

A REVIEW ON GASTRO RETENTIVE SUPER POROUS HYDROGELS AND ITS GENERATIONS

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ABSTRACT

This review gives a detailed idea about super porous hydrogels and its generations. Generally super porous hydrogels (SPH) are different from superabsorbent polymers. On administration they instantly swell in the gastric media along with maintaining integrity, losing density and remains float. After 24 hours they are fragmented into small pieces and then eliminated from the body. This is one of the new drug delivery technologies allowing the use of new drug candidates and their development and to improve the effectiveness of existing drugs. SPH acts as a novel drug delivery system to control and retain drug release in gastric media i.e. gastro retentive systems.

KEYWORDS: Gastroretentive system, Superporous hydrogels.

1. INTRODUCTION

General problem for all the oral dosage forms that are encountered is the gastric residence time. For this, researchers attracted towards the novel drug delivery technologies to enhance drug residence time by formulating various gastro retentive systems. Dosage form retention in the stomach with the intention of prolonging oral gastro intestinal (G.I) transit time to achieve and improve drug bioavailability is the current target. The rigid crystalline structure and low elasticity in polymer leads to slow swelling of hydrogels and they take few hours to days for complete swelling.

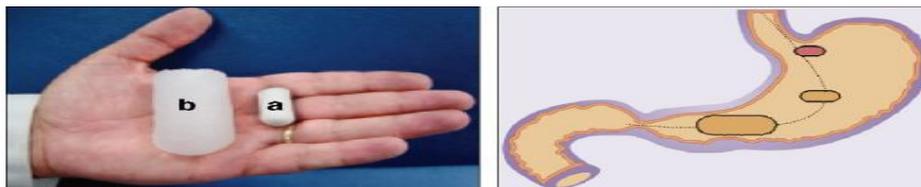


Figure1: Differentiation between dried SPH and swollen SPH and swelling of SPH in stomach

Diffusion of water through glassy matrix structure of hydrogel is the reason for its slow swelling. This property of hydrogel is responsible to make a controlled release dosage form. When faster swelling was required these may not serve the purpose. This is the reason behind the development of a new generation hydrogels, namely a super porous hydrogel (Figure1).

a.Super Porous Hydrogels (SPH): These are highly porous hydrophilic polymers with a three dimensional cross linked network like structure having pores in μm range. Due to these pores they have a property of absorbing large amount of water in a very short time and then expand their volume. This ideal property of SPH makes them in to usage as gastro retentive carriers. Mainly these are classified in to 3 generations.

a.1.The First generation SPH named as conventional SPHs: Ingredients that are used in the preparation of conventional SPHs contain monomers with high water absorbing affinity. The cross linking agent, foam stabilizer chemical initiator pair, distilled water and a buffer to adjust the pH are also present. Acrylic acid, acetic acid and hydrochloric acid are commonly used as monomers in SPH and are interact with sodium, ammonium, potassium carbonates after addition of initiator and a blowing agent both polymerization and foaming takes place which enhances the viscosity of reaction mixtures that leads to trapping of bubbles that are formed in foaming reactions.

For the first time in 2000, Chen prepared a SPH with fast swelling and super absorptive properties. In the formulation they used vinyl monomers and they are cross linked in presence of a blowing agent, foam stabilizer and alcohol, which was used as a dehydrating solvent. The process of dehydration decreases drying time and it preserves porous structure of hydrogel. The major problem faced with this conventional hydrogel is its mechanical strength. These are fragile and structure can easily break under low pressures. For this reason researchers make their attention towards second generation SPH composites.

a.2. Second generation hydrogels named as SPH composite: In this type SPH composite an extra material called super disintegrant was added i.e. swellable filler. These have good mechanical property with stands up to pressure of $2N\text{ cm}^2$. Baek (2001) was made modifications to conventional SPH to form this second generation super porous hydrogel composite by adding super disintegrant. Composite material doesn't show any pharmacological effects but they enhance the mechanical strength of hydrogels.

a.3. Third generation super porous hydrogel hybrids: A SPH with a high mechanical or elastic property are generally called as SPH hybrid. Due to addition of hybrid agent a cross linked structure of SPH was formed. Hybrid agent is a polymer that is soluble and dispersible in water. By undergoing physical or chemical cross linking it forms a cross linked SPH. Examples for hybrid agents include pectin, chitosan, polyvinyl alcohol, polysaccharides including sodium alginate. When compared with SPH composite SPH hybrids are highly elastic in swollen state. In 2003 Hossein Omidian prepared SPH hybrid using acrylamide, methylene bisacryl amide as monomers and cross linker.

	Structure	Swelling Property	Mechanical Property
First Generation	Polymer Chain Primary Crosslinker		
Second Generation	Composite Agent		
Third Generation	Hybrid Agent		

Figure 2: Generations of super porous hydrogels

b. Ingredients used in the preparation of super porous hydrogels and its generations: They are classified as following

b.1. Monomers: Acrylic Acid (AA), Acryl amide, 3- Sulpho propyl acrylate potassium (SPAK), Hydroxy ethyl methyl acrylate (HEMA), N-isopropyl acrylamide (NIPAM), Acrylonitrile (AN), Polyvinyl alcohol (PVA) etc.

b.2. Cross linking agents: N, N'-methylene bisacryl amide (BIS) is used most widely in blowing technique. Glutaraldehyde, formaldehyde (chemical cross linker), metal ions like calcium, iron and phosphorus are used in ion tropic cross linking of hydrocolloids.

b.3. Foam stabilizers: Pluronic F127, Pluronic P105, Silwet L7605, Span 80, Tweens etc.

b.4. Polymerization initiator pair: Ammonium per sulfate / N, N, N, N-tetra methyl ethylene diamine (APS/TEMED), Potassium per sulfate (KPS) /Sodium metabisulfite, ammonium per sulfate (APS) /Sodium metabisulfite, Azo-initiator etc.

b.5. Foaming agent: Bicarbonates like Sodium and Potassium bicarbonate.

b.6. Properties of SPHs

- For any SPHs to act as a gastro retentive system it should have following properties.
- The size of SPH must be small for easy swallowing.
- The size of the swollen hydrogel was large enough so it can retain in stomach.
- To overcome the gastric emptying by interdigestive myoelectric motor complex (IMMC) the swelling of SPH must be rapid.



Figure 3: Super porous hydrogels (bird shape) in dried and swelled form

c. Method of preparation of SPH

c.1. Gas blowing technique: This is the one of the method used in the synthesis of super porous hydrogel. In this method, a foaming agent was added to produce gas bubbles in the reaction mixture. Initially monomers, cross linking agent, foam stabilizer and distilled water was added in a test tube. The pH of the solution was adjusted to 5 with 5M NaOH. Low pH favors polymerization reaction, later foaming agent was added to the

reaction mixture which leads to formation of gas bubbles. During the addition of foaming agent, a polymerization initiator catalyst was added simultaneously. Both gellification and foaming reactions occurs simultaneously and they lead to entrapment of gas bubbles in the reaction mixture.



Figure 4: A) Reaction mixture in test tube B) Addition of foaming agent C) Formation of superporous hydrogel

d. Evaluation of superporous hydrogels

d.1. Swelling property of SPHs: Swelling is the main property shown by all the hydrogels when placed in contact with water. They undergo swelling within 20 minutes or less in stomach and escapes from premature emptying through house keeper waves there by act as gastro retentive systems. By using this swelling parameter equilibrium swelling time and equilibrium swelling ratio were determined.

d.1.1. Equilibrium swelling time: swelling time is the time taken by the hydrogel to attain its equilibrium swelling point. After this point the swelling of hydrogel was stopped. To measure this swelling time, the hydrogel was immersed in distilled water, 0.1NHCl and measure the time at which equilibrium in swelling process occurs.

d.1.2. Equilibrium swelling ratio: For this dried super porous hydrogel was taken and measured its weight and then it was allowed to hydrate in distilled water at room temperature. At various time intervals measured the swollen hydrogel weight. The Equilibrium swelling ratio was calculated by using the formulae

$$Q_s = \frac{W_s - W_d}{W_d \times 100}$$

W_s is the weight of the swelled hydrogel, W_d is the weight of the dried hydrogel and Q_s is the equilibrium swelling ratio.

d.1.3. Mechanical strength: In order to withstand the pressure exhibited by gastric contents and its contractions, any hydrogel must require showing mechanical strength. Mechanical strength was measured by using bench comparator and gastric simulator. Conventional super porous hydrogels showed low mechanical strength when compared with others.

d.1.4. Porosity measurement: In order to determine the porosity of a super porous hydrogel solvent displacement method was followed. A reweighed dried hydrogel was immersed in absolute ethanol for 24 hours; it absorbed ethanol and was swollen, which led to blotting of ethanol on the surface.

$$Porosity = \frac{M_2 - M_1}{\rho V}$$

Where M_1 and M_2 are the mass of the hydrogel before and after immersion in absolute ethanol and ρ is the density of absolute ethanol and V is the volume of the hydrogel.

d.1.5. Scanning electron microscopy (SEM): SEM analysis was performed to identify the morphology of a dried super porous hydrogel. The samples were coated with gold using Hummer sputter coater (Techniques, Ltd.), then carried using a Jeol JSM-840 scanning electron microscope (Jeol USA, Inc., Peabody, MA), and captured the images using a digital capture card and Digital Scan Generator 1 (Jeol). This picture clearly indicates the pores in its structure (figure 5).

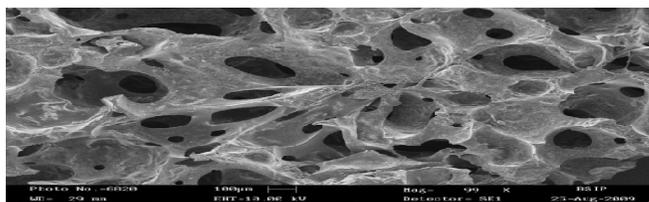


Figure 5: SEM image of metformin loaded super porous hydrogel composite

2. CONCLUSION

Super porous hydrogel acts as a novel polymer by releasing drug slowly for a long period of time. Drugs with narrow absorption window and absorbs mainly in stomach or upper part of intestine will be loaded in these hydrogels. Initially the size of the hydrogel is too small after administration it swells rapidly releases drug slowly after swelling its density decreases and then it floats. By floating in the stomach it promisingly acts as a gastro retentive system.

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