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SUPER POROUS HYDROGEL TABLETS: NOVEL DRUG DELIVERY APPROACH

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ABSTRACT

Super porous hydrogels (SPHs) are novel improvement in sustained release gastro retentive drug delivery system. Another gastro retentive drug delivery systems (GRDDS) includes mucoadhesive system, intragastric floating system (low density system), swellable system and high density system. SPHs system should swell instantly in stomach and should maintain their integrity in highly acidic stomach environment, while releasing the pharmaceutical active ingredients in stomach. First generation conventional SPH has poor mechanical strength that can be overcome by developing second generation composite SPH and third generation hybrid SPHs. Characterization can be performed by the measurement of porosity, apparent density, swelling studies and SEM studies.

KEYWORDS: Super porous hydrogels (SPHs), gastro retentive drug delivery systems (GRDDS), Composite SPHs, hybrid SPHs, etc.

Hydrogels have long been established in this field to control the release of a drug from a conventional solid dose formulation. It gradually swells in the aqueous medium and controls drug release by both diffusion and erosion. These types of hydrogels are non-crosslinked and ultimately dissolve over time in the presence of sufficient water or the swelling medium.[1,2]

Super porous hydrogels (SPHs) are porous hydrophilic crosslinked structures with the ability of absorbing aqueous fluids up to a few hundred times their own weight. Maximum swelling is generally reached in a fraction of a minute with SPHs having average pores of 200 mm in size.[3]

In the preparation of SPHs certain ingredients, including initiators, crosslinkers, foam stabilizers, foaming aids and foaming agents, are added into a water-diluted monomer. The foaming of SPHs is then driven by the interaction of acids and carbonates. For instance, acetic, acrylic and hydrochloric acids are commonly used with sodium, potassium and ammonium carbonates. Since the acid–carbonate interaction is only effective in aqueous media, the solution technique is the preferred method of polymerization in the preparation of SPHs.[4,5,9]

The third generation super porous hydrogels are the SPH hybrid (wherein a water-soluble counterpart, a hybrid agent is employed).[5]

Depending on the agent type and its associated treatment, various third generation SPHs can be created, ranging from high modulus to highly elastic and rubbery (in their water-swollen states). Water-soluble hydrocolloids, including sodium alginate, sodium carboxymethyl cellulose, pectin and chitosan, have been used alone or in combination as the preferred hybrid agents. Overall, these third generation SPHs are elastic super porous hydrogels having enhanced mechanical properties. [5-11]

Preparation of drug loaded SPHs

Hydrocolloid polymer solution (2%w/v) can be prepared by stirring in 0.1M glacial acetic acid solution using a homogenizer until the chitosan dissolves in acid completely. A 10% w/w aqueous PVA solution can prepared and mixed to the polymer solution. To this solution, 0.2 ml of formaldehyde solution (10% w/w of the dry weight of chitosan) should mix. Further, 0.2 ml of tween 80 should added and mixed thoroughly followed by 50 mg of sodium bicarbonate. The prepared mixture should stir well and kept aside overnight.

10 ml of 0.1 N HCL should take. To this 20 mg of drug and 100 mg of super porous hydrogel should added and mixed for 1 h at 50°C. Then acetone of 2ml should added and the hydrogel should repeatedly should be with distilled water to remove any unreacted material. Further it should dry at 40°C for 24h, finally powder and store in a well closed container. [15 -18]

Swelling studies

Completely dried super porous hydrogel should be weighed and then immersed in excess of 0.1 N HCl. At various time intervals, the hydrogel should be removed from the solution, blotted to remove excess of medium and then weighed.[16,18] Swelling ratio should be calculated according to the following equation:

$$Q = (M_s - M_d) / M_d$$

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

Porosity measurement: Dried hydrogels were immersed overnight in absolute ethanol and weighed after excess ethanol on the surface should be blotted. The porosity should be calculated from the following equation:

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.[16 -18]

Determination of void fraction: The void fraction should be calculated by the following equation:

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

The void fraction inside super porous hydrogels should be determined by immersing the hydrogels in 0.1 N HCl up to equilibrium swelling. The dimensions of the swollen.

Table 1: Formulations With Hydrocolloid Polymer: Superporous Hydrogel.

Ingredients (% w/w)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Chitosan	2	---		3	---	---	4	---	---
Pectin	---	2	---	---	3	---	---	4	---
Sodium alginate	---	---	2	---	---	3	---	---	4
Poly Vinyl Alcohol	4	4	4	4	4	4	4	4	4
Formaldehyde	10	10	10	10	10	10	10	10	10
Tween 80	0.2ml	0.2ml	0.2ml	0.2ml	0.2ml	0.2ml	0.2ml	0.2ml	0.2ml
Sodium Bicarbonate	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
API	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg

Determination of void fraction: The void fraction should be calculated by the following equation.

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

The void fraction inside super porous hydrogels should be determined by immersing the hydrogels in 0.1 N HCl up to equilibrium swelling. The dimensions of the swollen hydrogels were measured and thereby dimensional volume should be determined. In the meantime, the amount of absorbed buffer into the hydrogels should be determined by subtracting the weight. of dried SPHs from the weight of swollen SPHs and the resulting values were assigned as the total volume of pores in the SPHs.[16 -18]

Water retention capacity: The following equation should be used to determine the water retention capacity (WR_t) as a function of time:

$$W_{Rt} = (W_p - W_d) / (W_s - W_d)$$

Where, W_d is the weight of the dried SPHs, W_s is the weight of the fully swollen SPHs (after exposure for 1day), and W_p is the weight of the SPHs after exposure time of 6 hours. For determination of the water-retention capacity of the SPHs at 37°C, the water loss of the fully swollen polymer should be determined by gravimetry [16 -18].

Mechanical Properties: The tensile strength (T) of super porous hydrogel formulations, which is a measure of the stress necessary to cause diametral fracture of the compact, should be determined from the mean data obtained from the hardness test carried out on the SPHs (n = 3) using the Monsanto hardness tester. The T values were computed from equation below, $T = 2P / \pi D t$

Where, P is the load applied on the SPH that causes tensile fracture of the SPH of diameter, D, and t is the SPH thickness.[19,20]

Determination of drug content: A weight of super porous hydrogel containing 5 mg of drug in 100 ml volumetric flask should be treated with about 10 ml 0.1 N HCl of pH 1.2 mixed well and made up to volume. The mixture should be filtered and drug content should be determined using UV-Vis spectrophotometer at 286 nm.

FT-IR spectroscopy: FT-IR spectroscopy should be employed to ascertain the compatibility between the drug and the polymers. It should be also used to investigate the chemical structure of the synthesized SPHs. The FTIR spectrum should be recorded over the range of 400–4000 cm^{-1}using KBr pellet method by Fourier-Transform Infrared (FT-IR) spectrophotometer, (Bruker-Alpha-T-1020).

Scanning electron microscopy: The dried super porous hydrogels were used for scanning electron microscopy (SEM) studies to determine the morphology of the dried samples. A JEOL JSM-840 scanning electron microscope should be 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).

Precompression characterization: Powder blend of SPHs should be evaluated for various physiochemical parameters. Bulk density, tapped density, angle of repose and powder flow studies of the different formulations were studied.

Weight Uniformity Test: The 20 tablets were taken and their weight should be determined individually and collectively on a digital weighing balance. The average weight of one tablet should be determined from the collective weight. Test should be performed as per Indian Pharmacopeia (IP) 2010.[21]

Hardness: Hardness should be determined by taking six tablets from each formulation, using a Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.

Friability: The friability test should be performed using Roche friabilator.

Sample comprising the tablets equivalent to 6.5 g were rotated at 25 rpm for 4 min. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss should be calculated. Friability below 1% should be considered acceptable.[21]

***In-vitro* drug release study:** The *in-vitro* drug release study of tablets should be performed using United State pharmacopeia (USP) Type 2 apparatus at 37°C ± 0.5°C using 0.1N HCl (900 mL) as a dissolution medium at 50 rpm. At the predetermined time intervals, 5 ml samples were withdrawn and replaced with fresh dissolution media. Withdrawn samples should be filtered through a 0.45 µm membrane filter, diluted and assayed at suitable wavelength using a UV-VIS double-beam spectrophotometer. Cumulative percentage drug release should be calculated using an equation obtained from a calibration curve.[22]

Ideal characteristics of SPHs tablets

The functional features of an ideal hydrogel material can be listed as follows.[48]

- The highest absorption capacity (maximum equilibrium swelling) in saline.
- Desired rate of absorption (preferred particle size and porosity) depending on the application requirement.
- The highest absorbency under load (AUL).
- The lowest soluble content and residual monomer.
- The lowest price.
- The highest durability and stability in the swelling environment and during the storage.
- The highest biodegradability without formation of toxic species following the degradation.
- pH-neutrality after swelling in water.
- Colourlessness, odorlessness, and absolute non-toxic.
- Photo stability.
- Re-wetting capability (if required) the hydrogel has to be able to give back the imbibed solution or to maintain it; depending on the application requirement (e.g., in agricultural or hygienic applications).

CONCLUSION

Recently, many hydrogels based networks have been designed and tailored to meet the needs of different applications. The favourable property of these hydrogels is either ability to swell when put in contact with an aqueous solution. The presented review demonstrates the literature concerning classification of hydrogels on different bases, physical and chemical character-istics of these products and technical feasibility of the utilization. It also involved technologies adopted for hydrogel production together with process design implications, block diagrams and optimized conditions of the preparation process. An innovated category of recent generations of hydrogel materials was also presented in some details. Super-porous hydrogels are new materials that, regardless of their original size, rapidly swell toa large size. Different generations of SPHs evolved to address the needs for certain applications. Based on the literature sur-vey, it can be concluded that batch or semi-batch reactors are suitable reactors for polymerization processes. The variables for batch reactors include temperature, pressure, batch cycle time, the number of reactants, and the feed addition strategy. Optimization variables such as batch cycle time and amount of reactant are continuous variables with fixed values for a certain batch reactor system depends mainly upon material and energy balance. Ribbon mixer with a screw around the axis, screw mixer with four baffles, and double ribbon mixer are three Impellers known to be effective in high viscosity ranges.

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