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SYNTHESIS AND CHARACTERIZATION OF SITE SPECIFIC SUPERPOROUS HYDROGEL HYBRIDS OF LORATADINE

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Keywords:

Gastroretentive Drug Delivery, Interpenetrating Networks, Swelling Properties, Mechanical Strength

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ABSTRACT: The aim of present study is to formulate and optimize the site specific controlled release formulation for release of loratadine in upper gastrointestinal tract. Superposrous hydrogel hybrids (SPHH) were prepared by using ferric chloride as crosslinking agent and sodium carboxymethyl cellulose as composite agent. The Superporous Hydrogels were evaluated for swelling ratio, mechanical strength, density, porosity, scanning electron microscopic studies. Statistical software, Design Expert was used for optimization and chosing the final formulation. Loratadine hydrochloride was loaded in optimized formulation and characterized by Fourier Transform Infrared Spectroscopy, X-Ray Diffraction, Differential Scanning Calorimetry and *in vitro* drug release studies. Superporous Hydrogel Hybrids were prepared with desired mechanical strength and sufficient swelling ratio. Equilibrium Swelling Ratio of hydrogels followed the pattern SPHH < SPHC < CSPH. The pattern may be attributed to the additional crosslinking and decreased poresize. Reduced swelling ratio may be because of restricted polymeric chain flexibility. H- bonds between poly (AM-co-AA) and NaCMC reduced the polymer ability to form H-bonds with water molecules, limiting water absorption. Increase in mechanical strength is due to crosslinking with composite agent. FTIR, XRD and DSC studies confirmed the drug integrity in hydrogel polymeric network. Drug release studies showed that initial burst release followed by sustained effect.

INTRODUCTION: Developing new drug delivery technologies and utilizing them in product development is crucial for pharmaceutical companies to compete and survive in current era. Controlled release, site-specific technologies allow effective use of existing drugs, maximizing therapeutic efficiency with minimal side effects. One of such approach is to confine the dosage form in desired area in gastrointestinal tract (GIT). In case of site-specific drug delivery to GIT, less transit time of dosage form is the main factor responsible for suboptimal absorption of drugs.

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Various technical advancements in fabrication of dosage forms has been explored in this area to retain dosage form in upper part of GIT viz Bioadhesive Systems, Raft Systems, Expanding Systems, Low Density Systems, Swelling Systems. [1] Preparation of Superporous Hydrogels is one of the useful approaches for keeping dosage form in stomach for longer duration.

Superporous Hydrogels (SPHs) are 3-dimensional network of hydrophilic polymers that absorb a considerable amount of water in very short period of time due to presence of many pores with diameter on the micro-millimeter scale. [2] Superporous hydrogels characterized mainly by fast swelling and large swelling ratios have been developed since 1998. Conventional SPHs (CSPHs) are the first generation of SPHs, can swell to several hundred times within a few minutes.

But, they are mechanically very poor and difficult to handle without breaking. SPH composites (SPHCs) are the second generation of SPHs, possess improved mechanical properties with composite agents, which serve as the local point of physical entanglement of the formed polymer chains. [3]

The use of various polymers has been reported for making SPHCs and SPHHs. Chitosan [4], Alginates [5, 6] and Gelatin [7] are among the widely used natural polymers while polyacrylamide, poly (acrylic acid), PVP are among synthetic ones used to generate polymeric networks and enhance mechanical strength. SPHCs consist of two polymers where one polymer is crosslinked in intimate presence of other (composite agent).

Here, one linear polymer penetrates into network of another crosslinked polymer without any chemical bond formation between these two polymers which show much better properties than its constituent polymers. The primary polymer affords capillary based sorption properties while the strengthening polymer imparts significantly enhanced mechanical strength and elasticity to the Superporous hydrogel. [8]

However, SPHCs are still brittle and thus further improvement in mechanical properties is required. SPHHs, the third generation of Superporous hydrogels involves a mixture of two or more cross-linked networks that are dispersed or mixed at a molecular segmental level.

The present work features a method for formation of SPHCs and SPHHs using gas blowing technique involving ion equilibration incorporating loratadine as a drug candidate. Polyacrylamide was used as primary polymer and sodium carboxymethyl cellulose as secondary polymer.

Ferric chloride was used as physical crosslinker for making SPHH. Optimization of various batches was based on response surface methodology. The prepared SPHCs and SPHHs were evaluated by SEM, swelling and mechanical strength studies. Drug was loaded in selected SPHH, which were further characterized by FTIR, DSC, XRD, HNMR, in vitro drug release studies. Loratadine is second generation, tricyclic, piperidine derivative.

This H1 antihistaminic, nonseative antiallergic drug belongs to Class II of BCS. It is absorbed in the proximal part of GIT. It is stable in acidic pH, has a narrow therapeutic absorption window in GIT. [9] The presence of food enhances bioavailability. [10] This fulfills the criteria for selection of drug as candidate to be formulated as gastroretentive device.

MATERIALS & METHODS:

Materials: Loratadine HCl was kindly gifted by Abbott Healthcare Pvt. Ltd., Baddi, India; acrylic acid, acrylamide, Pluronic F (PF 127), ammonium persulfate, sodium carboxymethyl cellulose, sodium bicarbonate were purchased from Loba Chemie Pvt. Ltd., N, N, N', N' –tetra methylene 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. Synthesis of SPH by Gas Blowing Technique: Gas blowing technique was used to synthesize SPH, SPHC and SPHH. All the ingredients including monomers (acrylamide- 50%, sodium carboxymethyl cellulose -1.5%), crosslinker (BIS – 2.5%), foam stabilizer (PF 127- 10%), acrylic acid, reaction initiator pair (APS – 20%, TEMED – 20%) 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. The volume of final solution in the test tube increased to 2-10 times the original solution volume. The resulting SPHs were air dried.

SPHC were synthesized by simple addition of sodium carboxymethyl solution in reaction mixture. SPHH were synthesized by addition of sodium carboxymethyl solution in reaction mixture, followed by physical crosslinking with ferric chloride solution.

The composition of various SPH, SPHCs and SPHHs is shown in **Table 1**.

TABLE 1: COMPOSITION OF VARIOUS BATCHES

Ingredients	SPH		SPHC		SPHH
Acrylamide (50%)	1000µl	750µl	750µl	750µl	750µl
Sodium Carboxymethyl Cellulose (1%)	-	37.5 µl	225 µl	450 µl	450 µl
N,N-methylenebisacrylamide (2.5%)	200µl	200µl	200µl	200µl	200µl
Pluronic F 127 (10%)	100µl	100µl	100µl	100µl	100µl
Distilled water	460µl	460µl	460µl	460µl	460µl
Acrylic acid (pH- 5-6)	45µl	45µl	45µl	45µl	45µl
Ammonium per sulfate (20%)	50µl	50µl	50µl	50µl	50µl
N,N,N',N'-tetraethylmethylenediamine (TEMED) (20%)	50µl	50µl	50µl	50µl	50µl
Sodium bicarbonate	100mg	100mg	100mg	100mg	100mg
Ferric Chloride					1%, 2.5%, 5% for 1, 2, 4 hrs respectively (9 batches)

B. Evaluation of SPHC and SPHH (without drug):

Equilibrium Swelling Ratio & Equilibrium Swelling Time: Completely dried SPH were weighed and kept in excess of swelling medium (distilled water at 37^o 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 [14].

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

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:

$$Porosity = V_p / V_t.$$

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.

Void Fraction: Superporous Hydrogel were immersed 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

Mechanical Properties: Compression force (N) was determined using the TA-TX plus texture analyzer (stable micro systems) 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.

Scanning Electron Microscopy: 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.

C. Drug Loading: Loratadine HCl (10 mg) was loaded into selected SPHHs using the method of soaking on equilibrium or equilibration. The amount of water required for complete swelling

was determined and thereafter drug was dissolved in the pre-determined amount of water. The SPH sample was kept in the drug solution and left until all the solution was sucked up. Finally, the completely swollen hydrogels were air dried.

D. Evaluation of Drug Loaded SPHH:

D.1. Statistical Method (Experimental Design): RSM computation was performed using Design Expert Software (Trial Version StatEase Inc, Minneapolis, MN, USA). 3^2 factorial design method was adopted for this study. Two factors were varied at three levels as hypothesized by the design. The concentration of ferric chloride as crosslinking agent and crosslinking time were two variables studied at three levels as mentioned in **Table 2**.

TABLE 2: LEVELS OF VARIABLES FOR FACTORIAL DESIGN

	Level		
	-1	**0**	**+1**
Concentration of ferric chloride solution (as cross-linking agent)	1 %	2.5 %	4 %
Duration for cross-linking	1 Hr	2 Hr	3 Hr

Three response variables were recorded. **Table 3** summarizes the nine experimental runs studied, their factor combinations and response parameters.

TABLE 3: RESPONSE PARAMETERS AT DIFFERENT LEVELS OF VARIABLES

		Factor 1	Factor 2	Response 1	Response 2	Response 3
Std	**Run**	**A:Ferric Chloride Conc**	**B:Cross linking Time**	**Swelling Ratio**	**Mechanical strength**	**Drug Release**
		% w/v	**Hr**	**mg/mg**	**N/sq m**	**%**
1	1	-1	-1	100.7	3.117	97.1
2	5	0	-1	80.6	8.16	96.8
3	9	1	-1	36.1	16.216	85.2
4	8	-1	0	69.2	9.518	96.8
5	6	0	0	58.7	13.95	96.4
6	4	1	0	23	18.46	80.2
7	2	-1	1	7.7	20.6	46.4
8	7	0	1	5.1	22.1	45.9
9	3	1	1	2.8	24.6	40.2

D.2- Laboratory Experimentation:

Drug Loading Capacity: Ten samples of drug loaded SPHH were triturated and an equivalent weight of 10 mg of drug was dissolved in 100 ml of simulated gastric fluid (pH 1.2) and the mixture was filtered, diluted and the analyzed spectrophotometrically at 283nm (n=6).

Drug loading capacity: a/b * 100

Where a = amount of drug, b = theoretical amount of drug loaded.

FTIR: The IR spectra of drug, acrylamide, plain SPHH and drug loaded SPHH were recorded using KBr pallet method over scanning range of 4000 – 400 cm^{-1}. The FTIR spectrum was recorded to check the compatibility of drug with hydrogel.

X-RD Analysis: The X-RD studies were carried out to monitor the changes in crystalline characteristics of the drug when drug was loaded into hydrogel polymeric network.

***In vitro* drug release studies:** The *in vitro* drug release studies from various batches of SPHH were carried out using USP apparatus II at 37+-0.5C at the paddle speed of in 900 ml of SGF for 24 h at specified time intervals, 10ml of dissolution medium was withdrawn and an equivalent volume of fresh dissolution medium was replaced. The samples were analyzed at 283nm using UV-Vis spectrophotometer. The obtained data was fit into various models.

RESULTS AND DISCUSSION:

Synthesis of Superporous Hydrogels using Gas Blowing Technique: Superporous hydrogels of three different generations namely CSPHs, SPHCs and SPHHs prepared as shown in **Fig. 1.**

The final formulation was optimized by varying formulation variables that provide better elasticity and mechanical strength properties.

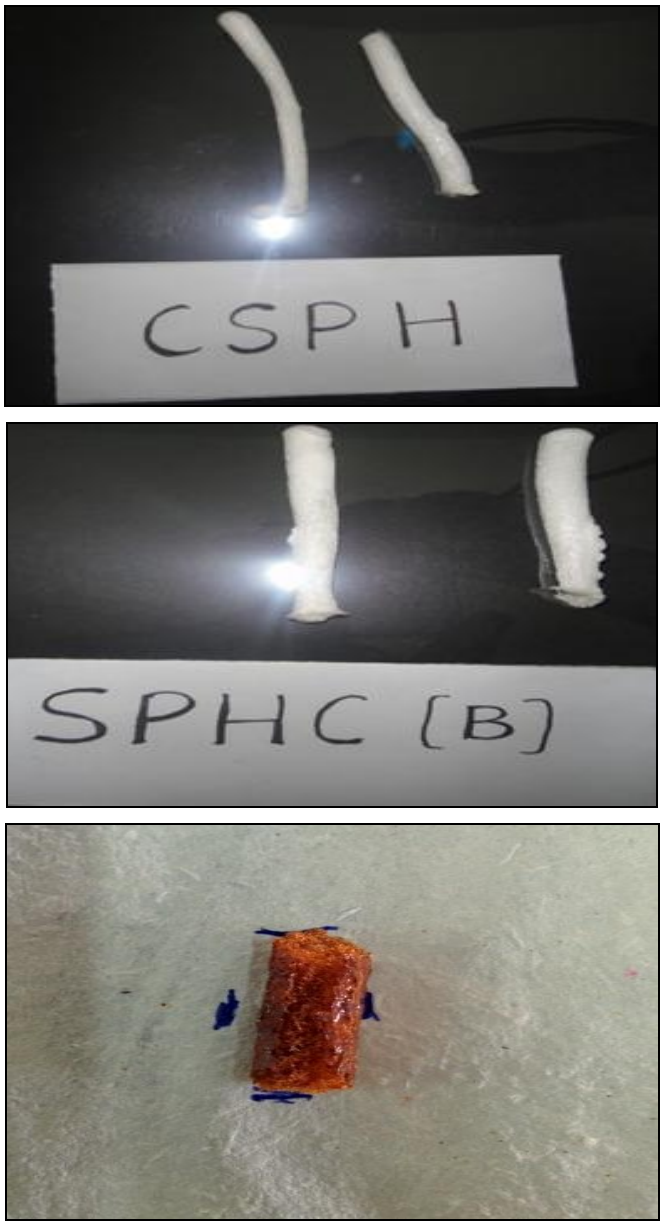


FIG. 1: VARIOUS GENERATIONS OF SUPERPOROUS HYDROGELS

B- Evaluation of SPHHs, SPHCs and CSPHs:

TABLE 4: PHYSICAL CHARACTERIZATION OF THREE GENERATIONS OF SUPERPOROUS HYDROGELS

Process	Parameter	CSPH	SPHC	SPHH
During synthesis	Texture	Soft, sticky, less flexible	Soft, less flexible	Soft, Flexible
	Colour	Completely White	Creamish white	Brown
	Porosity	Highly Porous	Highly porous	Porous
During ethanol dehydration/ crosslinker treatment		No immediate hardening	Hard and Brittle	Hard and Brittle
After drying	Texture	Hard and sticky	Non-sticky	Non-sticky
	Elasticity	Completely fragile	Less fragile	Elastic, not fragile
After swelling		Completely Transparent	No complete transparency, whitish	Completely brownish opaque

Swelling studies:

Equilibrium Swelling Ratio: Equilibrium Swelling Ratio of hydrogels followed the pattern SPHH < SPHC < CSPH as shown in **Fig. 2.** The pattern may be attributed to the additional crosslinking and decreased poresize. The data has been tabulated in Table. Reduced swelling ratio may be because of restricted polymeric chain flexibility. H- bonds between poly (AM-co-AA) and NaCMC reduced the polymer ability to form H-bonds with water molecules, limiting water absorption. Equilibrium Swelling Ratio had been considered as the characteristic parameter for optimizing the concentration of CMC as composite agent. Depending on the results found, 450 µl of 1% solution of CMC was optimized concentration for preparing SPHCs.

Equilibrium Swelling Time: Equilibrium Swelling Time was observed to be 3-6 min in CSPHs and 20-25 min in SPHCs, as mentioned in **Table 5**. The uniformity of capillary channels in ethanol dried SPHs led to less swelling time in CSPHs. Increase in density of crosslinking leads to comparative more swelling time in SPHCs.

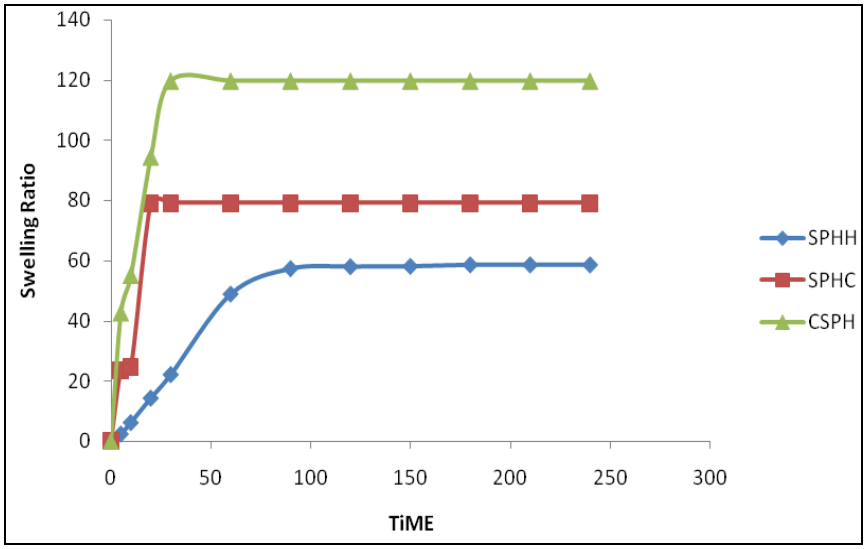


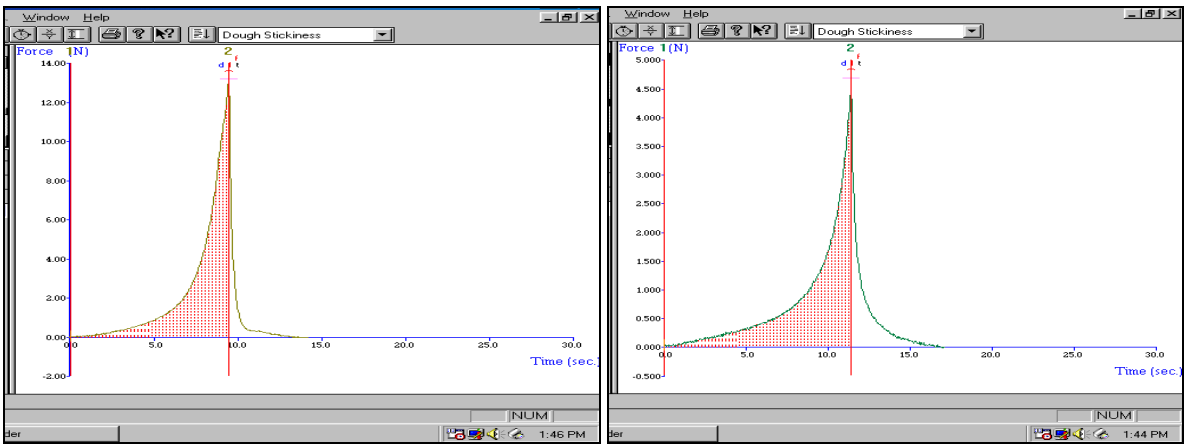
FIG. 2: RATE OF SWELLING OF SPHH, SPHC AND CSPH

Density, Porosity and Void Fraction: Density, porosity and void fraction of three formulations are given in Table 5. Presence of sodium CMC and ferric chloride decreases density, porosity and increases the void fraction because of interpenetrating polymer networks.

TABLE 5: EVALUATION PARAMETERS OF THREE GENERATIONS OF SUPERPOROUS HYDROGELS

Parameter	CSPH		SPHC		SPHH	
Density (g/cm^3)	0.86 ± 0.06 g/cm^3		0.67 ± 0.04 g/cm^3		0.42 ± 0.08 g/cm^3	
Porosity (%)	92.7 ± 0.8		76.5 ± 0.8		67.4 ± 0.5	
Void Fraction	33.6 ± 0.7		51.3 ± 0.9		54.3 ± 0.8	
Equilibrium Swelling Time	3 -6 min		20-25 min		75-90 min	
Equilibrium Swelling Ratio	DDW	SGF	DDW	SGF	DDW	SGF
	137.7 ± 2.6	8.2 ± 1.2	79.2 ± 3.6	15. 02 ± 2.6	58.7 ± 0.9	18.1 ± 4.2
Dimensions	DDW	SGF	DDW	SGF	DDW	SGF
Initial	0.6/1.7	0.6/1.2	0.7/2.8	0.65/2.9	0.6/1.0	0.6/1.5
Final	3.5/10.5	1.0/1.9	3.5/13.5	1.3/6.3	1.9/1.8	1.1/4.2
Mechanical Strength	-		4.5 ± 0.05 N/m^2		13.95 ± 0.97 N/m^2	

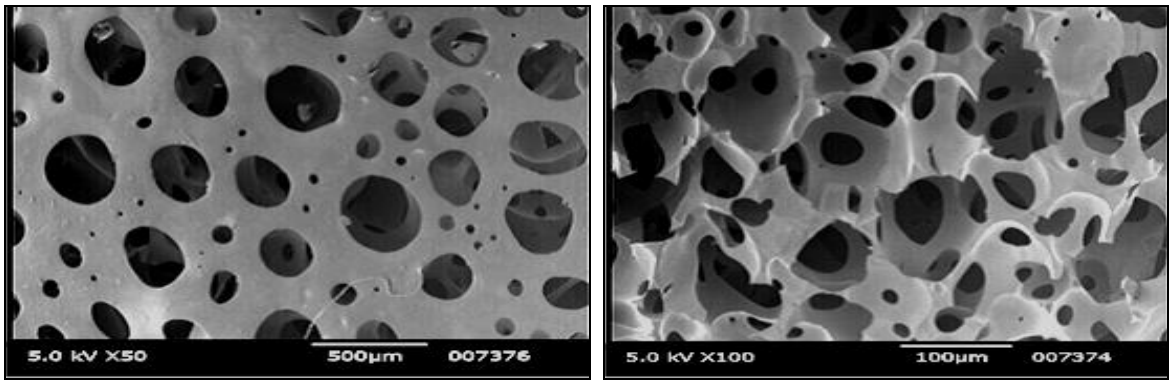
Mechanical Strength: The data for mechanical strength has been tabulated in **Table 5**. The CSPH were very fragile, so mechanical strength could not be recorded. The data for SPHC and SPHH are shown in **Fig 3**. This clearly indicates the mechanical strength is increased when secondary polymer and cross-linking agents are added.



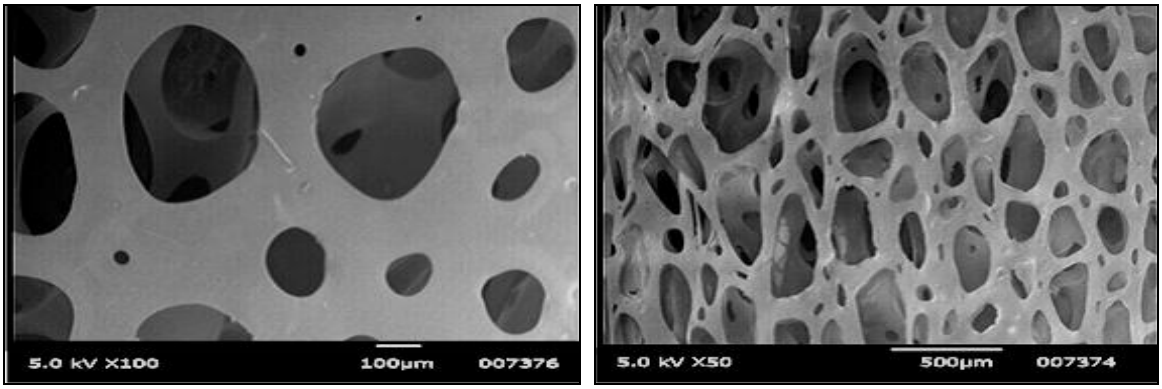
a: Mechanical Strength of SPHC b: Mechanical Strength of SPHH

FIG. 3: MECHANICAL STRENGTH OF SUPERPOROUS HYDROGELS

Scanning Electron Microscopy: The integrated pore structure with interconnected channels was observed in SEM images as shown in **Fig. 4**.



SPHC with Sodium CMC



SPHH (2.5% $FeCl_3$)

FIG. 4: SCANNING ELECTRON MICROGRAPHS OF SPHC AND SPHH

C- Evaluation of SPHHs after drug loading:

C.1- Statistical Evaluation (Optimization Data Analysis): Statistical model including interaction and polynomial terms was generated for all response variables. The general expression is

$$Y = \beta_0 + \beta_1 A + \beta_1 B + \beta_3 AB + \beta_4 A^2 + \beta_5 B^2 \quad (1)$$

Where, β_0, the intercept, is the arithmetic average of all quantitative outcomes of nine runs. B_1 to β_5 are coefficient computed from observed experimental values of Y, and A and B are the coded levels of independent variables. The term AB and A^2, B^2 are the interaction and polynomial terms, respectively. The main effects (A and B) represent the average result of changing one factor at a time from its low

to high value. The interaction term (AB) shows how the response changes when two factors are changed accordingly. The polynomial terms symbolizes nonlinearity.

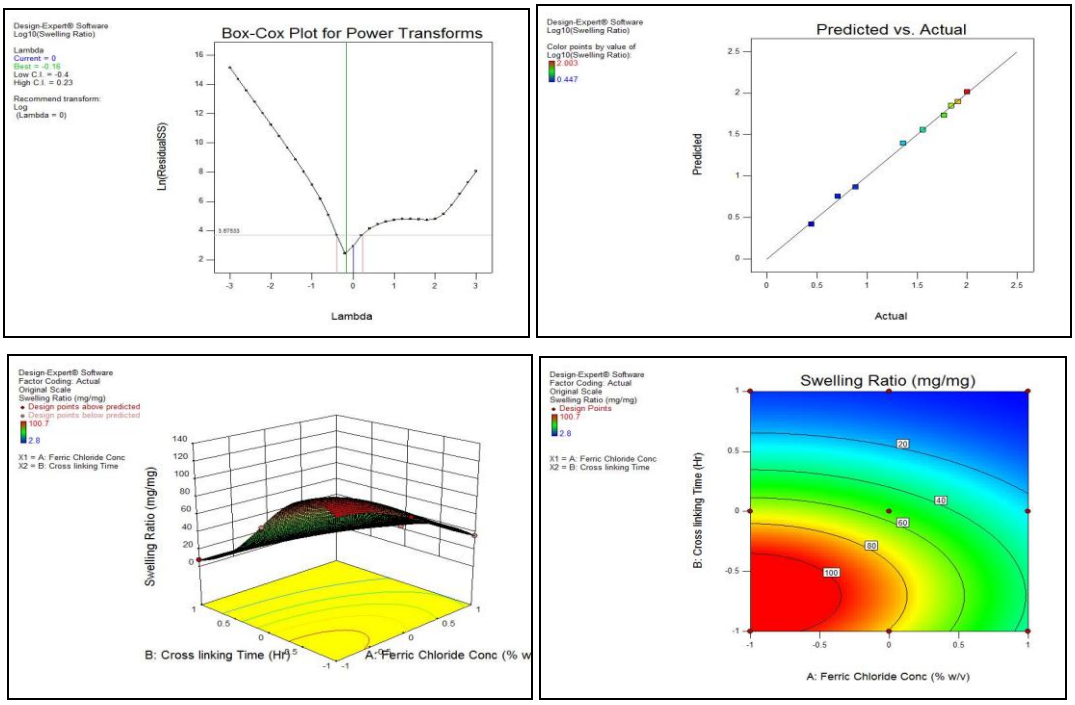


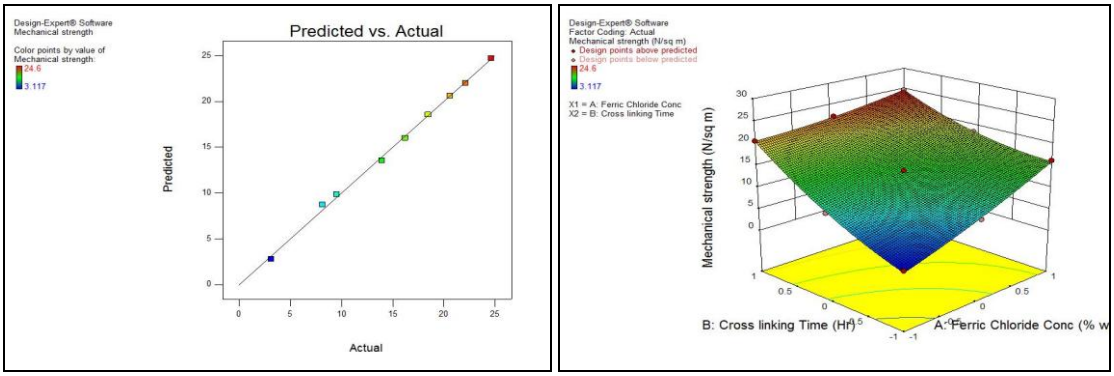
FIG. 5: RSM PLOTS OF RESPONSE PARAMETER, SWELLING RATIO

Transformation to log base 10 was recommended to get best fit value of lambda in box cox plot as shown in Fig 5-a. This transformation was recommended as the ratio of high to low value of swelling index was more than 10. Quadric model with F value of 88.17 (P = 0.0022) is most suitable for describing the relationship between variables and swelling ratio. The polynomial equation is

$$Log_{10}(\text{Swelling Ratio}) = 1.73 - 0.23 * A - 0.57 * B + 1.547E\text{-}003 * AB - 0.11 * A^2 - 0.41 * B^2 \quad (2)$$

The value of correlation coefficient (r^2) was found to be 0.9977. Equation 2 indicates that both concentration of cross-linking agent and cross-linking time have significant effect on swelling ration. Swelling ratio changes logarithmically with change in both the variables. Term A, B, A^2 and B^2 are significant terms. The effects may further be elucidated with help of diagnostic plots shown in **Fig 5**. The steeper ascent of crosslinking time (B) as compared to concentration of cross-linking agent (A) is clearly visible from both the plots, **Fig 5**-c,d. thus, appropriate selection of both the variables leads to better swelling properties of SPHH. **Fig. 5b** represents the observed response values compared with that of the predicted values depicting a good fit.

C.1.2: Effect of formulation variable on Mechanical Strength:



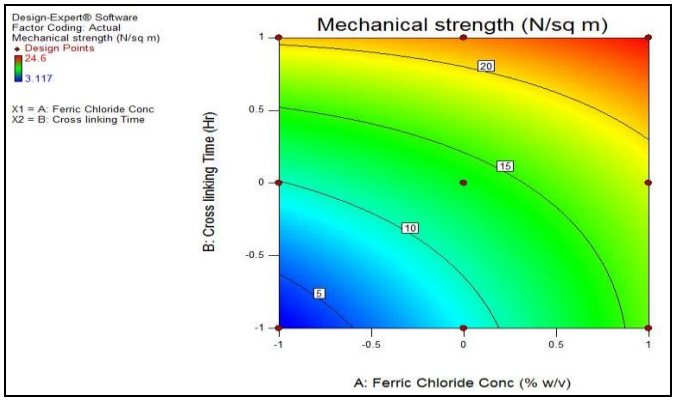


FIG. 6: RSM PLOTS OF RESPONSE PARAMETER, MECHANICAL STRENGTH

No transformation was needed in this data. Quadratic model with F value of 14.16 (P = 0.0296) is most suitable for describing the relationship between variables and mechanical strength. The polynomial equation is

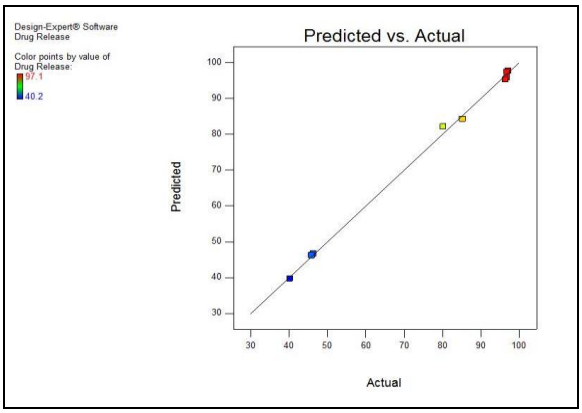
Mechanical strength = +13.52 +4.34 * A +6.63 * B -2.27 * AB +0.68 * A^2 +1.82 * B^2 (3)

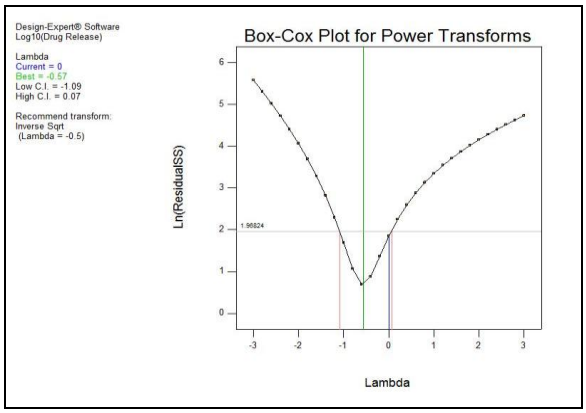
The value of correlation coefficient (r^2) was found to be 0.9980. Equation 3 indicates that A, B, AB, A^2 and B^2 are significant terms. The combined effect of A and B is further shown in plot 6– b,c. The steeper ascent of crosslinking time (B) as compared to concentration of cross-linking agent (A) is clearly visible from both the plots, Fig 6-b,c. Fig 6-a represents the observed response values compared with that of the predicted values depicting a good fit.

C.1.3: Effect of formulation variable on % Cumulative release in *in vitro* dissolution testing: Transformation to log base 10 was recommended for this data as shown in box-cox plot as shown in plot 7-a. Quadric model with F value of 312.21 (P = 0.0003) is most suitable for describing the relationship between variables and % drug release. The polynomial equation is

Log_{10}(Drug Release) = 1.98 -0.033 * A -0.16 * B -1.378E-003 * AB -0.031 * A^2 -0.15 * B^2

The value of correlation coefficient (r^2) was found to be 0.9989. Equation 4 indicates that both concentration of cross-linking agent and cross-linking time have significant effect on drug release. It changes logarithmically with change in both the variables. Term A, B, A^2 and B^2 are significant terms. The effects may further be elucidated with help of diagnostic plots shown in **Fig 7.** The steeper ascent of crosslinking time (B) as compared to concentration of cross-linking agent (A) is clearly visible from both the plots, **Fig. 7-c,d.** thus, appropriate selection of both the variables leads to better swelling properties of SPHH. Fig 7-a represents the observed response values compared with that of the predicted values depicting a good fit.(4)





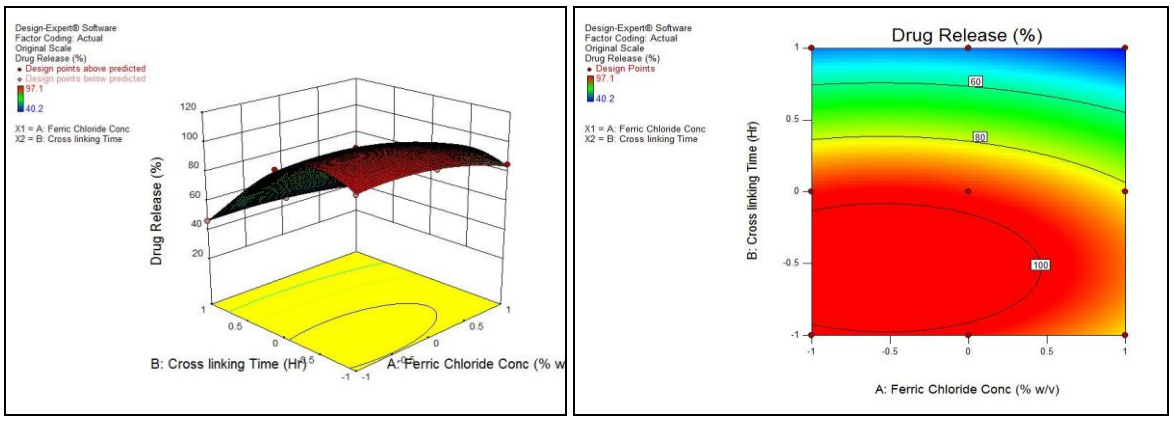


FIG. 7: RSM PLOTS OF RESPONSE VARIABLE %CUMULATIVE RELEASE

The formulation parameters were optimized using numerical optimization following desirability approach. The process was optimized by keeping target for swelling ratio as 60, mechanical strength as 14 N/m^2 and % cumulative drug release range between 95-100%. Confirmation Report is shown in **Table 6**.

TABLE 6: CONFIRMATION REPORT

Two-sided	Confidence =95%					
Factor	**Name**	**Level**	**Low Level**	**High Level**	**Std. Dev.**	**Coding**
A	Ferric Chloride Conc	0.46	-1.00	1.00	0.000	Actual
B	Cross linking Time	-0.43	-1.00	1.00	0.000	Actual

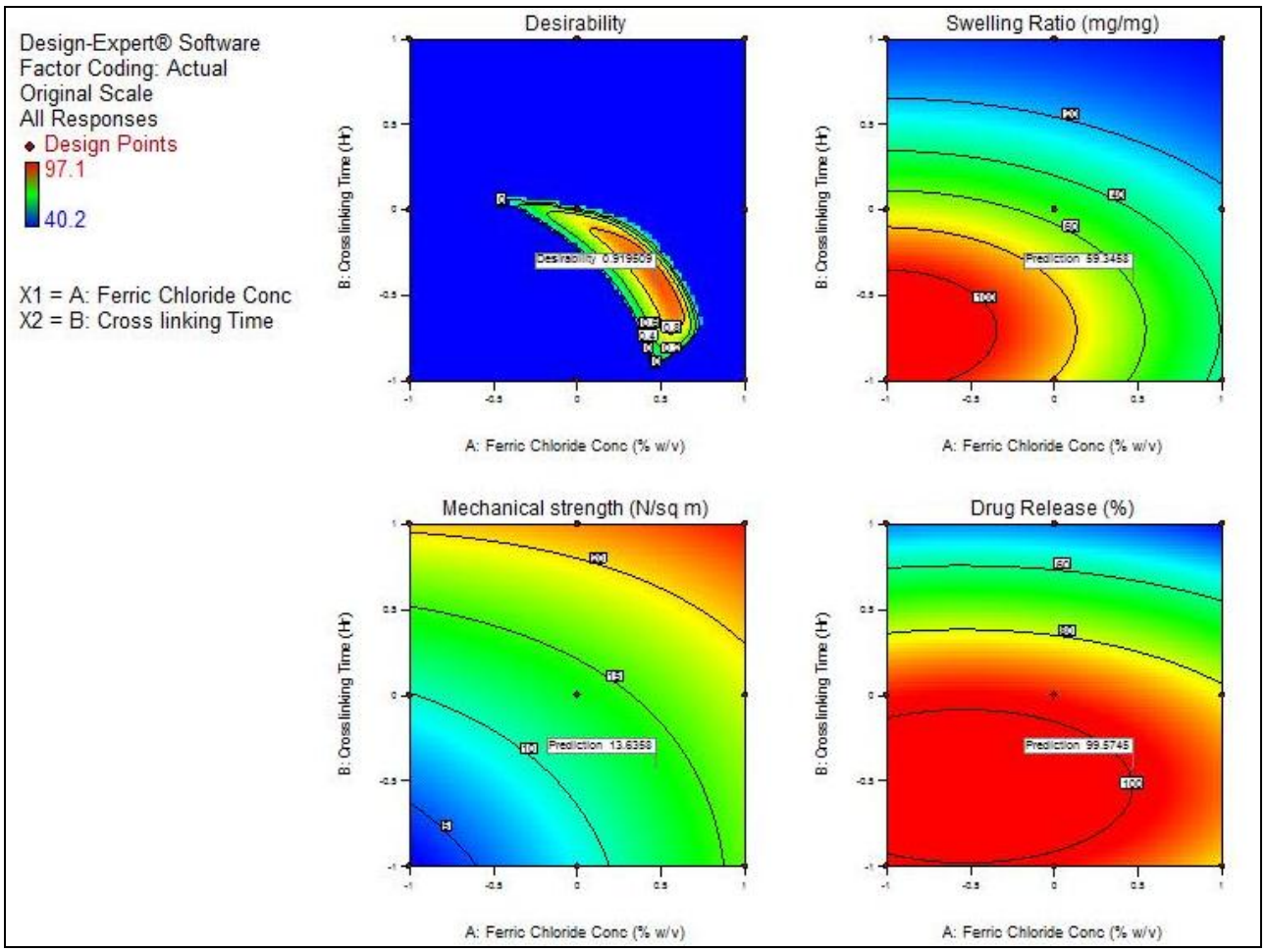


FIG. 8: DESIRABILITY PLOTS

The optimized formulation with coded factors as A = 0.46 (3.6 % concentration of ferric chloride) and B= -.042 (1.5 Hr cross-linking time) was observed with desirability value 0.92. The same formulation was prepared and prediction error was observed as shown in **Table 7**.

TABLE 7: PREDICTED AND OBSERVED RESPONSE VARIABLES OF THE OPTIMAL SPHH OF LORATADINE

	Swelling Ratio	Mechanical strength	Drug Release
Predicted Value	59.346	13.636	99.574
Observed Value	61.17	13.223	96.4
Predicted Error	1.83	-0.413	-3.2

The low prediction error of -3.2 to 1.83 indicates the high prognostic ability of RSM.

C.2: Laboratory Experimentation:

Drug loading capacity: The percent drug loading was found to be 98.2 ± 0.7 in final optimized formulation.

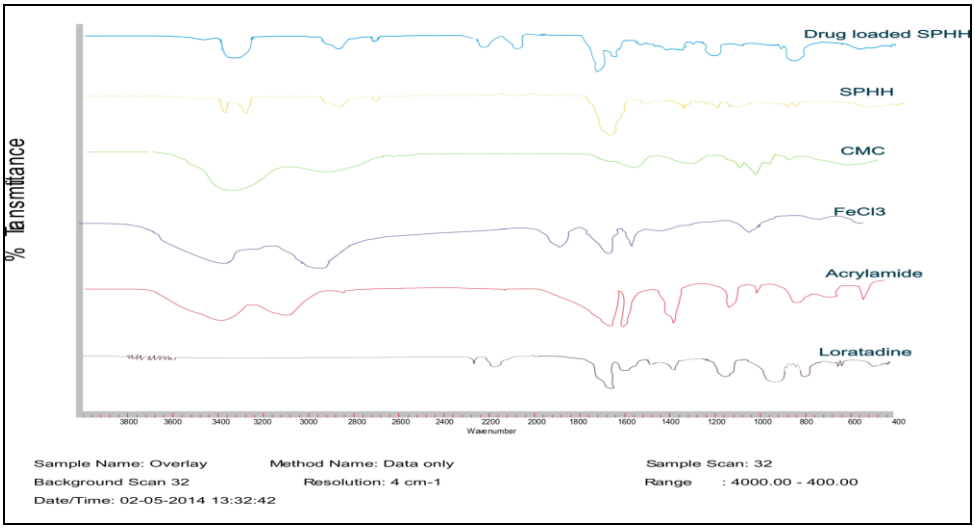


FIG. 9: OVERLAY DIAGRAM OF FTIR

The FTIR Spectra of pure drug Loratadine exhibits peaks at 2196, 1702, 1643, 1443, 1227, 998 and 862 cm^{-1}. An absorption around 1700 cm^{-1} attributes to amide group due to C=O stretching and N-H deformation. Absorption at 998 cm^{-1} is attributed to alkyl halide group due to C-Cl stretching. Absorption at 1443cm^{-1} is due to nitro group, N=O stretching. Absorption at 1227cm^{-1} is observed due to saturated and side chain aromatic groups present in the structure of drug. Absorption at 2196 cm^{-1} shows C= N stretch, at 1643 shows C=N stretch and at 862 shows =C-H stretch.

The FTIR of final formulation (Plain SPHH) shows peaks at 1721 and 1632 cm^{-1} reveals the presence of amide and carboxylic group, which confirmed the formation of poly(AA-co-AM) superporous hydrogels. Presence of band at 3410 cm^{-1} may be assigned o symmetric and asymmetric stretching of N-H group. The characteristic C=O stretching vibration bands of amide and acid groups have been observed at 1685 and 1652 cm^{-1}.FTIR spectra of CMC shows peaks at 3429 cm^{-1} due to OH vibrational stretching; symmetric stretching mode of methyl groups was found at 2937 cm^{-1} in which all the CH bonds extend and contract n phase; peak at 1614 cm^{-1} indicates the presence of stretching vibration in six membered cyclic rings. FTIR spectra of $FeCl_3$ shows peaks at 3369, 2977, 1665, 982 cm^{-1}. The FTIR study reveals that there is no drastic change in the absorption peaks of loratadine in final formulation. This attributes to observation that there is minimal drug excipient and/ or incompatibility. The overlay diagram is shown in **Fig. 9**.

X-Ray Diffractometry Report:

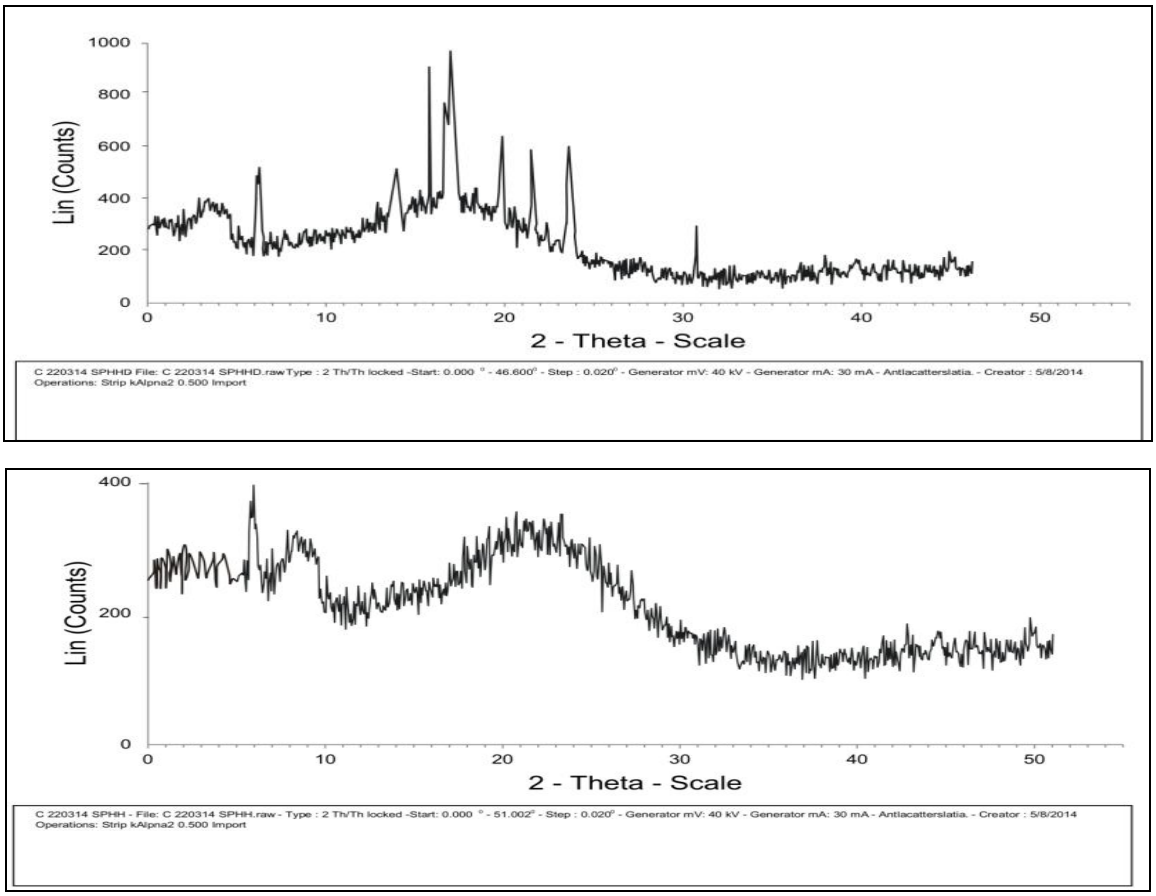


FIG. 10: X-RAY DIFFRACTOGRAMS OF PLAIN AND DRUG LOADED SPHH

The presence of characteristic peaks of drug in the diffraction pattern of drug loaded SPHH indicated that incorporated drug remains intact in its crystalline state within polymer network (Fig 10). The crystalline nature of the drug was still maintained. However, minor shifts in characteristic peaks and reduced diffraction intensity suggests reduction in quality of the crystals and presence of higher amount of amorphous drug along with polymer.

Diffraction Scanning Colorimetric Report: DSC of pure drug Loratadine HCl showed an endothermic peak at 138.0^{0}C. The DSC of drug loaded SPHH showed the same endothermic peak, but with decreased intensity indicating no interaction of drug with hydrogel polymeric network although some polymorphic changes during the formulation may have occurred as shown in **Fig. 11**.

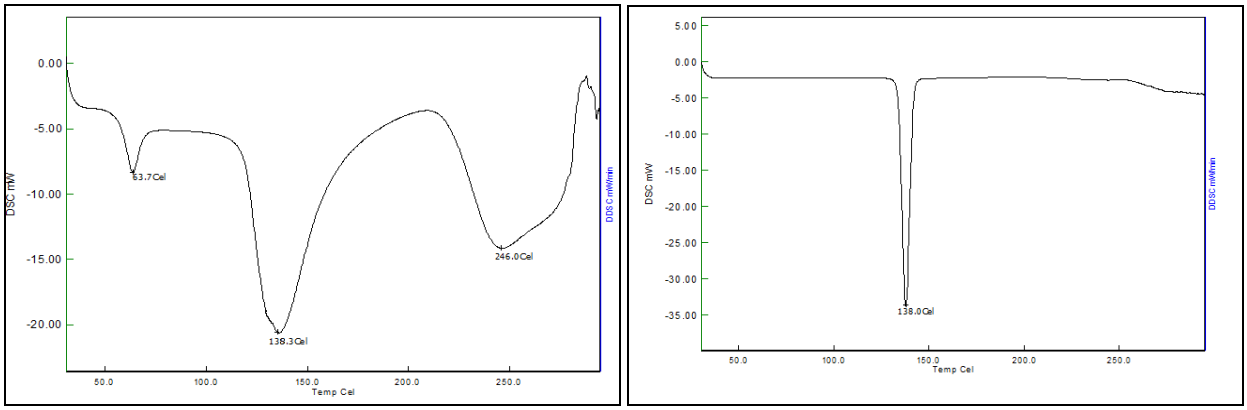


FIG. 11: DIFFERENTIAL SCANNING CALORIMETRIC DATA OF PLAIN AND DRUG LOADED SPHH

In vitro drug release:

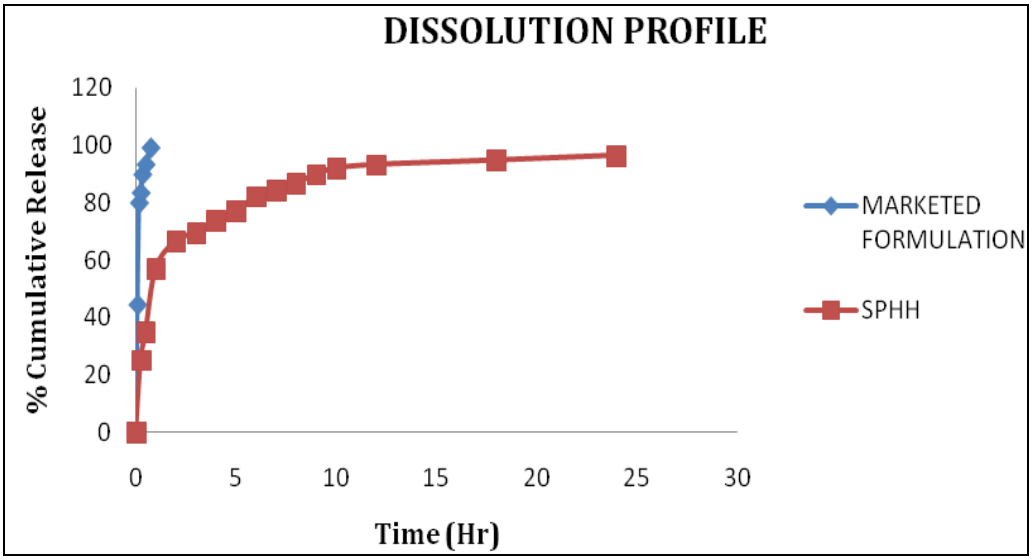


FIG. 12: *IN VITRO* DRUG RELEASE PROFILE OF MARKETED FORMULATION AND SPHH

It was observed that the drug release from SPHH continued upto 2 hours and then sustained effect was observed for 24 hours. Initial bust release may be attributed to drug present on the surface of SPHH. Compared to marketed formulation, SPHH shows sustained effect as shown in **Fig. 12**.

Drug Release Kinetics: The data of in vitro drug release was fitted into various models and regression coefficients were calculated as represented in **Table 8**. It shows Korsmeyer-Peppas Model best describes the kinetics of in vitro release of drug from optimized SPHH.

TABLE 8: DISSOLUTION RELEASE KINETICS

Model	Regression Coefficient Value
Zero Order Model	0.573
First Order Model	0.882
Higuchi Model	0.803
Hixon Crowell Model	0.732
Korsmeyer-Peppas Model	0.910

CONCLUSION: Different generations of superporous hydrogels were prepared and evaluated. Superporous hydrogel hybrids with enhanced mechanical strength, desired swelling rate and swelling ratio were obtained, which are potential candidates for gastroretentive drug delivery. This device deals with the challenge of gastric retention. The formulation has shown initial prompt followed by sustained release of loratadine.

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