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Development and Evaluation of Superporous Hydrogel Tablets of Cefditoren Pivoxil as a Gastroretentive System

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Abstract : Superporous hydrogels(SPHs) were originally developed as novel drug delivery system to retain drugs in the gastric medium. These systems should instantly swell in the stomach and maintain their integrity in the harsh stomach environment, while releasing the pharmaceutical active ingredient. The present review focuses on concept of development of cefditoren pivoxil as superporous hydrogel tablets, their applications and various evaluation techniques.The aim of this study is to prepare Gastroretentive dosage form based on SPH using cefditoren pivoxil as a model drug for swelling & prolonged drug release characteristics in acidic pH. The formulation is based on preparation of third generation SPHs with three different polymers, such as, Formaldehyde, Urea-Formaldehyde and Sodium tripolyphosphate with chitosan as crosslinking agent were used with different concentrations by crosslinking technique to get the desired sustained release profile over a period of 8 hrs. The characterization studies for SPH were performed by measurement of apparent density, porosity, swelling studies, mechanical strength, scanning electron microscopy(SEM) and FT-IR.All formulations were evaluated for stability, drug content,kinetic drug release & invitro drug release profile. It is concluded that the proposed gastroretentive drug –deliverysystem based on SPHs is promising for stomach specific delivery of Cefditoren Pivoxil.

Key Words: Gastroretentive dosage forms, Superporous hydrogels, chitosan, swelling, Cefditoren Pivoxil.

Introduction[1,2]

A superporous hydrogel (SPH) is a three-dimensional network of a hydrophilic polymer that absorbs a large amount of water in a very short period of time due to the presence of interconnected microscopic pores. When applied as drug carriers, these highly swollen hydrogels remain in stomach for a long time, releasing almost all loaded drugs, since their volumes are too big to transport through the pylorus and their sheer bulk hinder their transport to the next organ via the narrow pylorus. This unique swelling property allows them to be used as gastric retention carriers providing a sustained release through long residence in the stomach. In order to be used as an effective gastric retention device, the hydrogels are required to possess not only fast swelling but also following properties: biocompatibility, biodegradability, high swelling capacity, high mechanical strength, and stability in acidic condition.

Many drugs having narrow absorption window, i.e. mainly absorbed from the proximal small intestine, bioavailability of those drugs would be increased by gastric retention. For drugs which are absorbed rapidly from the gastrointestinal tract (GIT), should have slow release from the stomach to improve the bioavailability. Gastric retention devices can also be used for those drugs that are poorly soluble at an alkaline pH or drugs that

are degraded in the colon (eg, metoprolol). 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. The weak mechanical property of fully swollen SPHs limits their practical application which can be overcome by making SPHs composites.

Advantages of SPHs:

Superporous hydrogels has three unique properties that conventional hydrogels do not have.

1. The swelling rate is very fast.
2. The Superporous hydrogels swell completely within a min regardless of the size of the dried superporous hydrogel.
3. Superporous hydrogels swell to such an extent that the weight of fully swollen superporous hydrogel is higher than the weights of dried superporous hydrogels.
4. Though the superporous hydrogels contain small percentage of solid content of the total weight, it can exert significant expansion force during swelling.
5. Superporous hydrogels can also be made elastic, which minimizes their rupture.

Materials and Methods

Materials:

Cefditoren pivoxel was obtained as a gift sample from aurobindo pharma ltd. Chitosan , Formaldehyde, Urea formaldehyde, Sodium Tripolyphosphate, Sodium bi carbonate, Microcrystalline cellulose, Magnesium stearate were obtained from SD fine chemicals Mumbai. All the other chemicals are of analytical grade and were provided by Spectrum pharma labs for research.

Methods:

Drug excipient compatibility study:

The drug and excipient compatibility was observed using Fourier Transform – Infra Red spectroscopy (FT-IR). The FT-IR spectra obtained byy KBr pellet method from Bruker FT-IR Germany (Alpha T). The spectra were recorded over the wave number of 8000 to 400cm^{-1}.

Scanning electron microscopy:

The dried superporous hydrogels were used for scanning electron microscopy (SEM) studies to determine the morphology of the dried samples. A JEOL JSM-840 scanning electron microscope (Jeol USA, Inc., Peabody, MA) was used after coating the samples with gold using a Hummer Sputter Coater (Technics, Ltd.). Images were captured using a digital capture card and Digital Scan Generator 1 (JEOL)

precompression parameters:[3,4]

Angle of repose(θ):

It was determined by fixed funnel method by measuring the radius and height of the pile. It can be obtained from the formula

$$\mathbf{Tan\ \theta = \frac{h}{r}}$$

Therefore, $$\theta = \frac{\tan^{-1} h}{\mathbf{r}}$$

Where h = height of pile.
r = radius of the base of the pile.
θ = angle of repose.

Bulk density:

A definite amount of blend was transferred carefully to measuring cylinder which was initially passed through sieve no: 20. It is expressed as gm/ml and calculated using the equation.

$\mathbf{P = W/V_b}$
Where P = bulk density.
W = mass of the powder blend.Vb = bulk volume of powder blend.

Tapped density:

Tapped density is the ratio of mass of powder to the tapped volume. A certain amount of powder (about 5gm) was passed through sieve no: 22 and transferred to the graduated cylinder fixed on the bulk density apparatus. The timer knob was set for 50 tapping and the volume was noted after the specified taps.

$\mathbf{P_{b,\,max} = W/V_{50}}$
Where Pb, max = tapped density.
W = mass of the powder blend.
V50 = volume of powder blend at 50 taps.

Carr's consolidation Index:

This property is also known as compressibility. It is indirectly related to the relative flow rate, cohesiveness and particle size. It was calculated by using following formula

$$\text{Consolidation Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Table1: Formulations of Cefditoren Pivoxil Tablets Prepared by Direct compression Method.

S.NO.	Ingredients (in mgs)	F1	F2	F3	F4	F5	F6
1	Cefditoren Pivoxil	200	200	200	200	200	200
2	Formaldehyde	25	50	75	100	_	_
3	Urea-Formaldehyde	_	_	_	_	25	50
4	Sodium Tripolyphosphate	_	_	_	_	_	_
5	Sodium bicarbonate	25	25	25	25	25	25
6	Micro crystalline cellulose	242.5	217.5	192.5	167.5	242.5	217.5
7	Magnesium stearate	7.5	7.5	7.5	7.5	7.5	7.5
8	Tablet weight	500mg	00mg	500mg	00mg	00mg	500mg

S.NO.	**Ingredients (in mgs)**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
9	Cefditoren Pivoxil	200	200	200	200	200	200
10	Formaldehyde	_	_	_	_	_	_
11	Urea-Formaldehyde	75	100	_	_	_	_
12	Sodium Tripolyphosphate	_	_	25	50	75	100
13	Sodium bicarbonate	25	25	25	25	25	25
14	Micro crystalline cellulose	192.5	167.5	242.5	217.5	192.5	167.5
15	Magnesium stearate	7.5	7.5	7.5	7.5	7.5	7.5
16	Tablet weight	500mg	500mg	500mg	00mg	500mg	500mg

Formulation of Cefditoren Pivoxil Superporous hydrogels:[5,6]

1) Crosslinking with Formaldehyde:

Procedure:

Chitosan solution (2%w/v) was prepared by stirring in 3ml of 2%(v/v) glacial acetic acid solution using a homogenizer until the chitosan dissolves in acid completely.To this solution,2 to 3 drops of formaldehyde solution(10%w/w of the dry weight of chitosan) , 0.5 ml of 0.1 N HCL were added and mixed for 1 h at 500C.Then acetone of 2ml was added and the precipitated hydrogel was repeatedly washed with distilled water to remove any unreacted material.Further it was dried at 400C for 24h,finally powdered and stored in a well closed container.

2) Crosslinking with Urea Formaldehyde:

Procedure:

To a 2%(w/v) solution of chitosan in 2% (v/v) glacial acetic acid solution prepared by gently heating and stirring, the required amounts of i.e, 2 to 3 drops of urea-fromaldehyde (UF) (10% w/w of the dry weight of chitosan) and 1ml of 1.12 M H_2SO_4 were added and stirring was continued for 1 hour. Then 0.5 ml of acetone was added to precipitate the hydrogel and the obtained hydrogel was repeatedly washed with distilled water to remove any unreacted material. Further it was dried at 40^0C for 24 h; powdered and stored in a well closed container.

Crosslinking with Sodium Tripolyphosphate:

Procedure:

A 2% of chitosan was dissolved in 2% (v/v) glacial acetic acid solution by stirring to get clear solution. To this solution 10% (w/w of dry chitosan) of sodium tripolyphosphate (TPP) was added and kept at 40C for 1 hour and the solution was maintained at 5.5. Acetone was added to precipitate the hydrogel amd the obtained hydrogel was repeatedly washed with distilled water to remove any unreacted material.

Procedure for the preparation of superporous hydrogel tablets:

The ingredient except magnesium stearate were weighed accurately and transferred to a clean mortar and pestle.The powder blend was mixed for 5 minutes after which lubricated magnesium stearate to ensure completemixing was added to the blend and the mixing was continued for another few minutes. After obtaining a uniform blend, it was passed through sieve no: 60 and was prepared for compression. Tablets containing Cefditoren Pivoxilequivalent to 500mg were compressed by using 12mmdiameter, spherical tablet and adjusting thickness and hardness accordingly punches on a 16 station rotary compression machine.

Evaluation of tablet (post compression parameters):[7,8]

Tablets are evaluated for its parameters like various quality control tests such as Tablet thickness and Diameter, Hardness, Friability, uniformity of weight and content uniformity of drug and other specific evaluation tests for GRDDS like swelling studies & Release rate of drug.

Tablet thickness and Diameter:

Thickness and diameter were measured using Vernier calipers. The tablet thickness should be controlled within a ± 5% variation of astandard value. It is expressed in millimeters (mm).

Hardness:

The hardness of the tablets was determined using pfizer hardness tester (cisco). It is expressed in Kg/cm2 and a crushing strength of 4 kg/cm2 is usually considered to be the minimum for satisfactory tablets.

Friability:

The friability of tablets was determined by using Roche friabilator (Lab India, FT 1020) and expressed in %. Ten dedusted tablets were initially weighed [$W_{(initial)}$] and transferred to friabilator and are subjected to fall from 6 inches height. After completion of 100 rotations, the tablets were weighed again [$W_{(final)}$]. The friability (f) was calculated by the formula

$$f = \left[\frac{W_{(initial)} - W_{(final)}}{W_{(initial)}}\right] X\ 100$$

Weight variation:

Ten tablets were selected randomly from each batch were weighed individually and together in a single pan balance. The average weight was noted and standard deviation calculated.

$$\%\ Deviation = \frac{individual - Averageweight}{Averageweight} \times 100$$

Drug content uniformity:

10 tablets were collected randomly and powered using a mortar and pestle. A quantity of the powder equivalent to the weight of one tablet (100mg drug) was transferred to a 100ml volumetric flask and was dissolved in 1.2 pH buffer and volume was made up to 100ml to give a concentration of 1000µg/ml. 1ml of this solution was taken and diluted to 10ml to give a concentration of 100µg/ml. The absorbance of the prepared solution was measured at 270 nm using UV Visible spectrophotometer

$$\%\ Drug\ content = \frac{Drug\ content}{Labeled\ claim} X\ 100$$

Swelling studies:[1]

The dried superporous hydrogel (100 mg) was immersed in excess of the swelling medium (20 ml) at 37^{o}C. The swelling behavior of a dosage form was measured by studying its weight gain or water uptake. Water uptake was measured in terms of percent weight gain, as given by the equation.

$$WU = \frac{(W1 - W0) \times 100}{W0}$$

Wt = Weight of dosage form at time t.
W0 = Initial weight of dosage form

Porosity measurement:

For porosity measurement, the solvent replacement method was used. Dried hydrogels were immersed overnight in absolute ethanol and weighed after excess ethanol on the surface was blotted. The porosity was calculated from the following equation:

$$Porosity = (M2 - M1) / \rho V$$

Where M1 and M2 are the mass of the hydrogel before and after immersion in absolute ethanol, respectively; ρ is the density of absolute ethanol and V is the volume of the hydrogel.

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.

In-vitro Drug release studies:

*In-vitro*drug release of the samples was carried out using USP– type II dissolution apparatus (paddle type). The dissolution medium, 900 ml 0.1N Hcl solution, was placed into the dissolution flask maintaining the temperature of 37 ± 0.5°C using 50rpm. Samples measuring 5 ml were withdrawn at regular intervals upto 8 hours using 5 ml syringe. The fresh dissolution medium (37°C) was replaced every time with the same quantity (5ml) of dissolution medium. Collected samples were suitably diluted with 0.1N Hcl and analyzed at 270 nm using 0.1N Hcl as blankby using a double beam UV spectrophotometer (T60 UV-VISIBLE spectrophotometer).

Accelerated Stability study:[6]

To determine its shelf life i.e. stability study same formulations were subjectedfor further stability study. For this packed final sample was packed in aluminum foil and sealed it and kept above packed formulation at following condition for 30days.

1. **40^0C± 2^0C/ 75%RH ±5% RH**
2. **25^0C±2^0C/60% RH ± 5% RH**
3. **30^0C±2^0C/65% RH ± 5% RH**

Results and Discussion

Drug excipient compatibility:

Drug and excipient compatibility was confirmed by comparing spectra of FTIR analysis of pure drug with that of various excipients used in the formulation.The ft-ir graphs showing the compatibility of drug with the polymers as shown in fig 1&2.

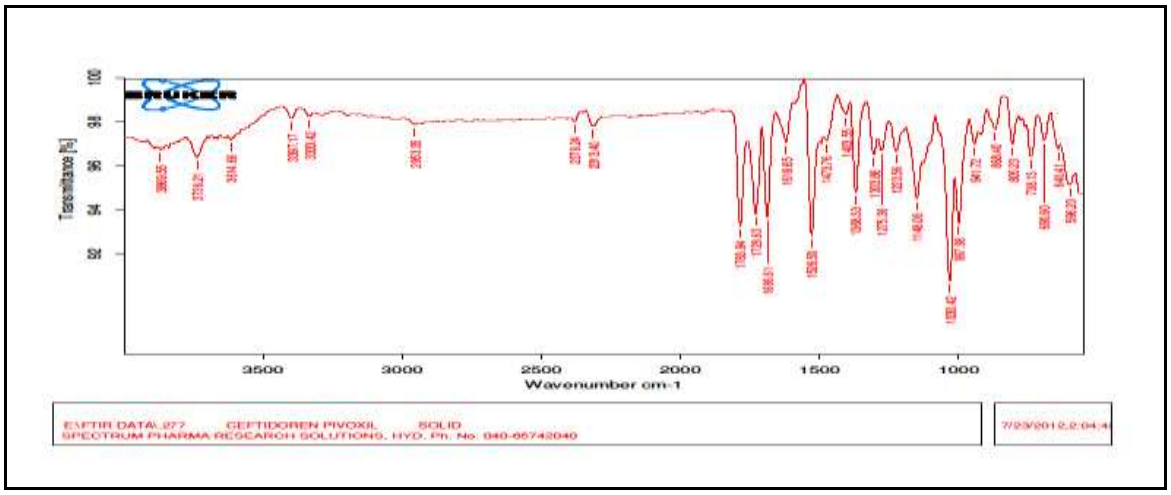

Fig 1: FT-IR spectra of pure drug Cefditoren pivoxil

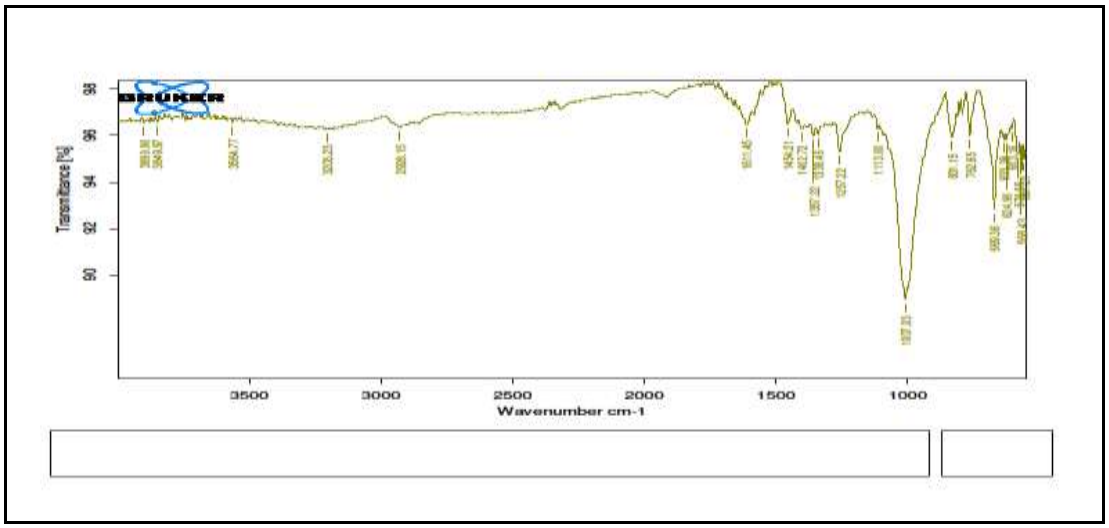

Fig 2: FT-IR spectra of best formulation F4

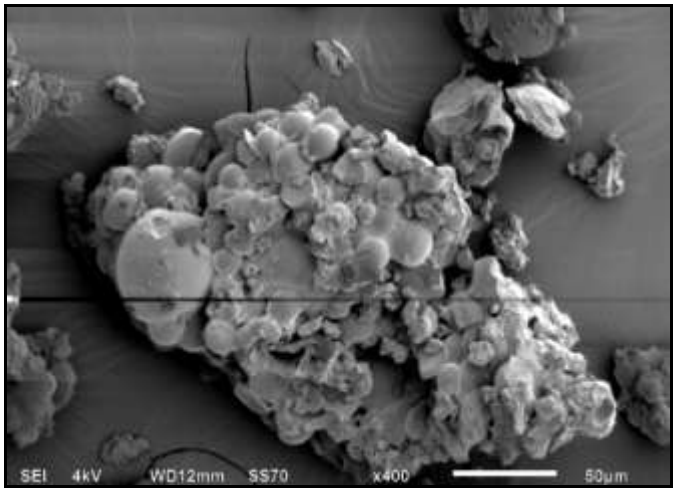

Fig 3: Scanning electron microscopic photograph of formulation IV recorded at 400X magnification with scale bar of 50µm showing porous surface.

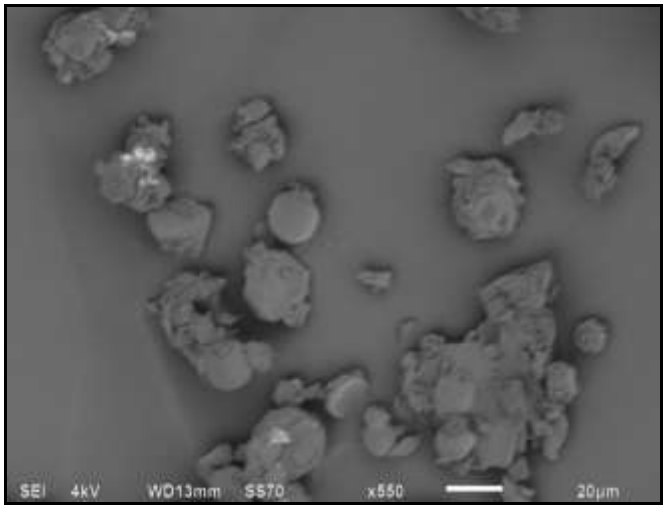

Fig 4: Scanning electron microscopic photograph of formulation IV recorded at 550X magnification with scale bar of 50µm showing porous surface.

Scanning electron microscopy:

The scanning electron microscopic photograph of superporous hydrogel shown in Figure.3&4 clearly shows the presence of pores on the surface. The superporous hydrogel has high porosity and is responsible for faster swelling of superporous hydrogels.The mechanical strength was significantly increased.

Evaluation of Dry Mixed Powder Blend for Pre-Compressional Parameters:

Bulk density may influence compressibility, tablet porosity, dissolution and other properties and depends on the particle size, shape and tendency of particles toadhere together. The bulk density and tapped density of powder blend was found to be between 0.532 ± 0.03 to 0.559 ± 0.02g/cm3 and 0.399 ± 0.03 to 0.471 ± 0.03. This indicates good packing capacity of powder blend .Carr's index evaluated interparticulate cohesive properties with angle of repose measurements and studied the effects of packing geometry of solids with bulk and tapped density.

This ratio, percent compressibility, was used as an index of flow. Adhesive/cohesive forces of particles are related to flow behaviour. Values of Carr's index below 15 % usually show good flow characteristics, but readings above 25 % indicate poor flow ability. Carr's index was found to be between 13.05 ± 1.21 to 14.93 ± 0.78. Hausner's ratio is simple method to evaluate stability of powder column and to estimate flow properties. Hausner's ratio was found 1.11 ± 0.11 to 1.18 ± 0.21.

Many different types of angular properties have been employed to assess flow ability. Angleof repose is suited for particles >150 m. Values of angle of repose $\leq 30^0$ generally indicate the free flowing material and angle of $\geq 40^0$ suggest a poor flowing material.The angle of repose is indicative of the flow ability of the material. The angle of repose of all the formulations fell within the range of $31.16^o \pm 0.622$ to $34.38^o \pm 0.231$ i.e. granules were of good flow properties. All rhe values are depicted in table 2.

Table 2 : Precompression parameters of all the SPH's Formulations:

Formulation Code	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	$32.31^o \pm 0.512$	0.533±0.03	0.407 ±0.013	14.18±0.19	1.16±0.11
F2	$33.39^o \pm 0.731$	0.537±0.01	0.418 ±0.017	14.13±0.41	1.16±0.45
F3	$34.36^o \pm 0.629$	0.541±0.03	0.454 ±0.021	14.11 ±0.32	1.17 ±0.19
F4	$32.28^o \pm 0.321$	0.532±0.03	0.399 ±0.073	15.03±0.84	1.18±0.02
F5	$33.07^o \pm 0.631$	0.539±0.08	0.407 ±0.066	14.05±0.71	1.16 ±0.07
F6	$31.38^o \pm 1.731$	0.559±0.02	0.471±0.033	13.50 ±1.21	1.16 ±0.12
F7	$31.16^o \pm 0.622$	0.554±0.08	0.399 ±0.091	14.93 ±0.78	1.17±0.03
F8	$32.35^o \pm 0.55$	0.538±0.02	0.422 ±0.038	13.05 ±1.21	1.16±0.12
F9	$33.19^o \pm 0.621$	0.554±0.08	0.443 ±0.031	14.28 ±0.23	1.18±0.02
F10	$34.36^o \pm 0.629$	0.537±0.01	0.422 ±0.038	14.28 ±0.31	1.16±0.30
F11	$34.38^o \pm 0.231$	0.554±0.08	0.399 ±0.031	13.50±1.21	1.11±0.11
F12	$31.38^o \pm 0.310$	0.537±0.01	0.407 ±0.049	14.28±0.21	1.18±0.21

Evaluation of Prepared tablets:

The tablets prepared of all formulations were evaluated for quality control parameters, Weight variation, Hardness, Friability, Drug content uniformity, and thickness. All formulations had average tablet weight in the range of 494-498 mg and thickness was within 4.4mm. The hardness of tablets varied from 4.9-6.5 Kg/cm^2.The friability of tablets is also depends on type of filler and moisture contents in it.The friability was in range of 0.201±0.04 to 0.703± 0.35and finally friability was less than 0.8% Drug content uniformity of all tablets was in the range of 98.84±0.69-100.1±0.83indicating good content uniformity in the all formulations.

The reading complies as per I P. That indicates drug was uniformly distributed throughout the tablet shown in Table 3.

Table 3: Evaluation of Prepared Cefditoren Pivoxil Superporous Hydrogel Tablets

Formulation Code	Hardness (Kg/cm^2)	Thickness (mm)	Friability%	Weight variation (%)	Drug content (%)	Swelling index	
F1	5.8 ±0.13	4.2 ± 0.02	0.501±0.04	498±2.5	98.95±0.88	47.35 ± 0.23	
F2	5.9±0.19	3.9 ± 0.02	0.502±1.15	496±3.2	100.1±0.83	58.00 ± 0.14	
F3	6.2±0.21	3.8 ± 0.07	0.602±0.03	497±2.7	99.73±0.87	40.00 ± 0.12	
F4	5.7 ±0.11	3.9 ± 0.05	0.571±0.04	495±2.5	100.8±0.64	72.60 ± 0.80	
F5	5.0 ±0.63	4.3 ± 0.03	0.520±0.04	488±3.2	99.4±0.58	52.75 ± 0.56	
F6	4.9±0.30	3.9 ± 0.07	0.460±0.06	495±3.5	99.99±0.8	74.50 ± 0.20	
F7	5.9 ±0.16	4.2 ± 0.05	0.501±0.04	496±3.2	99.8±0.42	48.80 ± 0.26	
F8	6.2±0.26	4.4 ± 0.24	0.602±0.03	498±3.5	99.9±0.5	69.40 ± 0.32	
F9	6.5±0.18	3.9± 0.05	0.703± 0.35	496±3.2	98.84±0.69	68.50 ± 0.16	
F10	5.1±0.47	4.2± 0.05	0.601± 0.04	497±2.7	99.98±0.62	78.42 ± 0.78	
F11	4.9 ±0.29	4.0 ± 0.06	0.201±0.04	494±4.3	98.8±0.42	74.40 ± 0.45	
F12	5.1±0.31	4.3 ± 0.03	0.401±0.26	497±4.2	99.9±0.5	65.38±0.92	

Water uptake study (swelling index):

Tablets composed of polymeric matrices build a gel layer around the tablets core when they come in contact with water. This gel layer governs the drug release.Kinetics of swelling is important because the gel barrier is formed with water permeation. Swelling is also a vital factor to ensure floating.The swelling index was in range 40.00 ± 0.12 to 78.42 ± 0.78.F10 tablet formulation having higher swelling index. The reason for higher swelling index values appeared to be CP act as channelling agent, thereby it allows more permeation of water into the gel layer and thereby it enhances the water retention property. This could be the reason for more moisture uptake by tablets from F10, F11 and F12 and moisture uptake values are given in Table 3.

Dissolution study of tablets:

The formulation Fl, F2, F3 F4 prepared with chitosan based formaldehyde shows tablet swelling in the range of 7±6min to 720±110 min respectively,The relases of Cefditoren Pivoxil from all the formulations were in the range of 24.60 to 99.21% at the end of 8hrs.The formulations F5, F6, F7, F8 which are prepared by using chitosan based urea-formaldehyde releases Cefditoren Pivoxil from all the formulations were in the range of 50.6 to 98.9% at the end of 8hrs.The formulations F9, F10, F11, F12 which are prepared by using chitosan based sodium tripolyphosphate releases drug from all formulations were in the range of 10.6 to51.3% at the end of 8hrs. The detailed in-vitro release data of all the formulations were given in Table 4at the end of 8hrs.

Table 4: Cumulative % drug release profile ofCefditoren Pivoxil Superporous Hydrogel tablets prepared by Direct Compression Method.

Time (hours)	Cumulative % drug release					
	F1	F2	F3	F4	F5	F6
1	45.64	40.54	35.63	24.65	67.80	61.20
2	62.31	59.30	46.81	37.80	85.60	80.30
3	71.60	68.20	55.87	46.20	93.83	89.41
4	83.47	79.31	69.70	59.30	98.90	91.60
5	91.87	87.62	80.23	71.30		100.20
6	99.85	98.41	90.89	83.82		
7			100.21	91.41		
8				99.20		
Time	Cumulative % drug release					

(hours)	F7	F8	F9	F10	F11	F12
1	59.30	50.67738	10.65	9.20	10.16	5.42
2	80.30	78.79516	21.51	12.81	15.62	9.61
3	83.41	85.66113	23.80	17.81	18.34	11.21
4	87.62	87.29588	33.40	23.82	20.20	15.62
5	98.81	95.46965	35.80	29.81	23.60	19.32
6		98.73916	39.41	40.10	29.45	25.60
7			45.61	42.31	34.81	29.45
8			51.30	47.83	38.90	32.30

Curve fitting analysis for different formulations:

In-vitro drug release data of all the formulations was subjected to goodness of fit test by linear regression analysis according to zero order and first order kinetic equations, Higuchi‟s and Korsmeyer–Peppas models to ascertain the mechanism of drug release. The results of linear regression analysis including regression coefficients are summarized in Table 5.

Table 5: Curve fitting analysis for different formulations

FC	Zero order (R^2)	First order (R^2)	Higuchi's (R^2)	Peppa's (R^2)
F1	0.878	0.527	0.996	0.474
F2	0.901	0.545	0.998	0.494
F3	0.951	0.557	0.988	0.539
F4	0.980	0.604	0.970	0.625
F5	0.764	0.568	0.955	0.386
F6	0.755	0.515	0.952	0.409
F7	0.755	0.515	0.948	0.409
F8	0.754	0.486	0.946	0.441
F9	0.966	0.653	0.971	0.693
F10	0.989	0.752	0.913	0.764
F11	0.969	0.664	0.951	0.674
F12	0.991	0.808	0.907	0.825

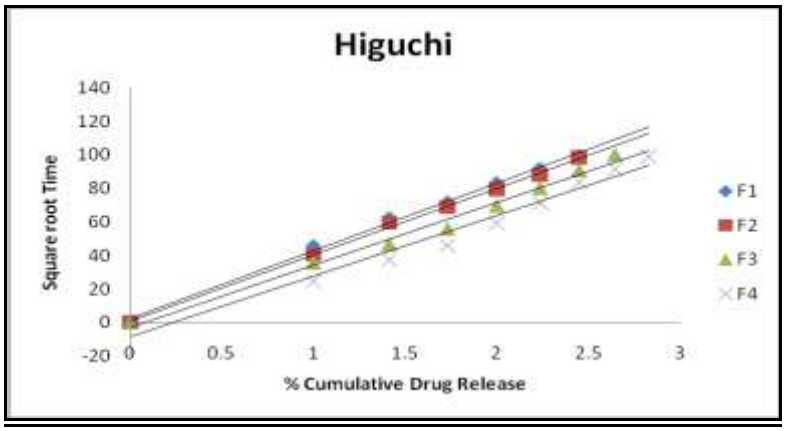

Fig 5: Cumulative percent drug released vs Square root of time (Higuchi's plot) Of formulation F1, F2, F3, F4(with formaldehyde).

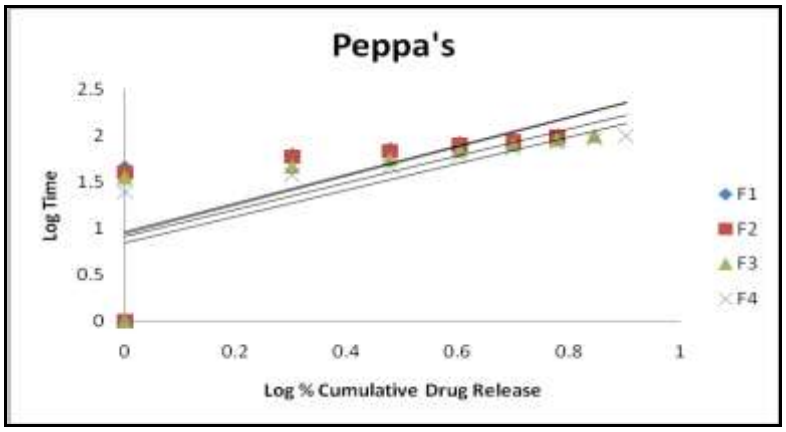

Fig 6: Log cumulative percent drug released vs Log time (peppas plot) of formulation F1, F2, F3, F4(with formaldehyde).

stability studies:

The most promised formulations were selected stability studies. Three month stability studies were performed as per ICH guidelines at a temperature of 450 ± 10C over a period of three month on the promising SPH's tablet formulation F4.Sufficient number of tablets (10) were packed in aluminium packing and kept in stability chamber maintained at 45 ± 10C / 75 ± 5 % RH for 3 months. Samples were taken at weekly intervals for drug content estimation. At the end of three weeks period, dissolution test and in-vitro floating studies were performed to determine the drug release profiles, the estimation of drug contents and data of dissolution and in-vitro dissolution studies are shown in table 6.

Table 6: Drug Content Data Stability Formulation F4

Sl. No.	Trial No.	st 1 Day (%)	th 30 Day (%)	th 60 Day (%)	St 90 Day (%)
1.	I	99.98	99.80	99.96	99.90
2.	II	99.95	99.38	99.88	99.91
3.	III	99. 53	99.32	99.42	99. 43
4.	Mean	99.57	99.50	99.75	99.78

Conclusion

The results conclusively demonstrated that Superporous Hydrogel tablets of Cefditoren Pivoxilwere effectively prepared with desired properties.Superporous Hydrogel tablets of Cefditoren Pivoxil were prepared by direct compression method. The directly compressed formulations exhibited better in-vitro drug release profiles. The formulation F4 prepared by direct compression containing chitosan based formaldehyde prepared by cross-linking technique exhibited good swelling index and maximum rate of drug release. So, this formulation was considered to be the optimized formulation. The prepared tablet formulations are evaluated for different pre-compressionaland post compressional parameters the results revealed that the all formulations shows good pre-compressional properties showing better flowability, hardness is maintained in the range of 4.9 to 6.9 kg/cm2 which provides good mechanical strength to the tablet. Other parameters like weight variation, friability, thickness, drug content are in the range of prescribed limits of IP.Thus the formulated Superporous Hydrogel tablets of Cefditoren Pivoxiloffer a superior alternative over conventional marketed dosage forms in regards of Localized action and Sustained release of drug.FTIR studies combined with stability studies proved the integrity of the developed tablets along with sem analysis gives improved information of the formulation by showing porous formation.Therefore the prepared tablets shows improved bioavailability with increased drug release.

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