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GASTRORETENTIVE SUPERPOROUS HYDROGEL DRUG DELIVERY SYSTEM: A REVIEW

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Abstract

Oral administration is the most easy and frequently used drug delivery system offering various advantages like ease of dosing administration, better patient compliance. Drugs which easily absorbed from gastrointestinal tract and have short Half-Life get eliminated quickly from the systemic circulation and frequent dozing of these drugs is required to have therapeutic effect. To overcome this problem development of oral controlled release formulation is an attempt to release the drug slowly into the gastrointestinal tract and maintain the effective drug concentration in the blood plasma for a long time. Super porous hydrogels are new advancement in gastro retentive drug delivery system which comprises of controlled release swellable system. The superporous hydrogel absorbs Gastrointestinal fluids swell in stomach. SPHs hold large amount of water in very short time interval. The SPHs consist of first generation, second generation and third generation SPH hybrids. This review discusses the various advantages and disadvantages, principle involved in the gastric retention of superporous hydrogels, methods of preparation, classification of superporous hydrogels.

Keywords: Superporous Hydrogels, Controlled Release, Gastrointestinal Tract, swellable system, Half-life.

Introduction

The control release dosage form increases the gastric retention time improve bioavailability, increase the duration of drug release and also improve the drug solubility which have good solubility in acidic media [1]

Gastroretentive drug delivery is an approach to prolong gastric residence time of drug and increase drug release in the upper gastrointestinal tract for local as well as systemic effect. Various gastroretentive Drug Delivery approaches are like high density system that is retained in the bottom of the stomach, low density floating system which causes buoyancy in gastric fluid [2], mucoadhesive system in which drug stick to stomach mucosa, Swellable systems like SPH (Superporous Hydrogels) which swells after absorbing large quantity of gastrointestinal fluids and prevent their passage from pyloric sphincter of stomach [3]. Fig 1.

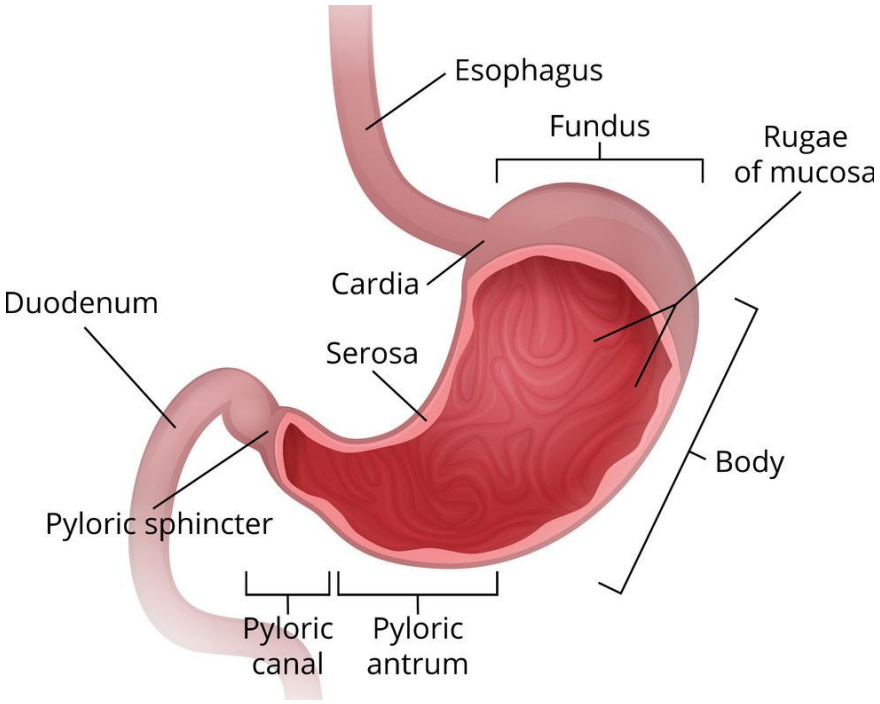

Figure 1: Structure of the stomach and its various parts

Source: https://www.vectorstock.com/royalty-free-vector/the-anatomy-of-the-human-stomach-vector-11092545

Drugs Which Are Suitable For Gastroretentive Drug Delivery System

Following are the Suitable drugs useful as Gastro retentive Drug Delivery System

1. Drugs having local action in stomach example antacids and drugs used against helicobacter pylori.
2. Drugs rapidly absorbing from GIT for example Metronidazole and Tetracycline.

3. Drugs having narrow absorption window for example Theophylline and Atenolol.
4. Drugs having low solubility in intestine for example Quinidine and Riboflavin.
5. Normal Flora disturbing drugs for example antibiotics which are used for helicobacter pylori.
6. Drugs which get destroyed in colon for example Metformin hydrochloride and Captopril.
7. Drugs having variable bioavailability for example Sotalol hydrochloride.
8. Drugs having good absorption from upper GIT for example calcium supplements and Cinnarazine.

Advantages

a. Better patient compliance
b. Reduced dosage frequency
c. More gastric residence time.
d. Drug Targeting to stomach can be achieved.
e. Increased bioavailability and fluctuation in blood drug concentration is avoided.
f. Uniform drug release from dosage form
g. Sustained effect for a long period of time.

Disadvantages

a. Drugs unstable & insoluble in acidic media cannot be administered as GRDDS.
b. Drugs causing gastric irritation cannot be administered by this route.
c. This system requires fed state to prolong gastric emptying.
d. Not suitable for drugs undergoing first-pass metabolism.
e. Gastric retention can be influenced by various factors which changes mainly in diseased state.

Superporous Hydrogels (SPH)

Superporous hydrogel (SPH) is a 3-dimensional network of a hydrophilic polymer which absorbs a large amount of water in a very short period of time due to the presence of Interconnected microscopic pores[4] SPHs are hydrogel that have numerous super size pores inside them. Swelling of superporous hydrogels is done by capillary wetting rather than by diffusion. In the preparation of SPHs certain ingredients, including initiators, crosslinkers, foam stabilizers, foaming aids and foaming agents, are added into a water-diluted monomer. 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 the stomach. Second

generation Superporous hydrogels composites are developed which shows fast swelling, medium swelling ratio and improved mechanical properties, while third generation superporous hydrogel hybrid possess high elastic properties[5]

Principle of the gastric retention of superporous hydrogels [6]

The gastric retention of superporous hydrogels is based on their fast swelling property. After oral administration, it swells rapidly in the gastric fluid to a large size. So that its emptying into the intestine is prevented[7] When the gastric contraction reaches the hydrogel, the gastric tissues slide over the hydrogel. As it is elastic, slippery and high mechanical strength it able to withstand gastric contraction and also due to the low density of superporous hydrogel than the gastric content it floats and releases drug in upper part of GIT[6].

Advantages of SPH

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

Methods for Preparation of Superporous Hydrogels

There are four methods for preparing the gastroretentive superporous hydrogel,

1. Porosigen technique
2. Cross linking technique
3. Phase separation technique
4. Gas blowing or foaming technique.

Porosigen Technique

Porous hydrogels are prepared in presence of dispersed water soluble porosigen. Various porosigen are used to prepare the superporous hydrogel. These porosigen are hydrophilic in nature[8] The pore size generates in the hydrogel depends on the size of porosigens[9]

Cross linking technique

Crosslinking 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 particles Individual hydrogel particles can be crosslinked to form crosslinked aggregates. This technique is limited to absorbent particles with chemically active functional groups on surface[10]

Phase separation technique

Phase separation is very critical process in generating superporous hydrogel because there is no much control over the porosity. In solution polymerization, monomers are usually mixed in diluent that is good for both monomers and polymers. 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[11]

Gas blowing or foaming technique

This is most widely used, Initially monomers, cross linking agent, foam stabilizer and distilled water are added in atest tube of specific dimensions pH adjust 5 to 6 with 5M NaOH. 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[12] After synthesis, Superporous hydrogels are subjected to washing, drying using different methods.

Classification of superporous hydrogel

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

First generation SPH (conventional SPHs, CSPHs)

Conventional SPH (CSPH) was first discovered by with fast swelling kinetics and super absorbent properties in 1999 [11] 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 ethanol. 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. By incorporating wetting agent the rate of water uptake is also enhanced [13,14]

Second generation SPH (SPH composite, SPHCs)

In this type super porous hydrogel an extra material called super disintegrant is added (swellable filler). These have good mechanical property withstands pressure up to 2N cm2. Baek in 2001 were made modifications to conventional super porous hydrogel to form second generation super porous hydrogel by adding super disintegrant[15] Composite material, which does not show any pharmacological effects but they enhance mechanical strength of hydrogels. Superporous hydrogel composite is a matrix of continuous phase having a dispersed phase incorporated within. A composite agent used in hydrogel composites is cross-linked water-absorbent hydrophilic polymer that can absorb solution of monomer, crosslinker, initiator and remaining components. Composite agent in hydrogel composites improves mechanical properties. But superporous hydrogel composites are still brittle and breakable.

Third generation SPH (SPH hybrid, SPHHs)

The third generation of SPHs was developed based on SPH hybrids. The third generation SPHs are modified versions of the second generation and assume an integrated IPN structure. A water soluble hybrid agent is introduced in SPH formulations in case of SPHHs. Although the SPHs of the second generation could provide a hydrogel with a

better strength. This triggered the development of the third SPH generation, also called superporous hydrogel hybrids (SPHHs), with superior mechanical properties. 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[12]

Although the mechanical properties of SPHs can be significantly enhanced after an ion treatment, the ion composition was foundto be a useful tool for better controlling the swelling and mechanical properties. 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. displays the fundamental structural differences between the second, the third, and the modified SPH generations. SPH hybrids are prepared according to conventional SPH formulations but a water soluble and ionogelling polymer (synthetic or natural) is added during hydrogel preparation[16] After preparation, the SPH is treated in an ion solution to become strong and elastic.

Conclusion

The SPHs are used efficiently for oral controlled drug deliver for long term retention, the cross linked polymer having network structure consisting of acidic, basic and neutral monomers are able to imbibe large amount of water. Nowadays a lot of work is going on gastroretentive drug delivery and in future SPHs will proved to be potential candidate for gastric retention.

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