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Superporous Hydrogel Composites of Acrylamide Using Starch-silicone Dioxide Coprecipitate as Composite Agent

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Authors' contributions

This work was carried out in collaboration between all authors. Authors MN and GAD designed the study protocol, interpretation of data and final draft of manuscript. Authors AG and SB performed the experimental work, complete literature survey, the analysis of data, and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aim: Present study includes the development and evaluation of superporous hydrogel composites of acrylamide using starch silicone dioxide coprecipitate (SSC) as composite agent.
Methodology: Gas blowing method was used for synthesis of superporous hydrogels. Different ingredients were mixed in specified amount in test tube and foaming agent was added at last. Simultaneous foaming and gelation lead to formation of porous hydrogel networks. Effect of different treatments (acetone dehydration and simulated gastric fluid (SGF) treatment) and drying conditions on the porous structure was evaluated. The prepared superporous hydrogels were evaluated for density, porosity, equilibrium swelling ratio, equilibrium swelling time, mechanical strength, scanning electron microscopy studies. The pure drug (Verapamil Hydrochloride) mixed with Carbopol 934 (1:0.5 and 1:1 ratio) was loaded into the selected batches of SPHC using *in situ* method of drug loading

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(drug added directly into the reaction mixture). The *in vitro* drug release was carried out using USP II dissolution apparatus.
Results: Acetone dehydrated superporous hydrogel composites were observed as better floating devices due to least density and maximum porosity values. Maximum swelling ratio was found in case of oven dried conventional superporous hydrogel and superporous hydrogel composites with equilibrium swelling time of more than 25 min. On the other hand, acetone dehydrated SPH showed less equilibrium swelling ratio with equilibrium swelling time of 5-10 min. Minimum swelling ratio was observed in case of SGF treated hydrogels with equilibrium swelling time of 15-19 min. Mechanical strength was improved by addition of starch silicone dioxide coprecipitate as composite agent. SGF treatment also leads to enhanced mechanical strengthbut compromised swelling characteristics. SEM images showed uniformity in pore structure in case of acetone dehydrated hydrogels. Acetone dehydrated SPHC showed sustained drug release behavior with 71.14% and 57.84% of verapamil released in 12 h in the batches with Drug: Carbopol 934ratio of (1:0.5 and 1:1) respectively.
Conclusion: Acetone dehydrated SPHC were found to be promising formulations with sufficient swelling and mechanical properties for achieving sustained drug delivery.

Keywords: Composite agent; gas blowing; starch silicone dioxide coprecipitate; mechanical strength; equilibrium swelling.

ABBREVIATIONS

SPH: Superporous hydrogel; SPHC: Superporous hydrogel composite; SSC: Starch silicone dioxide coprecipitate; SGF: Simulated gastric fluid; CSPH: Conventional superporous hydrogel; APS: Ammonium persulfate; TEMED: N, N, N', N'- tetraethylmethylene diamine; AM: Acrylamide; AA: Acrylic acid; BIS: N, N'-methylene bisacrylamide; PF 127: Pluronic F127; PEI: Polyethyleneimine; PVP: Polyvinylpyrollidone.

1. INTRODUCTION

The development of novel drug delivery systems with the aim of increasing the peroral bioavailability of existing drug molecules is an ongoing process in pharmaceutical science. Oral route of administration is of great interest due to patient compliance. The poor bioavailability of drugs after oral administration is due to interplay of low drug permeability, first pass effect, rapid degradation by proteolytic enzymes etc. Therefore, oral controlled release systems should be designed so as to overcome these limitations to achieve predictable and reproducible absorption in therapeutics doses [1]. Hydrogel polymers are structurally loosely cross-linked networks which have the ability to absorb considerable amounts of water or aqueous fluids and the absorbed water is hardly removed under some pressure. Hydrogels with well-defined physicochemical properties and reproducible drug release profiles can be obtained by using an ordered polymer network composed of macromers with well-defined structure. Versatility of hydrogels in various applications such as development of engineering scaffolds, biosensors, suitable drug carriers is broadening due to the development of functional monomers and macromers [2,3].

Superporous hydrogels (SPH) has been explored using acrylamide based matrices in 1999 for pharmaceutical drug delivery applications. SPH tend to swell very quickly due to their highly porous structure [4]. The difference between SPH and SPHC is their swelling ratio and mechanical stability. SPH swells more quickly but of poor mechanical strength whereas

SPHC are more stable mechanically but their swelling is less [5]. Ac-di-sol was reported as most widely used composite agent with vinyl monomers to improve the mechanical strength of SPH [1,6,7]. Various other polymers such as Carbopol, Polyethyleneimine (PEI) have also been incorporated for the preparation of SPHC [8,9].

Recently, modified excipients with improved physical characteristics have been widely used in the development of novel drug delivery systems. For example, Modified chitin (chitin silicon dioxide coprecipitate), modified Polyvinylpyrollidone (PVP) (i.e. PVP crosslinked with glutaraldehyde) with improved compressibility characteristics and tableting properties has already been reported [10,11]. Modifications in starch have been reported for its superdisintegrant action (starch silicon dioxide coprecipitate) [12].

Verapamil hydrochloride, a calcium channel antagonist is used in the treatment of hypertension, arrhythmia and angina pectoris. The extensive first pass effect of the drug leads to higher pharmacokinetic variability and low bioavailability (22±8%). Moreover short half-life (4±1.5h) of the drug makes it a suitable candidate for controlled release application. Therefore, controlled release of verapamil in novel hydrogel carriers may improve patient compliance by reducing the dosing frequency and associated side effects [13].

In the present study, superporous hydrogel composites of verapamil hydrochloride based on acrylamide and starch silica co-precipitate (SSC) as composite agent were synthesized and evaluated for equilibrium swelling ratio, equilibrium swelling time, density, porosity, mechanical strength, SEM analysis and *in vitro* drug release studies.

2. MATERIALS AND METHODS

2.1 Materials

Verapamil hydrochloride waskindly gifted by Abbott Healthcare Pvt. Ltd. Baddi. Silicon dioxide and Starch were kindly gifted by Ipza Pharmaceuticals, Baddi and Helios Pharmaceuticals, Baddi respectively. Pluronic F127 was obtained from Sigma Life Sciences. All other ingredients used were of analytical grade.

2.2 Methods

2.2.1 Synthesis of SPHs using gas blowing technique

Various formulations ofSPH(CSPH and SPHC) were prepared by gas blowing technique [4].Various ingredientsin specified quantities (acrylamide (AM), N,N'-methylene bisacrylamide (BIS), water, Pluronic F127 (PF 127) and acrylic acid (AA)) were added sequentially in a test tube followed by the addition of ammonium persulfate (APS) and N,N,N',N'- tetraethylmethylene diamine (TEMED) solution. Sodium bicarbonate ($NaHCO_3$) was added at last step which led to foaming and polymerization and eventually the formation of superporous hydrogels. The amount of acrylic acid (varied from 20-45µl) and sodium bicarbonate (varied from 75-150 mg) was optimized to obtain simultaneous polymerization and foaming process resulting in uniform SPH (Table 1). Superporous hydrogel composites (SPHC) were prepared in similar manner by the addition of starch silica coprecipitate (200 and 250mg) before the addition of APS and TEMED. The composition of CSPH and SPHC is shown in Table 1.The effect of amount of composite agent on swelling and mechanical properties was also evaluated. The prepared superporous hydrogels were given different

treatment conditions (kept in acetone for 2h for acetone dehydrated; kept in SGF for 2h for SGF treated) followed by oven drying at (50-55ºC) for 24h. Various SPH formulations with formulation codes are shown in Table 2.

Table 1. Composition of CSPH and SPHC

S. No	Ingredient	CSPH	SPHC
1.	Acrylamide (50%) (µl)	1000	1000
2.	N,N-bisacrylamide (2.5%) (µl)	200	200
3.	Water(µl)	460	460
4.	Pluronic F-127(10%) (µl)	100	100
5.	Acrylic Acid (µl)	20- 45	20
6.	Ammonium Per Sulfate (20%) (µl)	40	40
7.	TEMED (20%) (µl)	40	40
9.	SSC (mg)	-	200-300
10.	Sodium bicarbonate(mg)	75-150	75

Table 2. Formulation codes of various SPH formulations

Formulation code	Formulation code
CSPH1	Untreated
CSPH2	Acetone dehydrated
CSPH3	SGF treated
SPHC1	(SSC 200mg), untreated
SPHC2	(SSC 200mg) Acetone dehydrated
SPHC3	(SSC 200mg) SGF treated
SPHC4	(SSC 250mg), untreated
SPHC5	(SSC 250mg) Acetone dehydrated
SPHC6	(SSC 250mg) SGF treated

2.2.2 Evaluation of CSPH and SPHC

2.2.2.1 Equilibrium swelling ratio

Swelling experiments were conducted in DDW. Cylindrical shape hydrogel samples were weighed and measured in diameter and length. Samples were immersed into double distilled water (DDW) at room temperature. At predetermined time intervals, each sample was taken out of the water to measure the weight, diameter and length of the swollen sample using balance and an electronic digital caliper [6]. The equilibrium swelling ratios were calculated based on those measured data.

The Equilibrium swelling ratio (Q_v) is defined as per equation (1).

$$Q_v = V_s/V_d \qquad (1)$$

Where V_s is the volume of the swollen hydrogel and V_d is the volume of the dried hydrogel.

2.2.2.2 Equilibrium swelling time

Equilibrium swelling time was calculated by immersing the hydrogels in deionized water and calculating the time required to attain equilibration in swelling [6].

2.2.2.3 Density

For density measurement, the solvent displacement method was used. Dried SPH samples were weighed and immersed in a predetermined volume of hexane in a graduated cylinder. The increase in the hexane volume was measured as the volume of the hydrogel [8,14]. The density was calculated from the equation (2).

$$\text{Density (D)} = M/V \quad \ldots\ldots(2)$$

Where, Mis mass of the hydrogel and Vis the volume of solvent displaced by hydrogel.

2.2.2.4 Porosity

For porosity measurement, the solvent replacement method was used. Dried SPHwere immersed overnight in absolute ethanol and weighed after excess ethanol on the surface was blotted [15]. The porosity was calculated from equation (3).

$$\text{Porosity (P)} = (M_2 - M_1)/pV \quad \ldots\ldots(3)$$

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

2.2.2.5 Mechanical strength

Acetone dehydrated and SGF treated dried SPH formulations (CSPH and SPHC) were selected for further mechanical strength studies. The mechanical strength was determined at room temperature using a TA-TX Plus Texture Analyzer (Stable micro system Ltd., Surrey, UK) with a cylindrical aluminum probe. A disk of 6mm thickness was placed on platform and the probe was compressed into the sample at a rate of 1mm/s and a depth of 3mm. Then the probe was removed at 2mm/s and the recovery of the sample was also monitored.

2.2.2.6 Scanning electron microscopy (SEM)

SEM studies were carried out to determine the effect of treatment and drying conditions on the porous nature of hydrogels. Only SPHC batches were selected for SEM analysis as (i) composite agent has no effect on porosity and there would be no difference between whether these studies have been done for CSPH or SPHC; (ii) SPHC batches will be selected for drug loading due to high mechanical strength observed during mechanical strength studies. The samples were mounted on to aluminium stubs using double-sided adhesive tape and then coated with gold/palladium (150-200Aº) using fine coat ion sputter (JEOL, JSM-6100, JAPAN).The samples were then analyzed using Scanning Electron Microscope. The effect of freeze drying on porous structure of SPHC was also evaluated using SEM studies (only SPHC were frozen in deep freeze drier at -74ºC for 12 h and dried completely in 24 h).

2.3 Drug Loading

Drug loading was carried out in selected SPHC composition (SPHC containing 250 mg SSC). Drug (120mg) mixed with Carbopol 934 was directly added into reaction mixture before addition of reaction initiator pair. The resulting SPHC were frozen in deep freeze drier at -74ºC for 12 h. The SPHC samples were dried completely in 24 h. Three different drug loaded formulations of SPHCs were prepared (A1-A3) in drug to carbopol 934 ratio of 1:0, 1:0.5 and 1:1 respectively.

2.3.1 *In vitro* drug release

In vitro release of drug from drug loaded SPHC was evaluated in triplicate at 37±0.5ºC using the United State Pharmacopoeia (USP) dissolution test apparatus Type II (paddle method) at a rotation speed of 50 rpm in 900 ml SGF (pH 1.2) for 24 h. SGF was prepared by dissolving (2g) sodium chloride in (7ml) concentrated HCl and making the volume upto 1000ml(as specified in IP). At regular time intervals, 5 ml of the dissolution medium were withdrawn, replaced with an equivalent volume of the fresh dissolution fluid and analyzed for the drug using the UV- VIS spectrophotometer (Shimadzu, Japan) at 278 nm.

2.3.2 *In vitro* drug release kinetics

To analyze the *in vitro* release data various kinetic models were used to describe the release kinetics. The zero order model describes the systems where the drug release rate is independent of its concentration. The first order model describes the release from system where release rate is concentration dependent. Higuchi described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion. Koremeyer Peppas model describes the mechanism of drug release. Various plots were made: cumulative % drug release vs. time (zero order kinetic model); log cumulative of % drug remaining vs. time (first order kinetic model); cumulative % drug release vs. square root of time (higuchi model); log cumulative % drug release vs. log time (korsmeyerpeppas model).

3. RESULTS AND DISCUSSION

3.1 Synthesis of SPHs Using Gas Blowing Technique

Various trial batches of CSPH were synthesized using different amount of acrylic acid (20,25,30,45µl) and sodium bicarbonate (75, 90, 120, 150mg) as both these variables affect the foaming and polymerization process which should be in harmony to yield porous hydrogels. The various amounts of acrylic acid and sodium bicarbonate were selected on the basis of literature. The uniform porous hydrogels were obtained reproducibly at 20 µl of acrylic acid and 75 mg of sodium bicarbonate. This composition was further used for synthesis of CSPH and SPHC both. The addition of composite agent (i.e. SSC) did not affect the foaming and polymerization, therefore the composition remained same for SPHC also. The three different amounts (200, 250 and 300mg) of SSC were tried to evaluate the effect on mechanical strength. At 300 mg, non-uniform/non-porous SPHs were obtained which may be due to increased viscosity which hindered the process of simultaneous foaming and polymerization. Therefore SPHC containing 200 and 250 mg SSC were further used for mechanical strength studies. Final composition of various SPH formulations is depicted in Table 3.

Table 3. Final composition of CSPH and SPHC

S. No	Ingredient	CSPH	SPHC
1.	Acrylamide (50%) (µl)	1000	1000
2.	N,N-bis acryl amide (2.5%) (µl)	200	200
3.	Water(µl)	460	460
4.	Pluronic-127(10%) (µl)	100	100
5.	Acrylic Acid (µl)	20	20
6.	Ammonium Per Sulfate (20%) (µl)	40	40
7.	TEMED (20%) (µl)	40	40
9.	SSC (mg)	-	250
10.	Sodium bicarbonate(mg)	75	75

3.2 Evaluation of CSPH and SPHC

3.2.1 Equilibrium swelling ratio

The equilibrium swelling ratio of CSPH varied from 304± 25 in CSPH1, 301 ± 15 in CSPH2 and 116 ± 23 in CSPH3. SGF treatment reduces the swelling ratio of hydrogels. SGF treatment partially protonized the anionic SO_3^- group into the SO_3H group (acidification).The decrease of the overall charges on the surface of hydrogel leads to increase in interaction between the polymer chains that might substantially change the properties (swelling and mechanical) of hydrogels and surface hardening effect. The addition of composite agent leads to slight decrease in equilibrium swelling ratio (290 ± 23 in SPHC1, 286± 11 in SPHC2 and 106± 14 in SPHC3). The increase in the amount of the composite agent (200 mg to 250 mg) leads to the further decrease (minor) in the swelling ratio of the samples (278± 28 in SPHC4, 279± 16 in SPHC5 and 104± 13 in SPHC6). The physical crosslinking of composite agent with primary polymeric network may restrict swelling behavior. However this decrease is not significant as clearly seen in the results. Further increase in composite agent did not favor formation of SPHC (Fig. 1). Acetone dehydration did not affect the equilibrium swelling of both CSPH and SPHC.

3.2.2 Equilibrium swelling time

The equilibrium swelling time of the CSPH varied from 38± 6 min in CSPH1, 10± 2 min in CSPH 2 and 19± 4 min in CSPH3. The slow swelling in CSPH1 is due to disrupted capillary channels during drying in oven. This is also clearly visible in SEM images. During acetone dehydration (CSPH2), acetone replaces water in the hydrogel network. Acetone being a poor solvent for hydrophilic polymer leads to precipitation of polymer chains. This results in hardening and rigidity of polymer network which contributes to maintenance of capillary channels during drying [4]. This is responsible for fast swelling in CSPH2. SGF treated CSPH showed fast swelling in comparison to oven dried CSPH1 but not as fast as in case of acetone dehydrated. A slight disruption in capillary channels was observed during drying (as in SEM image).

The addition of composite agent reduces the time for equilibrium swelling as observed in SPHC 1- SPHC3 (26± 5 min, 6± 0.7 min and 15 ± 2 min respectively). The reason may be again that physical crosslinking by composite agent to primary polymeric network maintains the capillary channels of hydrogel which provide easy absorption of solvent, thereby reduces the swelling time. Increase in composite agent however did not further affect the equilibrium

swelling time as observed in SPHC4- SPHC6 (24 ± 4 min, 5 ± 0.5 min and 15 ± 3 min) (Fig. 1).

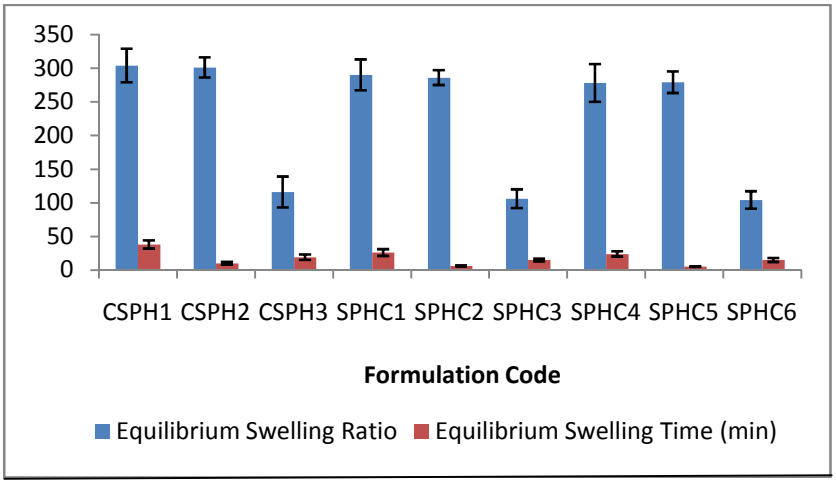


Fig. 1. Equilibrium swelling ratio and time of various SPH formulations

3.2.3 Density

Maximum density was observed in untreated hydrogels and the minimum density was found in the acetone treated samples (0.73 ± .06 in CSPH1, 0.32 ± .02 in CSPH2, 0.47 ± .04 in CSPH3). The removal of water during drying results in collapse of polymer chains due to high surface tension of water. The collapse of polymer chains leads to substantial shrinkage during drying as indicated by high density values observed in CSPH1. During acetone dehydration, replacement of water in the porous structure of hydrogel with acetone and during drying acetone gets easily evaporated which has low surface tension and no collapse of polymer chains as indicated by low density values observed in CSPH2 [4]. Addition of composite agent (SSC) decreases the density (0.68 ± .03 in SPHC1, 0.26 ± .01 in SPHC2 and 0.41 ± .03 in SPHC3). The increase in composite agent (250mg) further decrease the density (0.58± .04 in SPHC4, 0.2± .009 in SPHC5 and 0.37 ± .006 in SPHC6). This may be due to the reason that when composite agent was mixed with the monomer solution, it swelled so that monomers (Am and AA) and cross linker (BIS) were absorbed into the composite agent network. The composite agent (SSC) maintained the network structure during drying resulting in less shrinkage of SPHC. The resultant increased volume of SPHC lead to decreased density values. The density of various SPH formulations is shown in Fig. 2.

3.2.4 Porosity

Acetone dehydrated hydrogels have maximum porosity and untreated hydrogels showed least porosity (29.46 in CSPH1, 46.76 in CSPH2, 39.09 in CSPH3). The addition of composite agent (SSC) further leads to increase in porosity of hydrogels (35.67in SPHC1, 55.87 in SPHC2 and 42.45 in SPHC3) and further no significant increase was observed (38.57 in SPHC4, 59.68 in SPHC5 and 47.36 in SPHC6)]. The addition of SSC leads to higher crosslinked density of primary polymeric network leading to decrease in occupied volume [16]. The porosity of various CSPH and SPHC is shown in Fig. 2.

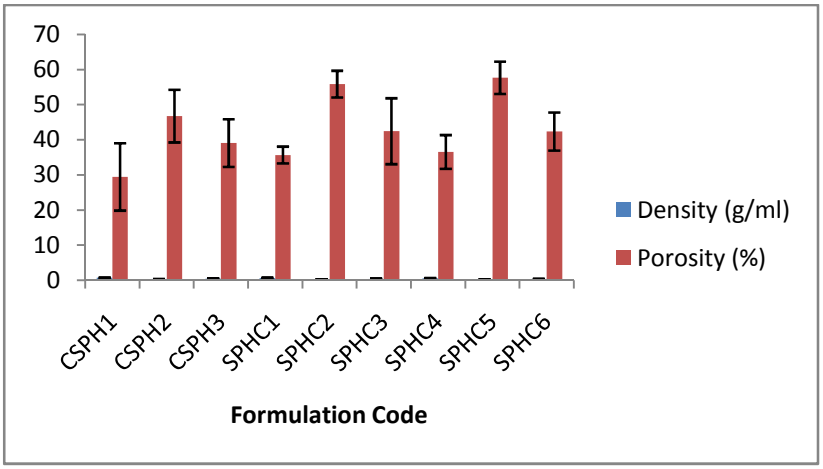
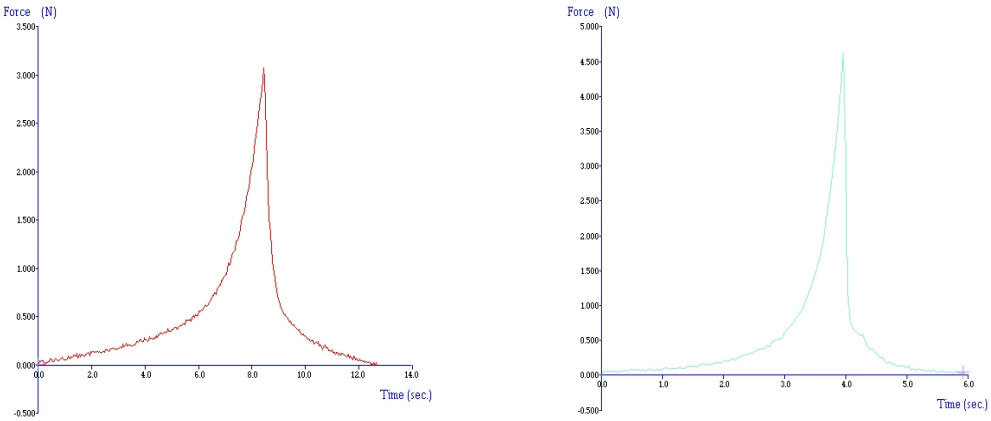


Fig. 2. Density and porosity data of various SPH formulations

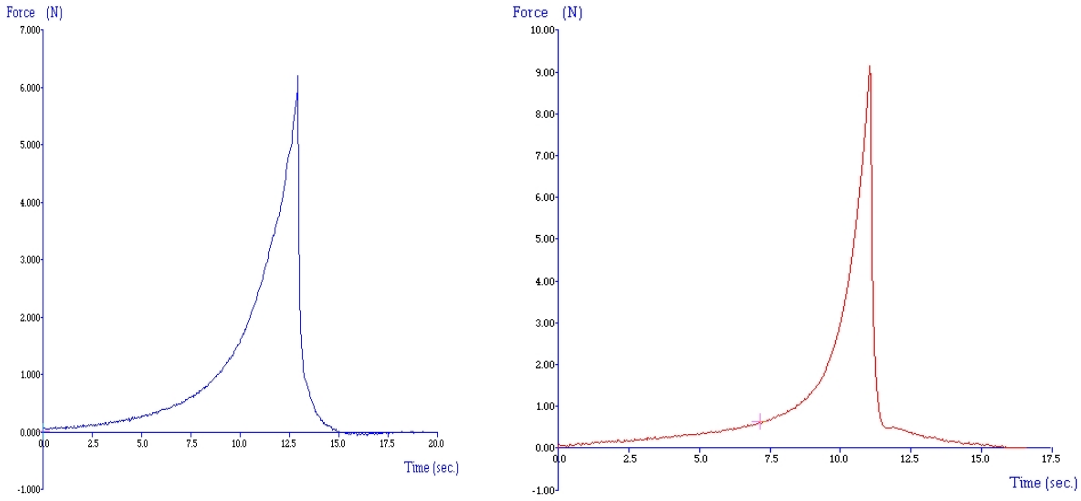
3.2.5 Mechanical strength

Force versus time plots for various SPH formulations are shown in Figs. 3, 4 and 5. The mechanical strength was less in CSPH i.e. CSPH2 tend to fragile under a force of more than 3N whereas compression strength of 4.5 N was observed in CSPH2 (Fig. 3). Strengthening of primary polymeric network due to physical crosslinking of SSC chains is clearly observed by increased mechanical strength of SPHC. Addition of composite agent (SSC) leads to increase in mechanical strength of acetone dehydrated and SGF treated CSPH (6N in SPHC 2 and 9N in SPHC3) (Fig. 4).



(a)CSPH2 (b)CSPH3

Fig. 3. Force versus time plot of (a) acetone dehydrated CSPH2 (b) SGF treated CSPH3

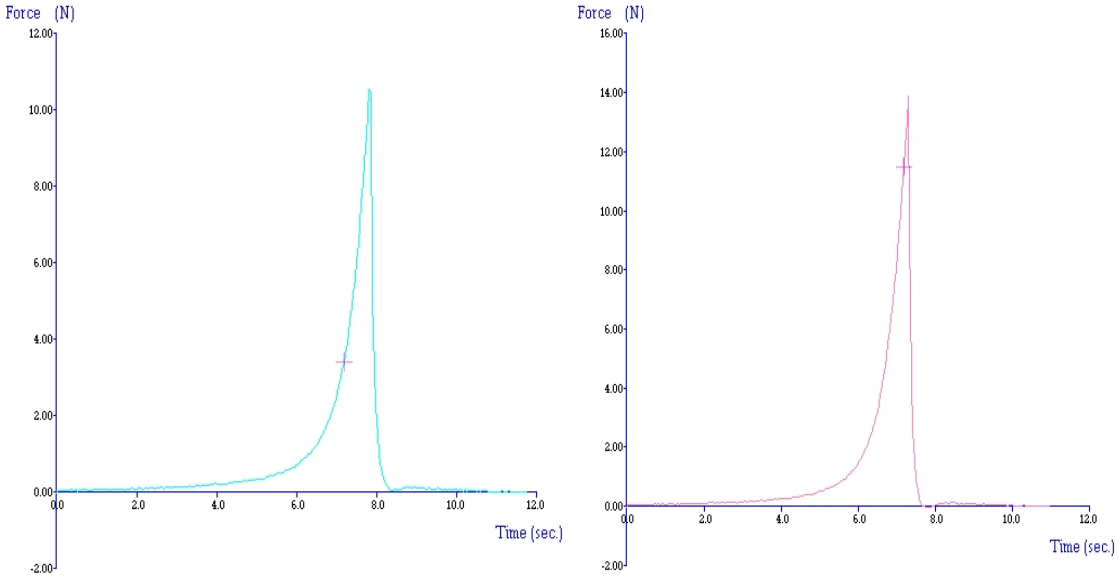


(a) SPHC2 (b) SPHC3

Fig. 4. Force versus time plot of (a) acetone dehydrated SPHC2 (b) SGF treated SPHC3

Increase in amount of SSC further leads to enhanced mechanical strength (10 N in SPHC5 and > 10 N in SPHC 6) (Fig. 5).

SGF treatment leads to acidification of hydrogel surface, decreasing the overall charge and increasing the polymeric network interaction. This results in increase in mechanical strength of superporous hydrogels.



(a) SPHC5 (b) SPHC6

Fig. 5. Force versus time plot of (a) acetone dehydrated SPHC5 (b) SGF treated SPHC6

3.2.6 Scanning electron microscopy

The dried Superporous hydrogels composites (SPHC) were used for scanning electron microscopy (SEM) studies to determine the morphology of the dried samples at 70X. SEM images of acetone treated (Fig. 6(a)) showed the uniformity in pore structure with preserved capillary channels. Untreated hydrogels showed completely distorted capillary networks (Fig. 6(b)) whereas slight disruption of porous polymeric network was also observed in SGF treated hydrogels (Fig. 6(c)).The porous network was also maintained intact with integrated capillary channels during freeze drying process (Fig. 6(d)). The freeze dried SPHC, however appeared less porous on the surface when observed visually but SEM studies confirmed about integrated porous structure. Also freeze dried SPHC were observed very light weighted in comparison to acetone dehydrated SPHC (can be better floating devices).

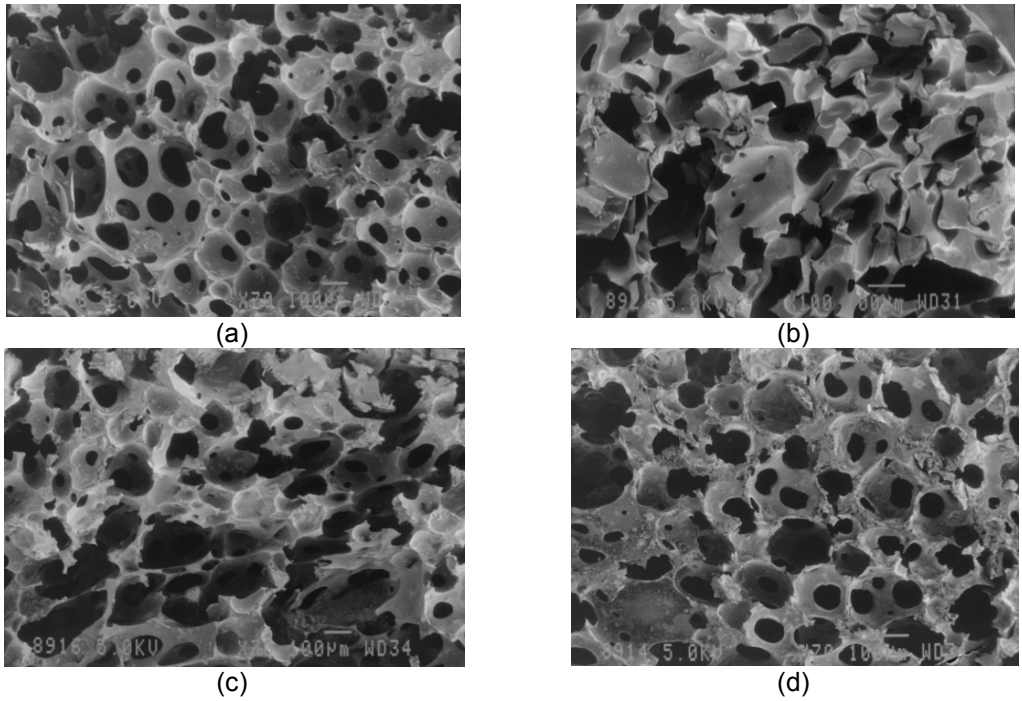


Fig. 6. SEM images of (a) oven dried, (b) acetone dehydrated, (c) SGF treated, (d) Freeze dried SPHC

3.3 Drug Loading

SPHC formulations containing 250 mg SSC were used for drug loading. Three drug loaded SPHC formulations (A1-A3) were successfully prepared by direct addition of drug and polymer carbopol 934 during synthesis. SPHC were retrieved from test tube and frozen in deep freeze drier at -74ºC for 12 h. SPHC were dried completely in 24 h. The dried drug loaded SPHC were very light weight porous networks. No ethanol dehydration was carried out as it may cause leaching of drug from hydrogel network causing loss of drug from the formulation.

3.3.1 *In vitro* drug release

The *in vitro* drug release profile of three SPHC formulations is shown in Fig. 7. Formulation A1 showed initial burst release (80% in 15 min) and 98% drug was released at the end of 12 h. Initial burst of the drug may be due to the drug particles present in outer side of capillary network of the hydrogel. Remaining drug was released from inside the capillary network via diffusion. Initial dose dumping may lead to drug related toxic effects. Addition of carbopol 934 leads to sustained release effect as observed in batch A2 (44.54% in 15 min and 71% in 12 h) and further increase in carbopol 934 in batch A3 further sustained release of drug from the polymeric network (32.64% in 15min and 57.84% in 12 h).The cross-linked carbopol 934 molecules may act as additional matrices for the drug therefore further sustained the drug release.

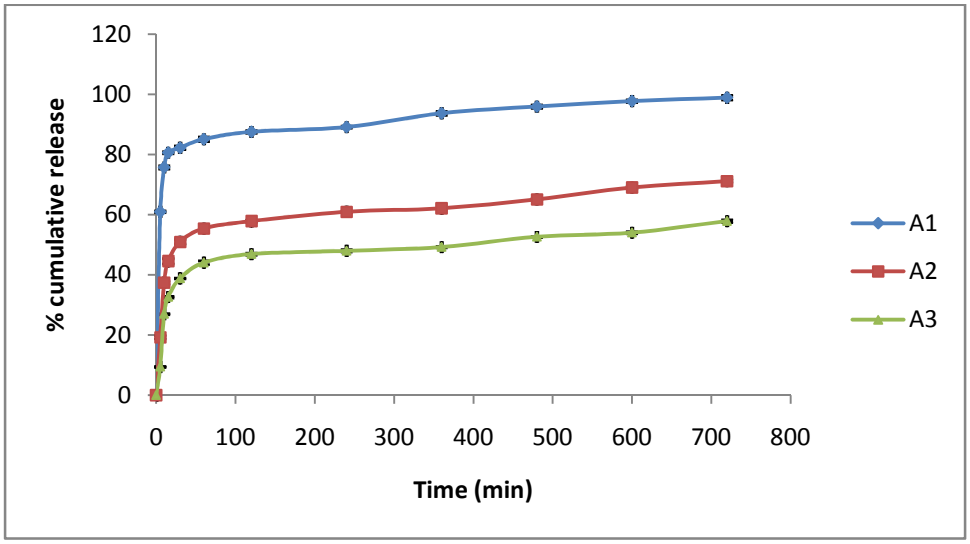


Fig. 7. *In vitro* drug release from SPHC formulations(A1-A3)

3.3.2 In vitro drug release kinetics

The values of regression coefficient for various kinetic models are shown in Table 4. *In vitro* drug release from the proposed formulation was best explained by Korsmeyerpeppas model (as indicated by R^2 values). The value of the release exponent in Korsmeyerpeppas model (n less than 0.45) was beyond the limits of the model, called as power law indicating that mechanism of drug release is not clear.

Table 4. Regression coefficient values of various release kinetic models

Formulation code	Zero order R^2	First order R^2	Higuchi model R^2	Korsmeyer-Peppas model n	R^2
A1	0.3112	0.8694	0.4666	0.05	0.9694
A2	0.5048	0.6696	0.6876	0.12	0.9355
A3	0.5287	0.6347	0.7127	0.14	0.9212

4. CONCLUSION

The study demonstrates the preparation of Superporous hydrogel composites for sustained delivery of verapamil hydrochloride. Various SPH formulations based on acrylamide were synthesized and evaluated for swelling and mechanical parameters. SSC (250 mg) proved as successful composite agent for enhanced mechanical strength of SPH formulations as in case of SPHC. SGF treatment significantly enhanced the mechanical strength of SPH but the swelling characteristics are compromised. The porous structure of SPH was maintained inacetone treated and oven dried formulations. The porous network was also maintained during freeze drying of even untreated formulations. The drug loaded SPHC (composed of 250 mg SSC) were freeze dried and evaluated for *in vitro* drug release behavior. Carbopol 934 proved as release retardant as it sustains the drug release from hydrogel network. However the release mechanism from the hydrogel network is not clear as indicated by drug release kinetic studies. SPHC composed of SSC as composite agent can act as sustained release drug delivery systems.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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