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Study of Effect of Initiators on Synthesis of Superporous Hydrogels as Gastroretentive Device

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ABSTRACT

The study emphasizes on studying the effects of redox initiators on synthesis of superporous hydrogels. Fast swelling highly porous superporous hydrogels are synthesized by crosslinking polymerization of various monomers as gastro-retentive devices. The swelling property, mechanical strength and Scanning Electron Micrograph pictures were investigated for such devices. Use of N,N,N'N'- tetramethylene diamine and Ammonium Persulfate (TEMED + APS) has already been reported for the preparation of first generation superporous hydrogels. In this study, riboflavin has been used along with TEMED + APS (Ribo + TEMED + APS). The result indicates that there is no significant difference in the swelling properties and mechanical strength of porous structure. The use of TEMED + APS may be preferred to reduce time and cost of the process. The process is simplified also.

INTRODUCTION

Oral route of drug administration is the most preferable route, taking patient compliance, flexibility of formulation into consideration. Drug absorption from GIT is a complex procedure and is subject to many variables. Magnetic systems, floating systems, expandable systems and mucoadhesive systems are various methods of increasing gastric residence time.[1] Superporous hydrogels have also been developed for prolonging the residence time of delivery system to gastrointestinal tract.[2] Superporous hydrogels are able to absorb water very rapidly due to the presence of interconnected microscopic pores.[3] The superporous hydrogels are able to absorb water and swell to equilibrium size in a very short period of time. Synthesis of superporous hydrogels involves copolymerization/ crosslinking of co-monomers using a crosslinking agent which is a multifunctional co-monomer.[4] The polymerization reaction is initiated by a chemical initiator. The rate of polymerization depends on the concentration of initiators, in turn, properties of resulting hydrogel also depends on the concentration of initiators. Increase in the concentration of initiators results in decrease in average polymer chain length.[5] The major advantage of riboflavin is that it is active in very low concentrations. When riboflavin is used with TEMED and ammonium persulfate, the total amount of initiator required is less.

MATERIALS AND METHODS

Materials:

Acrylic acid, acrylamide, Pluronic F (PF 127), ammonium persulfate, riboflavin, sodium bicarbonate were purchased from Loba Chemie Pvt. Ltd., N,N,N',N'-tetramethylene diamine was purchased from Central Drug House Pvt. Ltd., New Delhi. All the chemicals used were of analytical grade and used as received.

Methods:

A. Preparation of Superporous hydrogels:

Gas blowing technique was used to synthesize superporous hydrogels. All the ingredients including monomers (acrylamide- 50%), crosslinker (BIS – 2.5%), foam stabilizer (PF 127- 10%), acrylic acid, reaction initiator pair [(SH 1: APS – 20%, TEMED – 20%) and (SH2: APS – 20%, TEMED – 20%, 0.5% Riboflavin) were added sequentially in a test tube and

shake well after each addition. pH of monomer solution was kept between 5 and 6 using acrylic acid. Sodium bicarbonate (90 mg) was added immediately with stirring to uniformly distribute generated bubbles. Two formulation batches, namely SH1 and SH2, were prepared by varying the initiator system as per composition is shown in Table 1. The volume of final solution in the test tube increased to 2-10 times the original solution volume. The resulting SPHs were treated with ethanol and air dried.[6]

Table 1: Composition of CSPH

Name of ingredient	**CSPH**	
	SH 1	**SH 2**
Acrylamide (50% w/v)	1000 µl	1000 µl
N,N-methylenebisacrylamide (2.5%w/v)	200µl	200µl
Pluronic F 127 (10%w/v)	100µl	100µl
Distilled water	460µl	460µl
Acrylic acid (pH- 5-6)	25µl	25µl
Riboflavin (0.5% w/v)	-	50µl
Ammonium per sulfate (20%w/v)	50µl	15µl
N,N,N',N'-tetraethylmethylenediamine (20%w/v)	50µl	15µl
$NaHCO_3$	100 mg	100 mg

B. Evaluation of Superporous hydrogels

1. Equilibrium Swelling Ratio & Equilibrium Swelling Time

Completely dried SPH were weighed and kept in excess of swelling medium (distilled water at 37^0 C) until the equilibrium swelling was achieved and the hydrogel sample was again weighed (n=6).

The swelling ratio was calculated as:

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

Where Q is the swelling ratio, M_s is the mass of the hydrogel in swollen state; M_d is the mass of the dried hydrogel.

The swelling time was determined by dipping hydrogel samples in excess of swelling medium till equilibrium swelling was achieved.

2. Determination of Density

Solvent displacement method was used for determination of density. The pre-weighed hydrogel sample was immersed in hexane in a graduated cylinder. Initial volume of hexane was noted and the increased volume was observed (n=6).
Density was calculated as:

Density = Mass of Superporous Hydrogel/ Volume of solvent displaced

3. Determination of Porosity

Immersed dried SPH in hexane overnight. Blotted excess amount of hexane on the surface and weighed (n=6).

Porosity was calculated using the formula:

$$\text{Porosity} = V_p / V_t.$$

Where, V_t is the total volume of SPH,

V_p is the pore volume of SPH (V_t-V_l),

V_l is the volume of liquid displaced.

4. Determination of Void Fraction

Immersed Superporous Hydrogel in Hydrochloric acid (pH1.2) till equilibrium swelling was attained. The dimensions of the swollen SPH were measured and by using these values, SPH sample volume was determined as the dimensional volume. The amount of absorbed HCl into SPH was determined by subtracting the weight of dried SPH sample from the weight of

swollen SPH and the resulting values were assigned as the total volume of pores in the hydrogels (n=6).

Void fraction was calculated using the formula:

Void Fraction = Dimensional Volume of superporous hydrogel/ Total volume of pores

5. Mechanical Properties

Compression force (N) was determined using the TA-TX plus texture analyzer (stable microsystems) using a cylindrical aluminum probe (P75) having a pretest speed of 2.00 mm/s, test speed of 1 mm/s and posttest speed of 2 mm/s up to a distance of 3 mm. The swollen SPH sample was placed on a disk-shaped platform. Compression force was estimated as the peak value in the force versus time plot.

6. Scanning Electron Microscopic Studies

The dried hydrogels cut in transverse section and mounted on the double sided tape on aluminum stubs and were sputter coated with gold using the fine coat ion sputter and then micrographs were recorded using Scanning Electron Microscope to study the porous nature of hydrogels.

RESULTS AND DISCUSSION

Two batches of CSPHs were formulated to study the effect of initiator pair (Fig 1). SH1 was formulated with 50µl of 20% APS + 50µl of 20% TEMED and SH2 with 50 µl of 0.5%Riboflavin + 15µl of 20% APS + 15µl of 20% TEMED. The rate of polymerization depends on the concentration of initiators, in turn, properties of resulting hydrogel also depends on the concentration of initiators. Increase in the concentration of initiators results in decrease in average polymer chain length.[4] The major advantage of riboflavin is that it is active in very low concentrations. When riboflavin is used with TEMED and ammonium persulfate, the total amount of initiator required is less.

Conventional Superporous Hydrogels with APS and TEMED as Redox Pair Initiator (SH 1)

Conventional Superporous Hydrogels with Riboflavin, APS and TEMED as Redox Pair Initiator (SH 2)

The superporous Hydrogels were evaluated. Table 2 summarizes the physical characterization of superporous hydrogels.

Evaluation of superporous hydrogels

1. Equilibrium Swelling Ratio & Equilibrium Swelling Time

Equilibrium Swelling Ratio of hydrogels was observed to be 136.6 ± 0.8 for SH1 and 117.8 ± 0.9 for SH 2 formulation batch. The equilibrium swelling time is 3-6 min in both cases. The pattern may be attributed to the porous structure of superporous hydrogels. It follows that the pore structure is not hampered by addition of riboflavin as initiator. The uniformity of capillary channels in ethanol dried SPHs led to less swelling time in CSPHs.

Table 2: Physical characterization of Superporous hydrogels

Process	Parameter	CSPH	
		SH 1	SH 2
During synthesis	**Texture**	Soft, sticky, less flexible	Soft, less flexible
	Colour	Completely White	Creamish white
During ethanol dehydration/ crosslinker treatment		No immediate hardening	No immediate hardening
After drying	**Texture**	Hard and sticky	Hard and sticky
	Elasticity	Completely fragile	Completely fragile
After swelling		Completely Transparent	Completely Transparent
	Equilibrium Swelling Time	3-6 min	3-6 min
	Equilibrium Swelling Ratio	136.6 ± 0.8	117.8 ± 0.9
	Density (g/cm^3)	0.86 ± 0.06 g/cm^3	0.81 ± 0.12 g/cm^3
	Porosity (%)	92.7 ± 0.8	88.7 ± 0.9
	Void Fraction	33.6 ± 0.7	33.6 ± 0.7
	Dimensions		
	Initial	0.6/1.7	0.5/1.6
	Final	3.5/10.5	3.3/9.8
	Mechanical Strength	3.117	3.106

Rate of swelling to reach the state of equilibrium is shown in Fig 2.

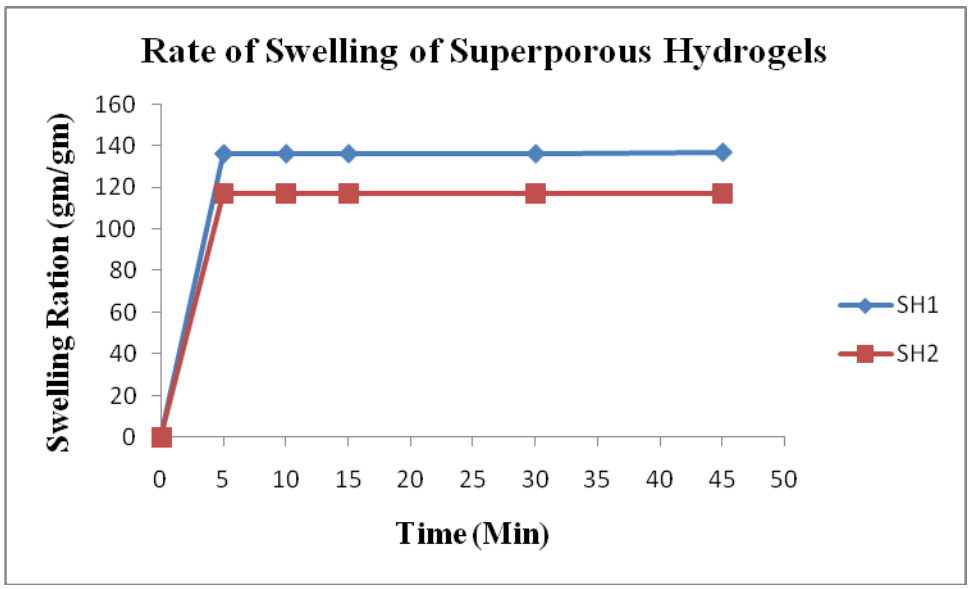
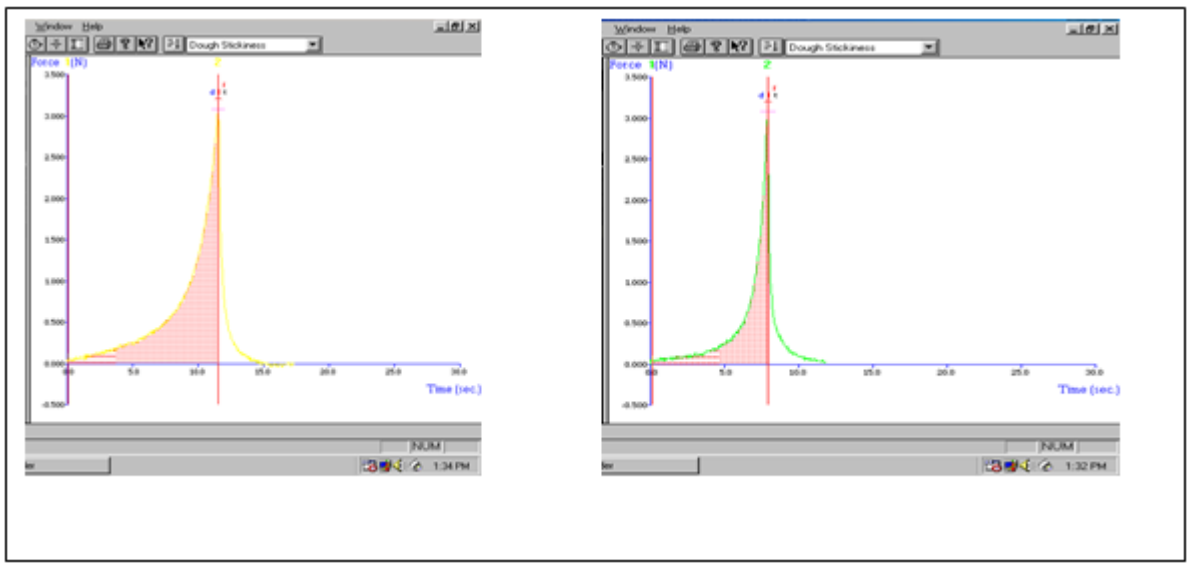


Fig 2: Rate of Swelling of Superporous Hydrogels

2. Density, Porosity and Void Fraction:

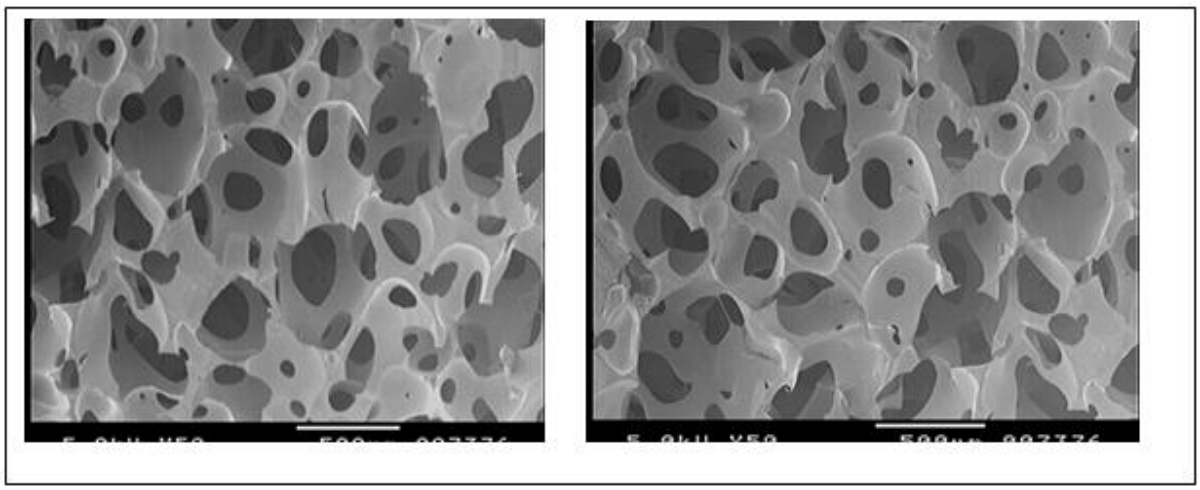
The experimental values of density, porosity and void fraction are given in Table 2. The observed values indicate that the porous structure is not very different in two formulations.

3. Mechanical Strength



The values of compression force were found to be 3.117 and 3.106 for the two test formulations. These values indicate that the formulations are fragile.

4. Scanning Electron Micrographs



The porosity of superporous hydrogels, at 500µm scale, is shown in scanning electron micrographs, is similar.

CONCLUSION

Addition of riboflavin didn't yield significantly better results, but delayed the process. The value of equilibrium swelling ratio, equilibrium swelling time, mechanical strength is also not significantly different. It takes comparatively more time for polymerization when riboflavin is added in initiator system. Thus, the process is simpler when we use TEMED + APS as redox initiator pair. Formulation batch SH 1 may be considered for formulation of second and third generation superporous hydrogels.

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REFERENCES

1. Grfning R., Werner M., Berntgen M., Georgarakis M. Peroral controlled release dosage forms with internal magnets and extracorporal magnetic guidance: investigations into the renal elimination of riboflavin. Eur. J. Pharm. Biopharm. 1996; 42:25– 32.
2. Lehr CM. Bioadhesion technologies for the delivery of peptide and protein drugs to the gastrointestinal tract. Crit. Rev. Ther. Drug Carr. Syst.1994; 11: 119– 160.
3. Dorkoosh F.A., Verhoef J.C., Borchard G., Rafiee-Tehrani M., Junginger H.E. Development and characterization of a novel peroral peptide drug delivery system. J. Control. Release. 2001; 71: 307– 318.

4. Chen J, Park H, Park K. Superporous hydrogels: fast responsive hydrogel systems. Proc ACS Div Polym Mat Sci Eng. 1998; 79: 236-237.
5. Menter P. Acrylamide Polymerization- A practical Approach. 2000: Bio-Rad Laboratories.
6. Kumar A, Pandey M, Koshy M K, Saraf SA. Synthesis of fast swelling superporous hydrogel: effect of concentration of crosslinker and acdisol on swelling ratio and mechanical strength. International Journal of Drug Delivery. 2010: 2;135-140.