It also increases the drug release duration, reduces drug waste. Prolonged gastric retention time (GRT) in the stomach could be advantageous for local action in the upper part of the small intestine e.g. treatment of peptic ulcer etc. It is an approach extends gastric residence time, by targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastro retentive dosage forms extend the gastric retention time (GRT) for extended periods. In the past, several gastro retentive drug delivery approaches were designed and developed, including: high density (sinking) systems that is retained in the bottom of the stomach, low density (floating) systems that causes buoyancy in gastric fluid [6], mucoadhesive systems that causes bioadhesion to stomach mucosa, unfoldable, extendible, or swellable systems which limits emptying of the dosage forms through the pyloric sphincter of stomach, superporous hydrogel systems [7], magnetic systems etc.

3.1 Advantages

1. Enhanced patient compliance.
2. Reduced dosage frequency.
3. Buoyancy leads to enhanced GRT (Gastric residence time).
4. Targeted drug delivery to stomach can be achieved.
5. Increased BA and fluctuation in blood drug concentration is avoided.
6. Uniform drug release from dosage form and no chance of dose dumping.
7. Sustained effect leads to prevention of mucosal irritation.

3.2 Disadvantages

1. Drugs unstable & insoluble in mucosal fluids cannot be administered as GRDDS.

2. Drugs causing gastric irritation cannot be administered via this route.
3. This system requires fed state to prolong gastric emptying.
4. Not suitable for drugs undergo FPM (first-pass-metabolism)
5. Gastric retention can be influenced by various factors which can never be constant all the time; these factors are variable & unavoidable.

4. SUPERPOROUS HYDROGELS (SPH)

A superporous hydrogel is a 3-dimensional network of a hydrophilic polymer that absorbs water in large amount in a short period of time due to the presence of interconnected microscopic pores as shown in Fig. 1. SPHs are a new type of hydrogel that have numerous super size pores inside them [8] and the swelling occurs by capillary wetting but rarely by diffusion. Certain ingredients, including initiators, cross linkers, foam stabilizers, foaming aids and foaming agents, are added into monomer diluted water in the preparation of SPHs. Superporous hydrogel do not have only fast swelling, but also properties like slipperiness, biodegradability biocompatibility, high swelling capacity, high mechanical strength, and stability in acidic condition of the stomach. Thereby, they swell completely within minutes regardless of their size due to absorption of water by capillary force rather than by simple absorption. Second generation superporous hydrogels composites are developed which has fast swelling, medium swelling ratio and improved mechanical properties, while third generation superporous hydrogel hybrid possess high elastic properties [9]. Gastric retention devices will 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 be absorbed primarily in the stomach.

4.1 Principle of the Gastric Retention of Superporous Hydrogels

The gastric retention of SPHs is primarly based on its fast swelling property. The initial volume of SPH is filled in a small capsule, which is easy to swallow but after oral administration, it swells rapidly in the gastric fluid to a large size, so that its emptying into the intestine can be prevented [10]. The gastric tissues move over the hydrogel, when the gastric contraction reaches the hydrogel. As it is elastic, slippery and has high mechanical strength it can able to withstand gastric contraction and also due to the low density, it floats and releases drug in upper part of GIT [11]. When a drug is released, it slowly undergoes degradation in the stomach by either mechanical force or chemical/enzymatic hydrolysis of the polymer chains constituting the hydrogel.

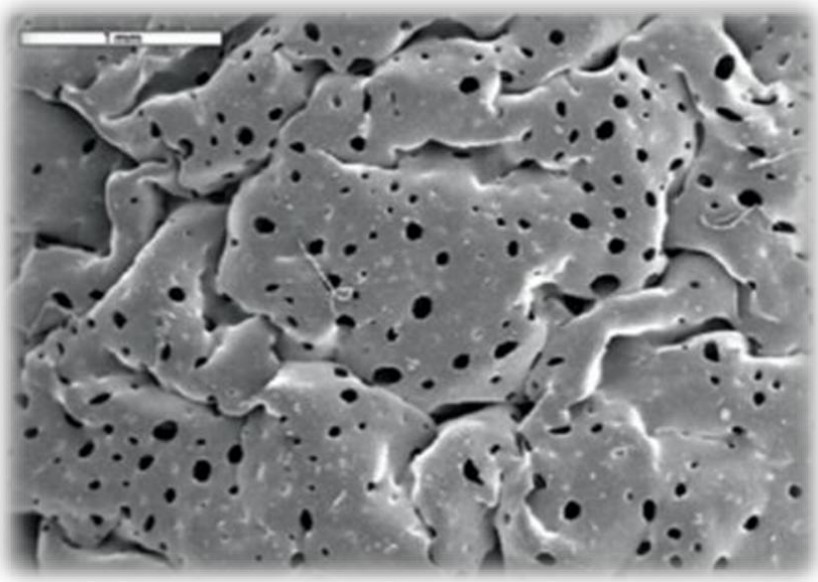

Fig. 1. Structure of superporous hydrogel under magnification of 1.00 mm showing porous surface

4.2 Advantages of Super Porous Hydrogels

- Regardless of the size of the dried superporous hydrogel, they swell completely within a minute.
- When it is swollen, itsweight is higher than dried state.
- They exert significant expansion force during swelling.
- To minimize their rupture, these can be made elastic.
- Can also be used for non pharmaceutical and non-biomedical applications.

4.3 Classification

1. First generation SPH.
2. Second generation SPH.
3. Third generation SPH.

4.3.1 First generation SPH (Conventional SPHs, CSPHs)

Conventional SPH (CSPH) was first discovered with rapid swelling kinetics and super absorbent properties in 1999 [12]. 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 hydrogels are hard and brittle, but the hydrophilic nature of the polymer results in moisture -induced plasticization. The porous structure collapses or gets shrink due to the surface tension of water, pulling the polymer chains together during the drying process and this happens when the SPHs are dried. To get rid of this problem, water inside SPHs is replaced with alcohol (e.g., ethanol), as the low surface tension of it prevents the porous structure from collapsing during drying. Under low pressures, these structures can be easily broken due to lack of desirable mechanical properties of the conventional SPHs. By incorporating wetting agent the rate of water uptake is also enhanced [13,14].

4.3.2 Second generation SPH (SPH composite, SPHCs)

An extra material called super disintegrant is added (swellable filler) for this type super porous hydrogel. These contain fine mechanical property that resists pressure up to 2N cm^2. Modifications were made to conventional super porous hydrogel to form second generation super porous hydrogel by adding super disintegrant [15]. They form complex material, which does not show any pharmacological effect but they intensify the mechanical strength of hydrogels as shown in Fig. 2. A complex agent is used in hydrogel composites which is cross-linked with water-absorbent hydrophilic polymer , cross linker, initiator and remaining components. SPH has a matrix of continuous phase having a dispersed phase incorporated within.

4.3.3 Third generation SPH (SPH hybrid, SPHHs)

Based on SPH hybrids, the third generation of SPHs was developed. These are the altered versions of the second generation and assume an integrated IPN structure. Although the SPHs of the second generation could provide a hydrogel with a better strength, much higher strength was felt to be needed, for the gastric retention application in particular. A water soluble hybrid agent is introduced in SPH formulations in case of SPHHs. This initiated the development of the third SPH generation, also called superporous hydrogel hybrids (SPHHs), with superior mechanical properties. The primary, secondary; and tertiary approaches have so far been disclosed. The SPH is prepared in a conventional way, but an active material is added during SPH synthesis, which is then treated in the ion solutions. While the primary approach is particularly useful in making SPHs with rubbery properties, SPHs with good mechanical strength can be obtained by adopting the secondary approach [13]. Although the mechanical properties of SPHs can be significantly enhanced after an ion treatment, the ion composition was found to be a useful tool for better controlling the swelling and mechanical properties [12]. Depending on the activity of the ion (sodium, calcium, aluminum and iron in particular), any ion composition can be used to modify and modulate SPH properties. SPH hybrids are prepared according to conventional SPH formulations but water soluble and ion gelling polymer (synthetic or natural) is added during hydrogel preparation [12]. After preparation, the SPH is treated in an ion solution to become strong and elastic [16].

4.4 Methods of Preparation

Preparation of gastroretentive SPH involves four methods. They are

- Porosigen technique
- Cross linking technique

- Phase separation technique
- Gas blowing or foaming technique.

4.4.1 Porosigen technique

In Porosigen Technique porous hydrogels are prepared in presence of dispersed water soluble porosigen. To prepare SPH various porosigen are used. These porosigen are hydrophilic in nature [10]. The pore size produced in the hydrogel depends on the size of porosigens [12].

4.4.2 Cross linking technique

Crosslinking of every particle of hydrogel particles lead to aggregates of particles. The pores in these structures are present in-between hydrogel particles. The size of pores are tiny than the size of particles. Individual hydrogel particles can be cross linked to form cross linked aggregates. This technique is limited to absorbent particles with chemically active functional groups on surface [16].

4.4.3 Phase separation technique

Phase separation is very critical process in generating superporous hydrogel. In solution polymerization, monomers are usually mixed in diluent that is good for both monomers and polymers. In addition, there is no control over the porosity of the gels when prepared by phase separation [13].

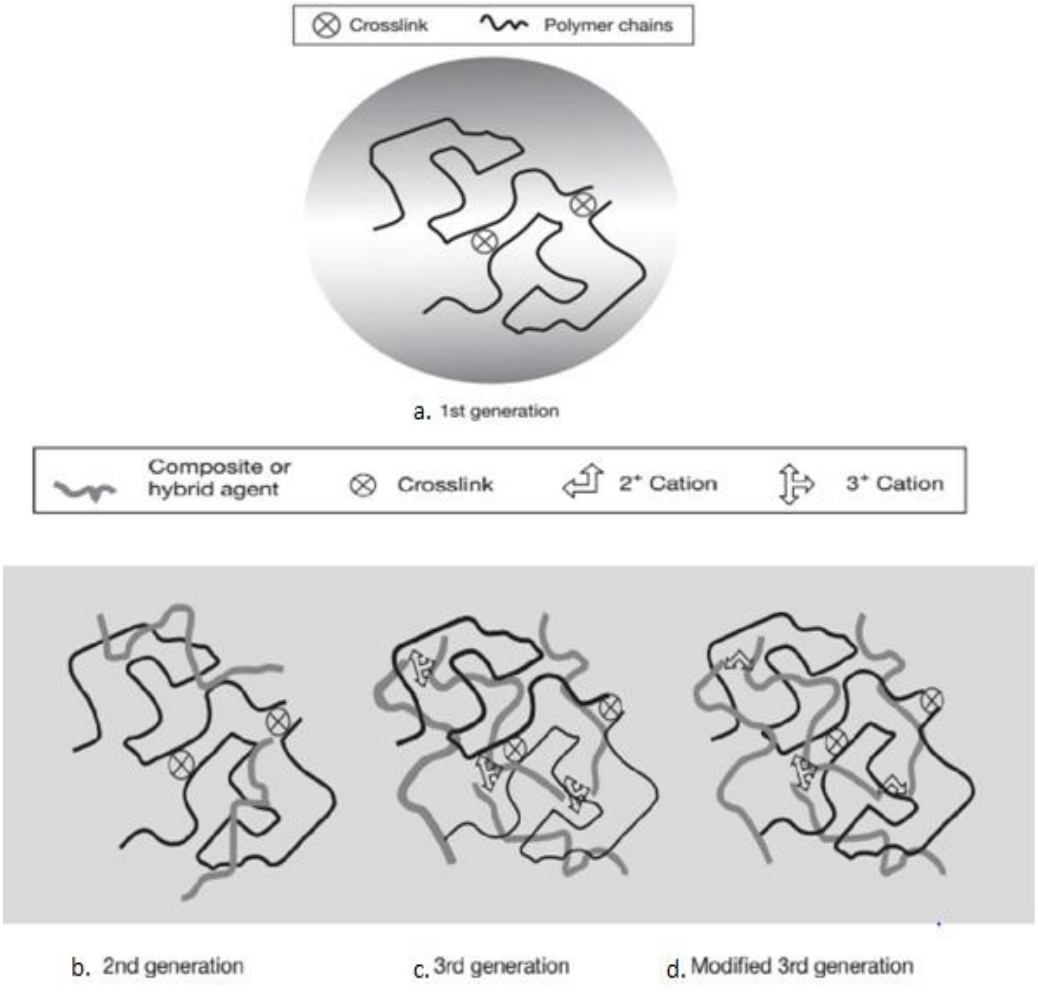

Fig. 2. Structures of superporous hydrogel generations a. 1st generation b. 2nd generation c. 3rd generation d. 3rd modified generation

4.4.4 Gas blowing or foaming technique

In this technique initially monomers, cross linking agent, foam stabilizer and distilled water are added in a test tube of specific dimensions pH adjust 5 to 6 with 5M NaOH [12]. 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 main 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 [10]. After synthesis, superporous hydrogels are subjected to washing and drying.

5. DRUG LOADING INTO SPH

Two techniques were suggested and reported for loading the drug into SPH delivery system.

1. Drug loading into SPH reservoir devices
2. Drug loading into SPH polymers

Drug Loading into Superporous Hydrogel Reservoir Devices: Two types of drug delivery systems has been designed

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

Core inside shuttle system: These systems are composed of two components: a core and a conveyor system [17,18] .Core is prepared in two different forms viz. micro particles and gross mass. Micro particles are prepared by dispersing the drug in melted polymers like PEG 6000 and cooling of the mixture to get gross mass. This mass is grinded in mortar and sieved through #400 µm, which are used as core material. As it has greater mechanical strength, SPHC is used as the body of the conveyor system and because of its high swelling ratio, SPH is used as the cap of the conveyor system 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 in the form of small tablets are prepared by dispersing the drug in melted polymer like PEG 6000 and sieving the mass through # 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 SPH Polymers: The required amount of water for complete swelling of specific weights of SPH and SPHC is determined. Drug is prepared using aqueous solution 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 [19].

6. DRYING OF SPH

Drying of SPH can be carried out under two different conditions.

Under condition I, swollen SPH are dried under blowing warm air (60°C) for a day in a food dehydrator.

Under condition II, swollen SPH are applied with 5–10 ml of absolute ethanol per each gel to dehydrate.

Further, SPH are dehydrated by placing them in a 50 mL of absolute ethanol several times to ensure replacement of all the water by ethanol. During this dehydration process, the soft and flexible SPH become hard and brittle. When the dehydration is completed, the excess ethanol from dehydrated SPH is removed by draining using paper towel and dried in an oven at 55°C for a day [20].

7. CHARACTERIZATION OF SUPERPO-ROUS HYDROGELS

7.1 Swelling Studies [21-23]

Completely dried, pre-weighed, disc-shaped SPH was weighed and then immersed in excess of

swelling medium. At various time intervals, the hydrogel was removed from the solution and weighed after excessive solution on the surface was blotted. Results were calculated according to the following equation:

$$Q = (Ms - Md)/Md$$

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

7.2 Measurement of Gelation Kinetics

As the polymerization reaction proceeded, the viscosity continuously increased until the full network structure (gel structure) was formed. The gelation time was defined as a period of time for gel formation following addition of glyoxal and measured by a simple tilting method after adjustment of pH to 5.0 with acetic acid. It was determined by the duration of time taken by the reactant mixture to become viscous and the viscous solution no longer descended in the tilted tube position [10,24]

7.3 Measurement of Density

It was difficult to measure the density of SPH directly. The apparent density of is determined by solvent displacement method [25]. Mass of SPH is measured and then placed in a graduated cylinder containing measured volume of absolute hexane [26]. Density is calculated as follows.

Density = MSPH / VSPH

where,

MSPH: Mass of SPH
VSPH: Volume of SPH

7.4 Porosity Measurement

Solvent replacement method was used for porosity measurement [22,10]. Dried hydrogels were immersed overnight in absolute ethanol and weighed after excess ethanol on the surface was blotted. The porosity was calculated from the following equation:

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

where M_1 and M_2 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 [13,27].

7.5 Mechanical Properties

The compressive strengths of various SPH formulations were determined using a bench comparator as shown in Fig. 3. Briefly, after the fully swollen hydrogel was put longitudinally under the lower touch of a bench comparator, different scale loads were successively applied on the upper touch until the point where the hydrogel could not support any more weight and completely fractured. The pressure at this point was defined as penetration pressure (PP) and calculated by the following equation:

$$PP = F_u/S$$

where F_u is the ultimate compressive force at complete breakage of polymer and *S* is the contact area of the lower touch [22,13].

Fig. 3. Mechanical strength of superporous hydrogel

7.6 Determination of Drug Content

A weight of SPH containing drug in 100 ml volumetric flask was treated with about 10 ml hydrochloric acid solution of pH 1.2 mixed well and made up to volume [22]. The mixture was filtered and drug content was determined using UV-VIS spectrophotometer [10,23].

7.7 Morphological Analysis

7.7.1 FT-IR spectroscopy

FT-IR spectroscopy was employed to ascertain the compatibility between the drug and the polymers. It was also used to investigate the chemical structure of the synthesized hydrogels. The FTIR spectrum was recorded over the range of 400–4000 cm^{-1} [13] using KBr pellet method by Fourier-Transform Infrared (FT-IR) spectrophotometer, (Shimadzu, FT- IR 8400S, Japan).

7.7.2 Scanning electron microscopy

The dried SPH were used for scanning electron microscopy (SEM) studies to determine the morphology of the dried samples (Fig. 4). A JEOL JSM-840 scanning electron microscope (Jeol USA, Inc., Peabody, MA) was used after coating the samples with gold using a Hummer Sputter Coater (Technics, Ltd.). Images were captured using a digital capture card and Digital Scan Generator 1 (JEOL) [23].

7.8 Drug Loading

The method of soaking or equilibration was employed for drug loading. In this method the amount of buffer necessary for complete swelling of SPH was determined. Thereafter the drug solution in the determined amount of buffer which was required for complete swelling was prepared. Subsequently, SPH was placed in the drug solution and left until all the drug solution was sucked up. Then the completely swollen SPH loaded with the drug was placed in an oven at 30°C overnight [28].

7.9 Stability Studies

The prepared batches are kept in airtight containers and stored in stability chamber at 40°C/75%RH for three months. Results for *in vitro* dissolution studies obtained after three months are compared with the data obtained at the time of preparation.

7.10 Evaluation of Degradation Kinetics

The degradation kinetics of the hydrogel is examined by measuring the swelling ratio as a function of water retention. The hydrogel are placed in pH 1.2 (0.1 M HCl) medium at 37°C for 12 h, and the samples are periodically weighed at 6 h interval. Water retention capacity (WRt) as a function of time is assessed as in equation.

$$WRt = (Wp - Wd|Ws - Wd)$$

where,

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

7.11 Determination of Void Fraction

The void fraction inside superporous hydrogels was determined by immersing the hydrogels in HCl solution (pH 1.2) up to equilibrium swelling. The dimensions of the swollen hydrogels were measured and by using the data, sample volumes were determined as the dimensional volume. In the meantime, the amount of absorbed buffer into the hydrogels was determined by subtracting the weight of dried hydrogel from the weight of swollen hydrogel and the resulting values were assigned as the total volume of pores in the hydrogels. Void fraction is calculated by the formula [2,18].

$$\text{Void fraction} = \frac{Dimensional\ volume\ of\ hydrogel}{The\ total\ volume\ of\ pores}$$

7.12 *In vitro* Release Studies

In vitro drug release from the superporous hydrogels was evaluated using a United States Pharmacopoeia (USP) Dissolution Test Apparatus Type 2 (paddle method) [10]. At regular time intervals, samples of the dissolution medium were withdrawn, replaced with an equivalent volume of fresh dissolution fluid and analyzed for the drug using a UV-Vis spectrophotometer [22].

8. APPLICATIONS

SPHs were generally proposed as gastric retention devices. However, SPHs may be tailor-made for applications other than gastric retention in the pharmaceutical and biomedical industries and these potential uses are also discussed below.

8.1 Gastric Retention Devices

There has been a multitude of approaches using well-established principles to prevent the dosage form from exiting the pylorus during gastric emptying over few decades. Gastric retention devices may be extremely useful for the delivery of many drugs. Such devices would be most beneficial for drugs that act locally in the stomach (e.g., antacids and antibiotics for bacteria-based ulcers), or for those drugs that are primarily absorbed in the stomach. For drugs that have a narrow absorption window (i.e., mainly absorbed from the proximal small intestine), such as

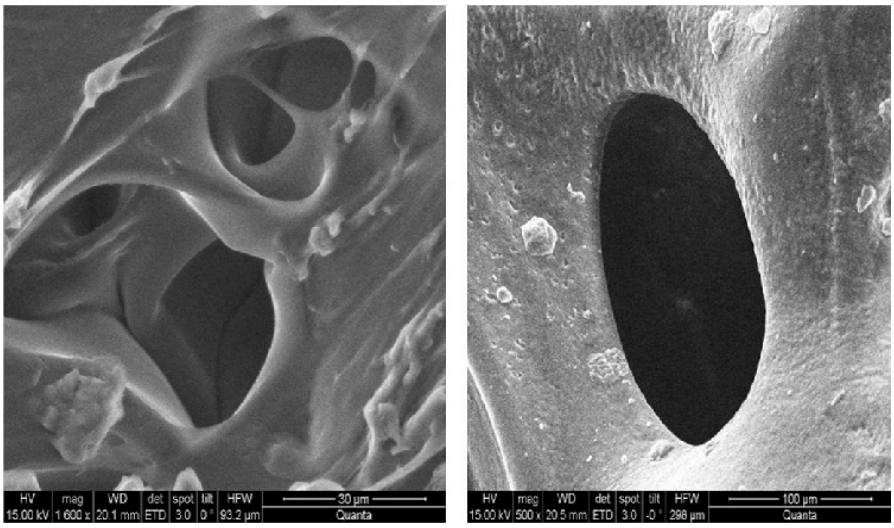

Fig. 4. SEM of Superporous hydrogels
(Gupta NV et al.)

riboflavin, levodopa, p-aminobenzoic acid, a controlled release in the stomach would improve bioavailability.

For drugs that are absorbed rapidly from the gastrointestinal tract, bioavailability could be improved by a slow release from the stomach. Gastric retention devices can further be used for drugs that are poorly soluble in an alkaline pH medium or for drugs that degrade in the colon (e.g., metoprolol). Prolonged gastric retention, however, is not desirable for all drugs. Gastric retention is not desirable for aspirin and non-steroidal anti-inflammatory drugs, or for drugs that are unstable in acidic pH. In addition, for those drugs that are primarily absorbed in the colon, a longer gastric retention may not be necessary because the time spent in the colon can sustain blood levels for up to 24 h [29].

8.2 Gastro Retentive Tablets

Processes which are used regularly such as dry blending and direct compression have been used to make gastro retentive tablets. The SPH particles of acrylic acid/sulfopropyl acrylate copolymers were mixed with gelatin and tannic acid, and thentabulated by direct compression [30]. Hydrogen bonding between gelatin, tannic acid and the carboxyl groups on the polymeric carrier, create an integrated matrix, which shows to be stable after swelling. The gastro retentive tablet could swell up to 30 times its own volume while maintaining its original shape in the period of 40 minutes. The swollen tablet can withstand up to 16 KPa compression force to reach its breaking point. Depending on the pH of the swelling medium, the gelatin can be replaced by carboxy methyl cellulose or other polysaccharides [31].

8.3 Fast-dissolving Tablets

Fast-dissolving tablets are orally administered without the need for water and swallowing. This feature is especially beneficial to children and the elderly. Freeze-drying, sublimation and direct compression are utilized to make fast-melting tablets. The first two methods make tablets that dissolve in 5–15 Ps, but the technology is rather expensive and tablets are not mechanically strong. One way of making fast-dissolving tablets by the direct compression method is to add fine particles of SPH to the granulation or powder formulation. The SPH micro particles within the tablet core expedite water absorption by an increased wicking mechanism. Tablets prepared by direct compression in the presence of SPH micro particles disintegrate in less than 10 seconds [32].

8.4 Peroral Peptide Delivery Systems

The feasibility of using CSPHs and SPHCs for peroral peptide delivery has been developed. 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 [17]. 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 is broken apart by the peristaltic forces of the gut by becoming over hydrated. Selection of proper type and thickness of enteric coating material will help to target to any specific site of small intestine and colon [18].

8.5 Development of Diet Aid

Diet soft drinks, meal replacement shakes, diet drugs and even surgical methods have been used to lose weight. Because of their rapid and extensive swelling, the SPHs can theoretically occupy most significant portion of the stomach space, leaving less space for food which causes suppressing of appetite. These types have the potential to facilitate weight loss in obese people. The major challenges to using SPHs as a weight loss aid will be to maintain the integrity and volume of the swollen SPH for a substantial period of time [32].

8.6 Chemoembolization and Occlusion Devices

Chemoembolization is a combined method of embolization and chemotherapy. Embolization has been used for cancer treatment by restricting the oxygen supply to the growing tumors. This method could be combined with chemotherapeutic agents to achieve local delivery and low systemic toxicity. A chemotherapeutic agent along with an anti-angiogenic agent could be loaded into SPHs for chemoembolization therapy. The strong SPHs would likely be better candidates for this application as they fit better in the blood vessels and provide better blocking. SPHs can also be used to develop biomedical devices for treating aneurysms. After determining the size and shape of an aneurysm site, smaller size of equivalent SPH is prepared. Because of its rapid and extensive swelling properties, the hydrogel will swell at the aneurysm site and clot the blood. Studies have shown that the SPH results in a 95% aneurysm occlusion without parent artery compromise and without inflammatory response [33].New occlusion devices are also under investigation. One such system, known as Hydrocoil, consists of SPH and platinum coils, and is currently under development by Micro-Vention.

8.7 Other Applications

Sodium CMC and hydroxyethyl cellulose cross-linked with diviny sulphone are used to remove fluids from body during surgery and also to treat edema. Sodium CMC, hydroxyethyl cellulose, poly ethylene glycol of different molecular weights were been used in development of orally administered hydrogels which absorb water. Superporous hydrogel microspheres are used in clinical evaluation of transcatheter arterial embolization for hypervascular metastatic bone tumor. SPH's have been potential to be used as scaffold for cell transplantation. For developing a PEG(poly ethylene glycol) based SPH with high pore interconnectivity photo cross linking reaction and foaming process were used which are applicable as tissue engineering where nutrient transport and tissue invasion are based on requirements [33].

Table 1. Literature survey of Research involving superporous hydrogels

S.No	Drug	Route of adminstration	Polymer	Method of preparation	Purpose
1	Metformin [34]	Oral route	Chitosan	Gas blowing technique	Treat type 2 diabetes
2	Pantoprazole[35]	Oral route	Eudragit L100	Gas blowing technique	Anti-ulcer drug
3	Rosiglitazone [36]	Oral route	Sodium carboxy methyl cellulose	Gas blowing technique	Treat type 2 diabetes
4	Amoxicillin [37]	Oral route	Chitosan	Gas blowing technique	Antibiotic
5	Carvedilol [38]	Oral route	Hydroxypropyl methyl cellulose	Gas blowing technique	Antihypertensive
6	Atenolol [39]	Oral route	Chitosan/Poly vinyl alcohol	Gas blowing method	Antihypertensive

9. CONCLUSION

Superporous hydrogels are a new class of hydrogel materials that swell to larger size regardless to their size and serves as a promising device for gastro-retentive delivery. Different generations of SPHs are investigated successfully for gastric retention. The network structure and possibility of rearrangements of hydrophobic/hydrophilic domains during swelling process, including entanglements and crystalline regions make these polymers water insoluble. A successful oral drug delivery platform that uses SPHs is expected to meet certain criteria including safety, effectiveness, desirable drug loading and release, feasible manufacturing as well as minimum interactions with gastric contents.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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