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DESIGN AND DEVELOPMENT OF SUPERPOROUS HYDROGEL OF AN ANTIHYPER-TENSIVE DRUG FOR GASTRORETENTIVE DRUG DELIVERY

Gopa Roy Biswas *, Simran Shaw, Sutapa Biswas Majee

Division of Pharmaceutics, NSHM College of Pharmaceutical Technology, NSHM Knowledge Campus, Kolkata-Group of Institutions, 124 B.L. Saha Road, Kolkata - 700053, West Bengal, India.

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Correspondence to Author:
Dr. Gopa Roy Biswas

Assistant Professor,
Division of Pharmaceutics,
NSHM College of Pharmaceutical Technology, NSHM Knowledge Campus, Kolkata-Group of Institutions, 124 B.L. Saha Road, Kolkata - 700053, West Bengal, India.

E-mail: gopa.biswas@nshm.com

ABSTRACT: Superporous hydrogels (SPHs) is originally developed as a novel drug delivery system to retain drugs in the gastric medium by instant swelling on water absorption through open porous structure and maintain their integrity in that harsh environment. Atenolol, an antihypertensive drug with a short half-life, limited bioavailability, unstable nature at basic pH potentiated the need for developing a gastro-retentive system, hence super porous hydrogel of Atenolol had been developed with cellulosic polymers, and adequate strength was imparted by the addition of Ac- Di- Sol. The structural morphology of hydrogel was investigated by SEM, and it was found that plenty of pores of different size ranges, like 1 µm, 2 µm, 10 µm were formed. Compatibility studies proved the integrity of the super porous hydrogel. Gelation time was found to vary with respect to the formulation. The setting time of super porous hydrogel was found to be increased with an increase in the concentration of HPMC K100M. The drug release from super porous hydrogels was sustained for 10 h. *In-vitro* drug release data obtained were fitted into various kinetic equations. The formulations obeyed Higuchi and Korsmeyer- Peppas kinetics of drug release. For further confirmation, the data were fitted to the Kopcha model to get the evidence of drug release by the combination of diffusion-controlled and chain relaxation–swelling mechanism. However, the diffusion mechanism predominated the process leading to quasi diffusion and anomalous diffusion mechanism.

INTRODUCTION: Oral controlled drug delivery system release drug from the systems predictably and reproducibly to achieve better bioavailability of basic drugs that have poor solubility at higher pH as well as drugs that have short elimination half-lives. A major drawback encountered with oral formulations is the inability to increase their retention time in the stomach and the proximal part of the small intestine.

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Many methods have been developed to prolong the residence time of drugs in the stomach. Different approaches to improve the gastric residence include dosage forms like mucoadhesive or bioadhesive systems, high-density systems, magnetic systems, superporous hydrogels, raft forming systems, low-density systems, and floating ion exchange resins [1]. Among these, superporous hydrogel system is one of the challenging approaches.

Hydrogels are cross-linked hydrophilic polymers with a network structure consisting of acidic, basic, or neutral monomers, and they have the ability to absorb large amounts of water. The swelling properties of hydrogels are closely related to so many factors like the elasticity of the network, the

presence of hydrophilic functional groups (such as -OH, -COOH, -$CONH_2$, -SO_3H) in the polymer chains, the extent of cross-linking, and porosity of the polymer. Hydrogel swells in water with some mechanical strength, but their swelling index and mechanical strength are not so enough to exhibit fast swelling properties [2]. Such slow swelling is beneficial for many applications, but there are many situations where a fast swelling polymer is more desirable. Therefore, a new generation of hydrogels that swell by absorbing water very rapidly, has been developed. Examples of this new generation are superporous hydrogel, which swells to an equilibrium size in a short period of time [3].

Atenolol is a beta-adrenoreceptor antagonist or more commonly known as a beta-blocker used in the treatment of hypertension and angina pectoris. The human jejunal permeability and the extent of absorption is low; thus, It has an oral bioavailability of only 50%, while the remaining is excreted unchanged in feces. It undergoes little, or no hepatic first-pass metabolism, and its short elimination half-life are 3 to 4 h favors development of a gastro-retentive superporous hydrogel tablets to improving its oral bioavailability.

Superporous hydrogels (SPHs) possess an average pore size of greater than 100 microns and swell to equivalent size within a minute because of rapid intake of water by capillary wetting through number of interconnected open pores [4]. SPHs have a tendency to swell to a large size with a swelling ratio of about 100 or more, and their mechanical strength should be high enough to withstand pressure when used as gastroretentive drug delivery. By incorporating hydrophilic particulate material Ac- Di- Sol (Cross carmellose Sodium) to the system, mechanical strength can be imparted. A superporous hydrogel is a 3-dimensional network of a hydrophilic polymer that absorbs a large amount of water in a very short period of time because of the presence of interconnected microscopic pores [5]. Due to porous structure, SPHs has hundred time's greater surface area and shorter diffusion distance than conventional hydrogels do. The superporous nature of dried SPHs enhances the swelling of it very fast to a very large size on contact with water. The drugs having a narrow absorption window, *i.e.,* mainly absorbed from the proximal small intestine, the bioavailability of those drugs can be well increased by gastric retention. For drugs that are absorbed rapidly from the gastrointestinal tract (GIT), should have a slow release from the stomach to improve the bioavailability. Gastro retentive dosage form can also be used for those drugs that are poorly soluble at an alkaline pH or drugs that are degraded in the colon. Several important properties of SPHs, like fast swelling capacity, large swelling ratio, and surface slipperiness, make them an excellent candidate to develop gastric retention devices [6.] The weak mechanical property of fully swollen SPHs reduces their practical application, and that can be overcome by making SPHs composites. To overcome this slow swelling property of dried hydrogels, the current inventors have synthesized a super SPHs. porous hydrogel that can swell within minutes despite the consequences of the size of the matrix. SPH has the ability to swell very fast regardless of their size, and this is due to the interconnected porous structure. The interconnected structural pores provide water absorption into the center of the SPHs by capillary force. Even though these super porous hydrogels provided drastically fast swelling kinetics and high swelling degree, the mechanical strength of the fully swollen super porous hydrogels was besides poor to be useful. In some cases, the abundant swollen super porous hydrogels could not be picked up and broke easily due to their very poor mechanical properties. Usually, mechanically strong super porous hydrogels can be made by increasing the cross-linking density, but this would result in a very small extent of swelling with a loss of the superabsorbent property [7].

EXPERIMENTAL SECTION:

Materials: Atenolol was a gift sample from Windlas Biotech Ltd., Dehradun, India. HPMC was obtained from Colorcon Asia Pvt. Ltd and Carbopol 971p from Mylan Laboratories Ltd. A.P. India. Ac-Di-Sol was obtained from Matrix Laboratories, Hyderabad. Triethanolamine was purchased from Loba Chemie Pvt., Ltd. All other ingredients used were of pharmaceutical grade.

Preparation of Superporous Hydrogels: Hydrophilic polymers had been selected to prepare superporous hydrogel of Atenolol. The polymers were used in different ratios. HPMC (Hydroxy

Propyl Methyl Cellulose) of different grades was first dispersed in double distilled water alone and also in combination of carbopol 971p. In the meantime, the required amount of drug, Atenolol was mixed to it. The mixture was stirred in magnetic stirrer until thickening occurred and then neutralized by drop-wise addition of 50% (w/w) triethanolamine, until a transparent gel appeared. The quantity of triethanolamine was adjusted to prepare gel with the desired pH. Gels were stored for 24 h at room temperature to stabilize [8] **Table 1**.

TABLE 1: COMPOSITION OF HYDROGEL FORMULATIONS

Ingredients	F1	F2	F3	R1	R2	R3	P1	P2	P3
HPMC K100M (mg)	200	150	100		-	-	100	75	50
HPMC K 4M(mg)	-	-	-	200	150	100	100	75	50
CARBOPOL 971P(mg)	100	150	200	100	150	200	100	150	200
SODIUM CHLORIDE (mg)	10	10	10	10	10	10	10	10	10
Ac - Di – Sol (mg)	20	20	20	20	20	20	20	20	20
ATENOLOL (mg)	50	50	50	50	50	50	50	50	50
TRIETHANO-LAMINE (drops)	7	7	7	7	7	7	7	7	7
DOUBLE DISTILLED WATER (ml)	20	20	20	20	20	20	20	20	20

Studies on Phase Transition: As the polymerization reaction proceeded by the addition of triethanolamine, the viscosity was continuously increased until the full network structure (gel structure) was formed. Sol-gel phase transition of superporous hydrogels was recorded using test tube-tilting method [9]. It was visually observed by tilting the test tubes, and conditions of superporous hydrogels could be defined as "flowing weak gels" and "non-flowing tough gels" respectively.

The time taken for the setting of superporous hydrogel was also noted **Fig. 4**. This parameter was based on the time taken until the formulation was no longer descending in the tilted tube position [10].

Swelling Studies: A completely dry, pre-weighed, disc-shaped superporous hydrogel was weighed and then immersed in excess of swelling medium (HCl-KCl buffer pH 1.2). At various time intervals, the hydrogel was removed from the solution and weighed after excessive solution on the surface was blotted. Data presented in this experiment were the mean values of triplicate measurements. Results were calculated according to the following equation:

$$Q = (Ms – Md) / Md$$

Where Q is the swelling ratio, Ms the mass in the swollen state and Md the mass in the dried state. The hydrogels were first swollen in pH 1.2 HCl solutions for 30 min[11].

Density and Porosity Measurements: For density measurement, the solvent displacement method was used. Dried SPHs were used for density measurements, which actually show the apparent densities of the SPHs. Pieces of SPHs were taken and weighed in order to determine the mass of each piece. A piece of the dried that was immersed in a predetermined volume of n- hexane in a graduated cylinder, and the increase in the volume of n-hexane was measured as the volume of the SPH. The density was calculated from the following equation.

$$Density = MSPH/VSPH$$

Where VSPH is the volume of solvent displaced by SPH, and MSPH is the mass of the SPH.

For porosity measurement, dried hydrogels were immersed in n-hexane overnight and weighed after excess hexane on the surface was blotted. The porosity was calculated from this equation.

$$Porosity = VP/VT$$

Where, VP (= VT - VSPH) is the pore volume of SPH, and VT is the total volume of SPH [12].

Determination of Void Fraction: The void fraction was calculated by the following equation:

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

The void fraction inside superporous hydrogels was determined by immersing it in HCl solution (pH 1.2) up to equilibrium swelling. The dimensions of the swollen SPHs were measured, and by using those data, sample volumes were determined as the

dimensional volume. In the meantime, the amount of absorbed buffer into the SPH was determined by subtracting the weight of dried SPH from the weight of swollen SPH, and the resulting values were assigned as the total volume of pores in the hydrogels [13].

Water Retention: The following equation was used to determine the water retention capacity (WRt) as a function of time:

$$WRt = Wp - Wd / Ws - Wd$$

Where Wd is the weight of the dried hydrogel, Ws is the weight of the fully swollen hydrogel, and Wp is the weight of the hydrogel at various exposure times like 15, 45, 90, and 150 min. For determination of the water-retention capacity of the SPHs as a function of the time of exposure at 37 ºC, the water loss of the fully swollen polymer at timed intervals was determined by gravimetry [14].

Mechanical Strength: Mechanical strength of the SPHs was measured by applying the weight on swelled Superporous hydrogels until the hydrogels fractured [15]. The strength was measured in gm.

Determination of Drug Content: A weight of superporous hydrogel containing 5 mg of drug in 100 ml volumetric flask was treated with about 10 ml of methanol. They were mixed well and made up to volume. The mixture was filtered, and drug content was determined using a UV-Vis spectrophotometer at 274 nm.

Scanning Electron Microscopy Analysis: Dried SPHs were cut to expose their inner structure and used for SEM studies. The morphology and porous structures of them were examined using ZEISS EVO 18, CARL ZEISS MICROSCOPY (PENTA FET X 3) OXFORD INSTRUMENTS with an operating voltage of 30 kV. Images were captured using a digital capture card.

***In-vitro* Release Studies:** *In-vitro* drug release of Atenolol from the superporous hydrogels was evaluated in triplicates at 37±0.5 ºC using a United States Pharmacopoeia (USP) Dissolution Test Apparatus Type 1 (Rotating Basket Apparatus) at a rotation speed of 50 rpm in 900 ml of 0.1M HCl (pH 1.2) for 10 h. For this study the capsule filled with hydrogel was kept into the basket, at regular time intervals, 10 ml of the dissolution medium were withdrawn, replaced with an equivalent volume of fresh dissolution fluid and analyzed for the drug using a UV-Vis spectrophotometer (UV-1700, Shimadzu, Japan at 274 nm [16] release mechanism, the parameters n and k of the Korsmeyer-Peppas equation were computed [17].

RESULTS AND DISCUSSION: A few representative photographs of prepared hydrogels are shown in **Fig. 1**.

FIG. 1: PHOTOGRAPHS OF PREPARED SUPER-POROUS HYDROGEL

They show the hydrogels in glass beakers just after preparation. The dried hydrogel is shown in **Fig. 2**.

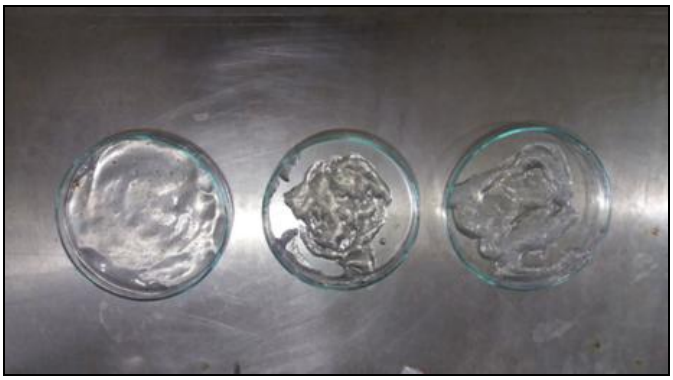

FIG. 2: PHOTOGRAPHS OF DRIED SUPERPOROUS HYDROGEL

It has been reported that if the amount of water in the polymerization mixture is higher than the swelling capacity of the gel, it cannot absorb all the water in the polymerization medium; thus, a phase separation occurs during the polymer formation [18]. Finally, an opaque gel is obtained. They also concluded that if the volume of swollen gel is higher than the volume of the just prepared-gel, no phase-separation is observed. Otherwise, the system will be two-phased and opaque in appearance.

Drug excipient interaction is an important study prior to the development of any formulations. Among the various methodologies available to study the drug - excipient interaction, common approaches are - FTIR Spectroscopy, DSC, IR Spectra, *etc*. FTIR Spectroscopy shows the interaction between the molecules at the functional groups. Here, drug excipient interaction was done using FTIR Spectroscopy **Fig. 3**. It was observed from the FTIR Spectra that there might be some physical interactions due to the generation of weak bonds as no such shifting of the peaks were marked.

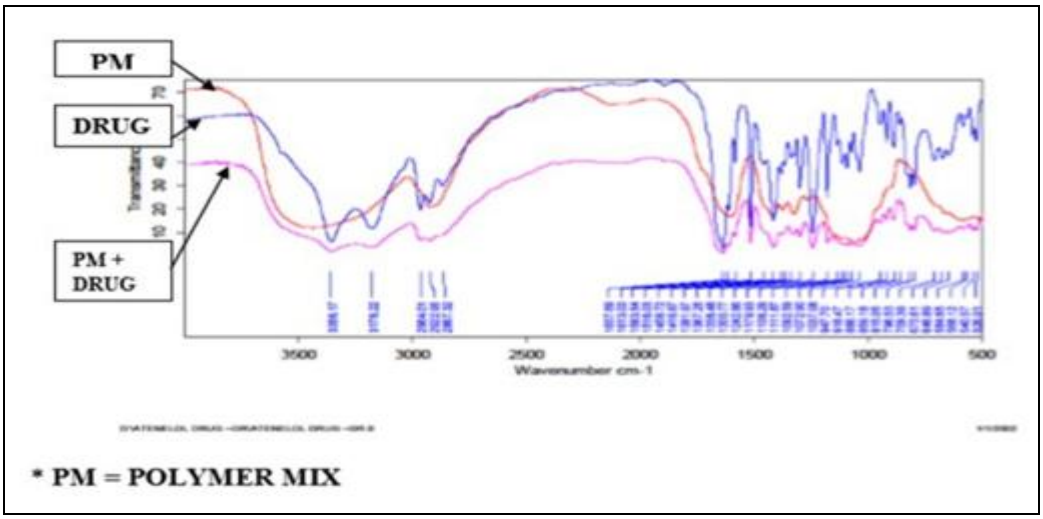

FIG. 3: OVERLAID FTIR SPECTRA OF DRUG (ATENOLOL), POLYMERS MIX AND DRUG WITH POLYMERS MIX

It is suggested by the FTIR spectra that there may be some physical interactions due to the generation of weak to medium intensity bonds as no major shifting of peaks was marked [19]. A mixture of polymers can change the rate of diffusion of drug molecules by changing entanglement in the polymeric network. Characteristic bands in the FTIR spectrum of the drug-polymer mixture were seen at 3355.54 cm^{-1} (the stretching vibration of the group $–NH_2$), at about 2962 cm^{-1} (the stretching vibration of –OH), Asymmetric and symmetric C=O were represented by two bands at 1145cm^{-1} (strong) and 1298 cm^{-1} (weak), respectively.

A superporous hydrogel has the fast swelling ability, because of the presence of large and uniform pores within the polymer structure, which is produced due to the formation of foam at the time of polymerization. In order to produce large and uniform pores, a porogen is introduced. That pores are made fixed by introducing Ac-Di-Sol. Ac-Di-Sol has the ability to increase the physical cross-linking of polymer chains so that the porous structure is maintained during drying of the SPHs [11]. Ac-Di-Sol is responsible for imparting mechanical strength to superporous hydrogels for their effective applications. The presence of triethanolamine increased the overall cross-linking density of the superporous hydrogels. This entanglement significantly improved the structural integrity of the hydrogel and decreased stress relaxation, which enhanced its ability to withstand pressure.

TABLE 2: PHYSICOCHEMICAL PROPERTIES OF SUPERPOROUS HYDROGEL (N=3, ±SD)

Formulation	Porosity	Void Fraction	Water retention	Density (gm/cm^3)	% Swelling index
F1	56 ± 2.02	1.161	0.575	1.76	43 ± 1
F2	94 ± 1.05	5.298	0.535	0.79	67.8 ± 1.12
F3	65.1± 3.14	2.19	0.746	1.43	50.16 ± 1.32
R1	59 ± 2.02	2.24	0.816	1.48	56.5± 1.16
R2	86 ± 1.09	8.4	0.526	0.75	76.9 ± 1
R3	22.75± 2.02	4.64	0.634	0.64	31.3± 1
P1	30.4± 3.05	6.26	0.864	1.92	34.6± 1.06
P2	38 ± 1.07	3.561	0.919	1.93	41.4± 2.12
P3	26.1 ± 0.97	5.26	0.454	1.98	35.02 ± 2

Porosity and void fraction measurements are shown in **Table 2**, the porosity of superporous hydrogels increased by the increase in the amount of triethanolamine. This is due to the incorporation of the higher crosslink density within the polymer structure, leading to a decrease in the occupied volume.

Gelation time was found to vary with respect to formulation **Fig. 4**. The setting time of superporous hydrogel was found to be increased with an increase in the concentration of HPMC K100M. Gelation time shows correlations with the density of the formulations. The time was shorter for less dense SPHs, whereas it was found to be in the higher side in comparatively dense SPHs. The superporous hydrogels were named as Flowing soft gels and non-flowing tough gels with respect to their followability.

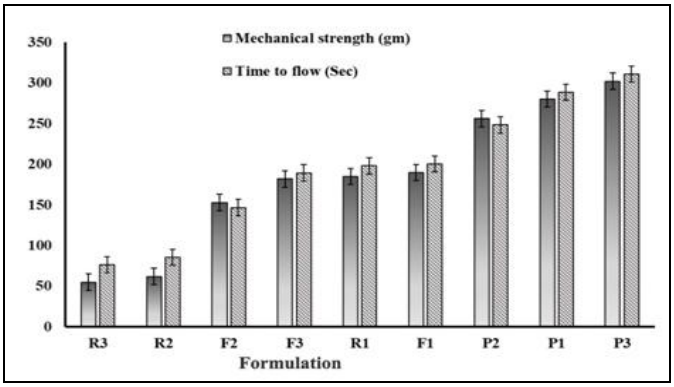

FIG. 4: COMPARISON OF MECHANICAL STRENGTH AND THE ONSET TO FLOW OF THE SUPERPOROUS HYDROGEL (±SD, N=6)

The drug content analysis showed that the drug loading is uniform it is distributed in the superporous hydrogels. Properly and the drug content was in the range of 96.5 - 98.6% of the total amount of the drug added.

The range of mechanical strengths was found to be 55-302 gm. For a gastric retention device, the swollen SPHs should be strong enough to withstand repeated peristaltic contractions. Thus, it was necessary to improve the mechanical property of SPHs. The presence of Ac-Di-Sol increased the cross-linking density of the SPHs by the physical entanglement of the polymer chains with its fibers. When Ac-Di-Sol fibers were added to the solution, they swelled and absorbed the polymer solution. The result confirmed the physical entanglements of polymer chains through the Ac-Di-Sol fibers. Hence the mechanical load gets shared between Ac-Di-Sol fiber and the polymer structure. However, there are variations in the mechanical strength irrespective of the same quantity of AC-Di-Sol used and that is because of the ratio of HPMC K100M and HPMC K4M incorporated. It has been found that mechanical strength was highest in P3 (302 ± 4 gm) and lowest in R3 (55 ± 2.5 gm). The results obeyed the coordination with the studies on phase transition and formation of "Flowing weak gels" or "Non-flowing tough gels".

Fig. 5-7 show the SEM pictures of the hydrogel formulation. The picture shows large numbers of pores, indicating the formation of hydrogel with a superporous structure. The fully swollen formulation was transparent in the water, and lots of bubbles could be seen within the hydrogel that appeared as netlike distribution.

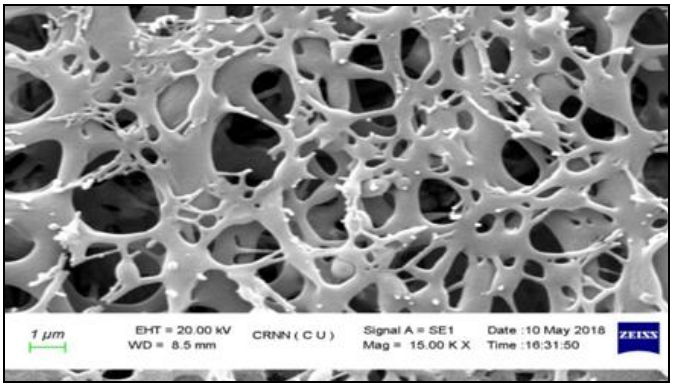

FIG. 5: SCANNING ELECTRON MICROSCOPE PHOTOGRAPH OF F1 AT X 15000

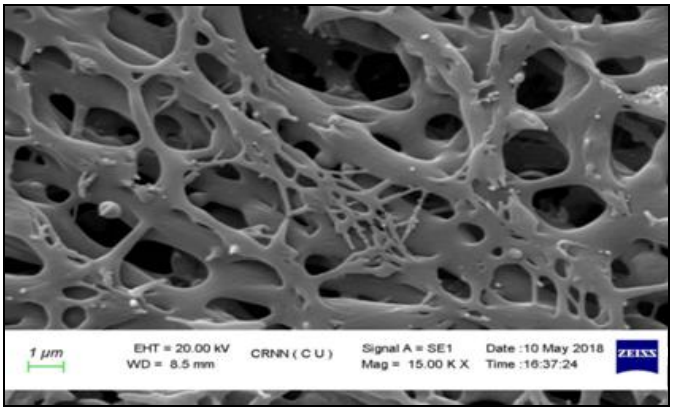

FIG. 6: SCANNING ELECTRON MICROSCOPE PHOTOGRAPH OF P1 AT X 15000

The scanning electron microscope photographs of superporous hydrogel **Fig. 5-7** clearly shows the presence of pores on the surface. The superporous hydrogel has high porosity and is responsible for faster swelling when compared to conventional

hydrogels. The pores are in different size ranges, like 1 µm, 2 µm, 10 µm.

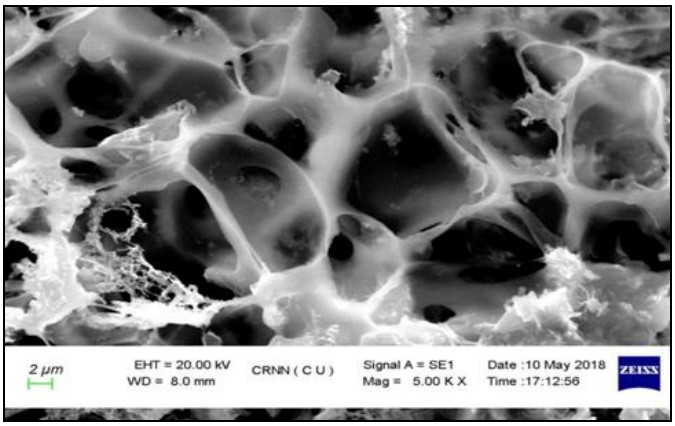

FIG. 7: SCANNING ELECTRON MICROSCOPE PHOTOGRAPH OF SUPER POROUS HYDROGEL AT X 5000 INDICATING THE PORES

Apparent densities and porosities of SPHs are shown in **Table 2**. Apparent density increases, while the porosity of SPHs decreases.

The swelling properties of the hydrogels were measured by weight, volume, and dimension at different time intervals to study the swelling rate or at equilibrium to measure swelling capacity. The swelling and mechanical properties of SPHs are generally sensitive to the type and nature of the swelling medium. The important factors for swelling are ionic strength, pH, salts, organic solvents, and pressure. Polymer--water interactions are also important and serve as the basis for the swelling process in all types of hydrogels [20]. The swelling process itself begins when an SPH is placed in water or other aqueous solutions. This process is first dominated by the attractive forces of the hydrophilic and ionic functional groups in the hydrogel structure. The swelling process continues until each of the functional groups is surrounded by the same amount of water. Next, as water tries to further dilute the polymer chains, an osmotic effect is created that continues to fill the open pores with water until opposed by the contractive forces of the cross-linked hydrogel structure.

It was observed from the data, as shown in **Fig. 8**, that ratio of HPMC K100 M and HPMCK4M and also the concentration of Carbopol 971p used affected the percentage release of drug from the formulations in the pH-1.2 buffer. It was found that the cumulative percentage of drug release from formulation was reduced when HPMC K 100 M is alone in the formulations along with less amount of Carbopol 971p. Whereas in the superporous hydrogels containing combinations of two grades of HPMC and more amount of Carbopol 971p, drug release is comparatively faster. It was due to the fact formulations that showed good porosity and swelling ratio allowed better absorption of buffer through polymeric structure, and hence drug release was prolonged upto 10 h.

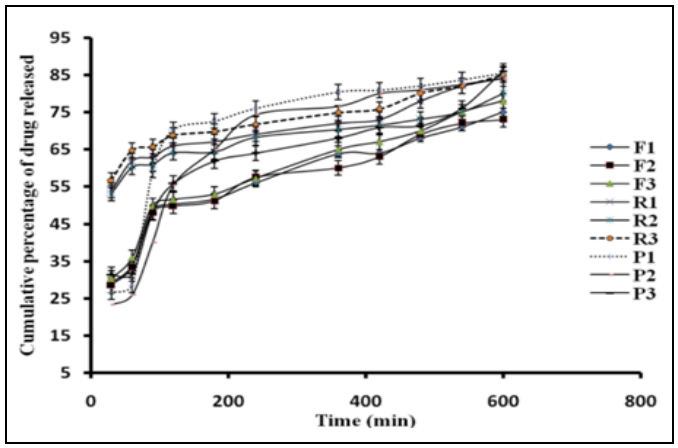

FIG. 8: CUMULATIVE PERCENT OF DRUG RELEASED FROM SUPERPOROUS HYDROGEL 0.1M HCl (pH 1.2) (± SD, N=6)

The formulations were analyzed for released kinetic studies by fitting them various mathematical models such as zero-order; first-order; Higuchi model; Korsmeyer model. Regression (R2) analysis of all formulation was determined. It had been found that the drug release pattern obeyed Korsmeyer model. Korsmeyer *et al*., (1983) derived a simple relationship which described the drug release from a polymeric system [21], Ritger and Peppas [22], and Korsmeyer and Peppas [23] developed an empirical equation to analyze both Fickian and non-Fickian release of drug from swelling as well as non-swelling polymeric delivery systems.

To find out the mechanism of drug release, first, 60% drug release data were fitted in Korsmeyer – Peppas model $M_t/M_\alpha = K t^n$ Where M_t/M_α is fraction of drug released at time t, k is the rate constant incorporating structural and geometric characteristics of the delivery system. n is the release exponent indicative of the mechanism of transport of drug through the polymer. The n value is used to characterize different release mechanisms [24]. As per Ritger-Peppas models, $0.45 < n < 0.89$ is for non-Fickian release (anomalous) from the cylinders (non swellable matrix) and $0.43 < n <$

0.85 for non Fickian release (anomalous) from non swellable spherical samples [22]. To find out the exponent n, the portion of the release curve Mt/Mα < 0.6 should only be used. The model is plotted as log cumulative percentage drug release versus log time. In the present study it was observed **Table 3** that the n varies from 0.3 to 0.6 representing quite a change in the drug transport mechanism. It is due to the change in the polymeric ratio. Among the nine batches, P1 and P2 followed anomalous diffusion (n=0.6) mechanism, whereas drug release from the rest is fully governed by Quasi-Fickian (n=0.45) mechanism.

TABLE 3: KINETIC PROFILE OF SUPERPOROUS HYDROGEL

Model And Parameters		F1	F2	F3	R1	R2	R3	P1	P2	P3
Zero-order	K (min^{-1})	21.96	89.32	101.5	0.111	75.96	57.40	47.6	39.85	43.41
	R^2	0.889	0.937	0.838	0.972	0.812	0.841	0.625	0.722	0.681
Higuchi	K_H ($min^{-1/2}$)	2.407	72.19	77.57	52.09	68.02	50.17	29.68	20.27	30.34
	R^2	0.933	.926	0.911	0.859	0.921	0.834	0.773	0.857	0.828
Korsmeyer-	N (min^{-n})	0.373	0.378	0.364	0.111	0.125	0.106	0.661	0.628	1.009
Peppas	R^2	0.942	0.933	0.929	0.972	0.872	0.969	0.841	0.917	0.925
Kopcha	A	5.711	5.586	5.988	11.29	11.23	11.87	5.163	4.179	6.037
	B	0.104	0.098	0.115	0.388	0.403	0.412	0. 29	0.091	0.119
	A/B	54.91	57	52.06	29.09	27.87	28.81	17.80	45.92	50.73

The diffusion rate of a drug depends on the physical structure of the polymer network and its chemical nature. When the gel gets fully hydrated, drug diffusion occurs through the pores present. In gels where lower hydration occurs, the drug is dissolved in the polymer and is transported between the chains. Cross-linking of the polymers is responsible for increasing the hydrophobicity of the gel formed at the outer surface and reduces the diffusion rate of the drug. For further confirmation, the data were fitted to Kopcha model, that showed the evidence of drug release by a combination of diffusion-controlled and chain relaxation–swelling mechanism. In the case of R1, R2, and R3 due to the presence of higher grade of hydroxyl propyl methyl cellulose (HPMCK100M), the gel became more hydrophobic and retarded the diffusion of Atenolol from the superporous hydrogel.

Evaluation of diffusion and erosion parameters in the Kopcha model showed a predominance of diffusion relative to swelling or erosion throughout the entire test period. This finding is supported by evaluation of the ratios of the exponent's A/B (*i.e.,* diffusional term A and erosional term B) derived from the Kopcha model [25]which were greater than 1 in all cases. The Kopcha model can also be used to quantify the relative contributions of diffusion and polymer relaxation to drug release. The data in Table clearly show that the value of A is far greater than that for B, suggesting that drug release from SPHs was primarily controlled by a Fickian diffusion process. Most of the formulations obeyed quasi Fickian mechanism and the formulations where HPMC K100M and HPMC K4M combinations are in a ratio of 1:1 and 2:1 with Carbopol 971P; they obeyed anomalous diffusion mechanism.

CONCLUSION: The work included the development of Atenolol loaded superporous hydrogel as gastro retentive dosage forms. HPMCK100M, HPMCK4M, Carbopol 971p have been employed for the formulations. NaCl was introduced as pore formers and Ac-Di-Sol to increase the physical cross-linking of polymer chains to fix it. SEM photographs of the formulations clearly indicated the formation of a large number of pores confirming it as superporous hydrogel. A significant variation is observed in the *in-vitro* release pattern of Atenolol from the SPHs in relation to change the ratio of two grades of HPMC to Carbopol 971p. There was variation in the transport mechanism from quasi diffusion to anomalous by changing the ratio of HPMCK100M and HPMCK4M. *In-vivo* studies can be considered as future prospects to get a clear picture of IVIVC.

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