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Design, Characterization and *In-vitro* Evaluation of Superporous Hydrogel Tablets of Nimodipine

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ABSTRACT

The present work was aimed to formulate Superporous Hydrogel tablets of Nimodipine using an effervescent approach for gastro retentive drug delivery system to improve its bioavailability by using different rate retarding polymers like plantago ovata, tamarind gum and carbopol, along with suitable excipients. All the formulations were prepared by direct compressionmethod. The prepared tablets of all the formulations were evaluated for physical characteristics, in-vitro drug release, hardness and friability. Optimized formulation F8 containing 0.3% of plantago ovata and carbopol each was considered as the best formulation with respect to in vitro drug release for 12 hours release action. The results showed that the drug release rate was decreased as the viscosity of the polymer was increased. The drug release kinetics was performed for the optimized formulation and it shows zero orderwith non-fickian transport drug release.

Keywords: Superporous Hydrogel tablets, Nimodipine, plantago ovata, tamarind gum and carbopol, non-fickian transport drug release.

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INTRODUCTION

Nimodipine is a 1,4-dihydropyridine calcium channel blocker originally developed for the treatment of high blood pressure. It acts primarily on vascular smooth muscle cells by stabilizing voltage-gated L-type calcium channels in their inactive conformation. By inhibiting the influx of calcium in smooth muscle cells, nimodipine prevents calcium-dependent smooth muscle contraction and subsequent vasoconstriction. Compared to other calcium channel blocking agents, nimodipine exhibits greater effects on cerebral circulation than on peripheral circulation. Nimodipine is used to act as an adjunct to improve the neurologic outcome following subarachnoid hemorrhage from ruptured intracranial aneurysm[1-6].

Superporous hydrogels (SPHs) were originally developed as a 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. 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.Maximum swelling is generally reached in a fraction of a minute with SPHs having average pores of 200mm in size. 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[7-11].

Superporous hydrogels are one of the important approaches to achieve gastric retention to obtain sufficient drug bioavailability. This delivery system is desirable for enhancing the bioavailability and produce prolonged action in GIT. Orally-administered Nimodipine is rapidly and completely absorbed from the gastrointestinal tract[8, 12-17].

This approach includes the development of Nimodipine Super porous Hydrogel tablets. Nimodipine is a calcium channel blocker which is originally developed in the treatment of high blood pressure.Nimodipine has a half-life of 8-9 h, the bioavailability of 13% and it has narrow

absorption window in upper part of the gastrointestinal tract (GIT), hence gastric drug delivery system (GDDS) is preferred for enhanced absorption and increased bioavailabilty of the drug[15, 18, 19].

MATERIALS AND METHODS

Materials:

Nimodipine purchased from Biophore India pharmaceutical Pvt.Ltd Hyderabad, Plantago ovata, Tamarind gum, Carbopol, Sodium bicarbonate, Citric acid, Glyoxal, PVA, Magnesium stearate, Talc, Micro crystalline cellulose and Hydrochloric acid were used. All the reagents used are of LR grade.

Method of Preparation of Tablets:

The drug loaded SPHs are prepared by direct compression method:

Hydrocolloid polymer solution (1%w/v) was prepared by stirring in distilled water using a homogenizer until the polymer dissolves in distilled water completely. A 1% w/w aqueous PVA solution was prepared and mixed to the polymer solution. To this solution, 0.2% of Glyoxal (10% w/w of the dry weight of polymers) was mixed thoroughly followed by 50 mg of sodium bicarbonate & 25mg of citric acid. The prepared mixture was stirred well and kept aside overnight. 10 ml of 0.1 N HCL was taken to this 30 mg of drug and 100 mg of superporous hydrogel were added and mixed for 1 h at 50°C. Then acetone of 2ml was added and the hydrogel was repeatedly washed with distilled water to remove any unreacted material. Further it was dried at 40°C for 24h, finally powdered and stored in a well closed container.

Preformulation Studies:

Determination of absorption maximum (λmax)[19, 20]:

Accurately weighed 10mg of Nimodipine was dissolved in 0.1N Hcl (pH 1.2) taken in a clean 10ml volumetric flask. The volume was made up to 10ml with 0.1N Hcl which will give stock solution-I with concentration 1000µg/ml. From the stock solution-I, 1ml was pipette out in 10ml volumetric flask. The volume was made up to 10ml using 0.1N Hcl to obtain stock solution-II with a concentration 100µg/ml. From stock solution-II, 1ml was pipette out in 10ml volumetric flask. The volume was made up to 10ml using 0.1N Hcl to get a concentration of 10µg/ml. This solution was then scanned at 200-400nm in UV-Visible double beam spectrophotometer to attain the absorption maximum (λmax).

Construction of calibration curve using 0.1 N HCL (pH 1.2) [19, 20]:

Standard calibration curve of Nimodipine in buffer pH 1.2:

- **Standard solution:** Accurately weighed 10mg of Nimodipine was dissolved in methanol taken in a clean 10ml volumetric flask. The volume was made up to 10ml with methanol which gives a concentration of 1000µg/ml.
- **Stock solution:** From this standard solution, 1ml was pipette out in 10ml volumetric flask and volume was made up to 10ml using 0.1N Hcl to obtain a concentration of 100µg/ml. From the above stock solution, aliquots of 0.5, 1, 1.5, 2, 2.5 and 3 ml each was transferred to a separate 10ml volumetric flask and solution was made up to 10ml using 0.1N Hcl to obtain a concentration of 5, 10, 15, 20, 25 and 30µg/ml respectively. The absorbance of each solution was measured at 292nm.

Drug excipient compatibility study: [19, 20]

The drug and excipient compatibility was observed using Fourier Transform – Infra Red spectroscopy (FT-IR). The FT-IR spectra obtained from Bruker FT-IR Germany (Alpha T) was utilized in determining any possible interaction between the pure drug and the excipients in the solid state. The potassium bromide pellets were prepared on KBr press by grounding the solid powder sample with 100 times the quantity of KBr in a mortar. The finely grounded powder was then introduced into a stainless steel die and was compressed between polished steel anvils at a pressure of about 8t/in^2. The spectra were recorded over the wave number of 8000 to 400cm^{-1}.

Flow properties: [19, 20, 21]

(Precompression Parameters):

1. Angle of repose: Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane. The flow characteristics are measured by angle of repose. A specific amount of powder was collected in a glass funnel by blocking the orifice with thumb at the stem opening. The funnel was fixed at a height of 2cm from a horizontal plate. After the adjustment is done the thumb is removed and the powder is allowed to flow over the plate to form a pile. The height of the pile was noted. A Circumference was drawn with a pencil on a graph paper and the radius of base of a pile was measured at 5 different points and average was taken for calculation.

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

Therefore,

$$\boldsymbol{\theta = \tan^{-1} h/r}$$

Where h = height of pile.

r = radius of the base of the pile.

θ = angle of repose.

Table No.1.1: Flow Properties and corresponding angles of repose

Flow Property	Angle Of Repose (degrees)
Excellent	25 – 30
Good	31 – 35
Fair (aid not needed)	36 – 40
Passable (may hang up)	41 – 45
Poor (must agitate, vibrate)	46 – 55
Very poor	56 – 65
Very, Very poor	> 66

2. Bulk density: The bulk density of a powder is the ratio of the mass of an untapped powder sample and its volume including the part of the interparticulate void volume. 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[19, 21].

$$\mathbf{P = W/V_b}$$

Where P = bulk density.

W = mass of the powder blend.

V_b = bulk volume of powder blend.

3. Tapped density: Tapped density is the ratio of mass of powder to the tapped volume. Tapped volume is the volume occupied by the same mass of powder after a standard tapping of measure. [19, 20]

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. The process of tapings was continued until concurrent volume is achieved. This final volume is tapped volume and the tapped density was calculated using the following equation and expressed as gm/ml.

$$P_{b,\,max} = W/V_{50}$$

Where $P_{b,\,max}$ = tapped density.

W = mass of the powder blend.

V_{50} = volume of powder blend at 50 taps.

4. 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 is simple, fast and popular method of predicting powder flow characteristics. It was calculated by using following formula:

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

Table No.1.2: Carr's index as an indication of granule flow properties

% CI	Properties
5-12	Free flowing
12-16	Good
18-21	Fair
23-35	Poor
33-38	Very poor
>40	Extremely poor

5. Hausner's ratio: A similar index has been defined by hausner in order to determine the flow property. Hausner's ratio greater than 1.25 is considered to be an indication of poor flowability. It was calculated by using following formula:

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Table No.1.3: Hausner ratio as an indication of granule flow properties

Hausner ratio	Properties
1.00 – 1.11	Excellent
1.12 – 1.18	Good
1.19 – 1.25	Fair
1.26 – 1.34	Passable
1.35 –1.45	Poor
1.46 – 1.59	Very poor
> 1.60	Extremely poor

Post compression parameters [18, 19, 20]:

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.

1) Tablet thickness and Diameter:

Thickness and diameter of tablets were important for uniformity of tablet size. Thickness and diameter were measured using Vernier calipers. The tablet thickness should be controlled within a ± 5% variation of a standard value. The thickness of the tablet is mostly related to the tablet hardness can be uses as initial control parameter. It is expressed in millimeters (mm).

2) 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. The tablet passes the test if not more than two tablets fall outside the percentage limit and none of the tablet differs by more than double the percentage limit.

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

Table No.1.4: IP Standard values of % deviation

Average weight	% deviation
80mg or less	10
More than 80mg but less than 250mg	7.5
250mg or more	5

3) Hardness:

Tablet hardness has been defined as the force required break ing a tablet in adiametric compression test. The hardness of the tablets was determined using pfizer hardness tester (cisco). Six tablets were picked randomly from each formulation for measurement. It is expressed in Kg/cm^2.

4) Friability:

The friability test was carried out to evaluate tablet surfaces and/or show evidence of lamination or capping when subjected to mechanical shock or attrition. The friability of tablets was determined by using Roche friabilator (Lab India, FT 1020) and expressed in %. Ten tablets 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 i.e., 25 rpm for 4 minutes, the tablets were weighed again [$W_{(final)}$]. The friability (f) was calculated by the formula

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

Values from 0.8-1.0% are regarded as the upper limit of acceptability

5) Drug content uniformity:

The test is used to ensure that every tablet contains the amount of drug intended with little variation among tablets within a batch. From each batch of the formulation, 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. The powder equivalent to 100mg drug 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 263 nm using UV Visible spectrophotometer (PG Instruments T60) and the drug concentration was determined from the standard calibration curve by using the regression equation. The preparation passes the test if individual drug content is 85-115% of the average content.

6) Swelling studies[18-22]:

i) Swelling Study:

The dried superporous hydrogel (100 mg) was immersed in excess of the swelling medium (20 ml) at 37°C. The swelling behavior of a dosage form was measured by studying its weight gain or water untake the dimensional changes could be measured in terms of the increase in tablet diameter and/or thickness over time. 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

ii) Measurement of density of superporous hydrogel:

The density (d) of the dried hydrogels was calculated.

d = Wd/Vd

where,

Wd = weight of dried hydrogel and Vd = volume.

The volume of the hydrogel was determined by the solvent displacement method using hexane as the displacement fluid. Hexane was used because it is very hydrophobic and superporous hydrogels do not absorb it.

iii) 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) / ρV

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.

iv) 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 the hydrogels in HCl solution (pH 1.2) up to equilibrium swelling. The dimensions of the swollen hydrogels were measured and by using these data, sample volumes were determined as the dimensional volume. In the meantime, the amount of absorbed buffer into the hydrogels was determined by subtracting the weight of dried hydrogel from the weight of swollen hydrogel and the resulting values were assigned as the total volume of pores in the hydrogels.

v) 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 = weight of the dried hydrogel, Ws = weight of the fully swollen hydrogel, and

Wp = weight of the hydrogel at various exposure times.

For determination of the water-retention capacity of the hydrogels as a function of the time of exposure at 37 °C, the water loss of the fully swollen polymer at timed intervals was determined by gravimetry.

7) 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).

8) 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 50 rpm. One Nimodipine tablet was placed in each paddle of dissolution apparatus. The apparatus was allowed to run for 12hours. Samples measuring 5 ml were withdrawn at regular intervals upto 12 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 263 nm using 0.1N Hcl as blank by using a double beam UV spectrophotometer (T60 UV-VISIBLE spectrophotometer). The cumulative percentage drug release was calculated. The graphs of time vs % release were plotted.To ascertain the order and mechanism of drug release the in vitro release data was

subjected to various kinetic equations.

Kinetic Models[22-26]:

Treatment of dissolution data with different kinetic equations:

To analyze the mechanism of release and release rate kinetics of the dosage form, the data obtained were fitted into Zero order, First order, Higuchi matrix,and Peppas.Based on the r- value, the best-fit model was selected.

1)Zero Order Kinetics:

A zero-order release would be predicted by the following equation:

$dQ/dt = K_0$

Where, Q = Drug released at time 't'

K_0= Zero-order rate constant (h-1).

When the data is plotted as cumulative percent drug released versus time, if the plot is linear then the data obeys zero-order release kinetics, with a slope equal to K_0.

2)First Order Kinetics:

To study the first order release rate kinetics, the release rate data were fitted to the following equation:

$dQ/dt = K_1Q$

Where, Q = Amount of drug remained at time 't'

K_1 = First-order rate constant (h-1).

When the data is plotted as log cumulative percent drug remaining versus time; yields a straight line, indicating that the release follows first-order kinetics. The constant 'K1' can be obtained by multiplying 2.303 with slope values.

3)Higuchi model[23]:

Higuchi developed several theoretical models to study the release of water soluble and low soluble drugs incorporated in semisolids and/or solid matrices. Mathematical expressions were obtained for drug particles dispersed in a uniform matrix behaving as the diffusion media. And the equation is,

$$Qt = KH \cdot t^{1/2}$$

Where, Qt = amount of drug released in time t,

KH = Higuchi dissolution constant

4) Korsmeyer and Peppas model[25]:

The release rate from sustained release polymeric matrices can be described by

the equation proposed by korsmeyer et al.

$$Q = K_{KP}tn$$

Where, Q = The amount of drug released at time 't'

K_{KP} = Kinetic constant incorporating structural and geometric characteristics of the tablets

'n' = The diffusional exponent, indicative of the release mechanism.

The release exponent, n, is the slope of log fraction of drug release versus log time curve.

Comparision with Marketed Product:

The dissolution time of optimized tablets were compared with marketed product Nimotop 30mg.

RESULTS AND DISCUSSION

Solubility study:

From the solubility studies it was observed that Nimodipine wasfoundtobemore soluble in 0.1N HCL pH1.2 buffer.

Melting point determination:

The melting point of Nimodipine was found to be 7°C

Determinationofλ_{max}

Wave length of maximum absorption of Nimodipine was found to be 263.40nm in 0.1N HCL buffer.

Calibration curve of Nimodipne at λmax of 263.40nm

Standard calibration data of Nimodipine was performed in 0.1N HCL.

Drug excipientinteraction (FTIR) study

FTIR Spectra were obtained for Nimodipine physical mixture, Nimodpine and excipients. The characteristic peaks of the Nimodipine were compared with the peaks obtained for physical mixture of Nimodipine and excipients. From the obtained spectra it appeared that there were no interaction between Nimodipine and excipients.

Surfacemorphology(SEM)

ThesurfacemorphologyoftheNimodipinetablets wasstudiedby SEM.SEM photographsof the optimizedformulationwere shown inthe Fig.1.5. Surface morphology of the formulated hydrogel indicates the porous nature of the hydrogel showing 10µ range.

Invitro dissolution studies:

From the invitro drug release studies it was observed that the formulations of gastro retentive superporus hydrogel tablets of Nimodipine formulated by using Plantago Ovata, Carbopol& Tamarind gum. The *invitro* performance ofNimodipine superporous hydrogel tablets showed sustained release of Nimodipine. As the polymer concentration was increased, the drug release from the hydrogels was found to decrease. Compared to Plantagoovata & tamarind gum, tamarind gum and carbopol, plantago ovate & carbopol shows optimum drug release at the end of 12 hours. The *invitro* release profiles of all the formulations(F1toF9) are shown in tables1.11 and Fig. 1.6to 1.9.

Release kinetics of Nimodipine superporous hydrogel tablets:

The invitro dissolution data for best formulation F8were fitted in different kinetic models i.e, zero order, first order, Higuchi and korsemeyer-peppas equation. Optimized formulation F8 shows R^2 value0.973. As its value nearer to the '1' it is conformed as it follows the zero order release. The mechanism of drug release is further confirmed by the Higuchi and peppas plot.

The 'n' value is 0.865 for the optimizedformulation (F8) i.e., n value was <0.89 this indicates non-fickian transport.

Comparision with Marketed product:

The dissolution time of optimized tablets were compared with marketed product Nimotop 30mg and optimized formulation F8 shown better dissolution profile compared with marketed tablets as shown in Table:1.13.

Table No.1.5: Wavelengthofmaximum absorptionof Nimodipine in 0.1N Hcl(pH1.2) buffer

Serial No:	Solvent	λmax
1	0.1N Hcl	263.40

Determination of absorption maximum (λmax):

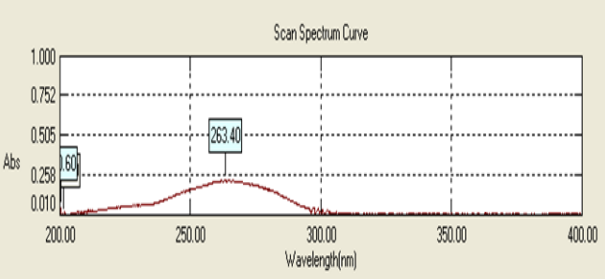

Fig 1.1: UV spectrum of Nimodipine

Table No.1.6: Standard graph of Nimodipine in 0.1 N Hcl (pH 1.2)

Concentration(µg/ml)	Absorbance
0	0
5	0.123±0.08
10	0.246±0.07
15	0.386±0.02
20	0.529±0.10
25	0.663±0.06
30	0.802±0.02

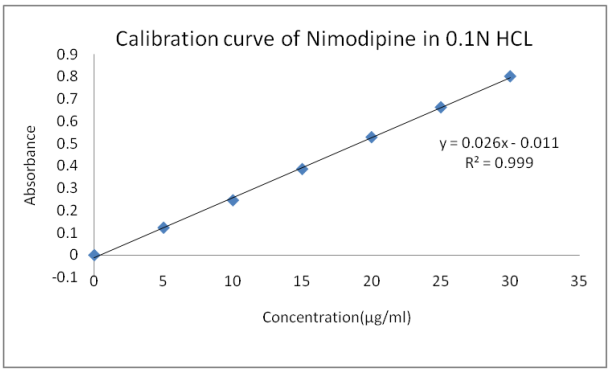

Fig 1.2: Calibration curve of Nimdipine

using 0.1 N Hcl (pH 1.2):

Table No.1.7: Formulations of Superporous hydrogel tablets of Nimodipine Prepared by Direct compression Method

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Nimodipine wt.equivalent to 30mg	30	30	30	30	30	30	30	30	30
sGlyoxal(%)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
PVA(%)	1	1	1	1	1	1	1	1	1
Plantago Ovata(%)	0.1	0.1	-	0.2	0.2	-	0.3	0.3	-
Tamarind gum(%)	0.1	-	0.1	0.2	-	0.2	0.3	-	0.3
Carbopol(%)	-	0.1	0.1	-	0.2	0.2	-	0.3	0.3
NAHCO3	50	50	50	50	50	50	50	50	50
Citric acid	25	25	25	25	25	25	25	25	25
MCC	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S.	Q.S	Q.S
Mg.stearate	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Talc	5	5	5	5	5	5	5	5	5
Tablet weight(mg)	250	250	250	250	250	250	250	250	250

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.

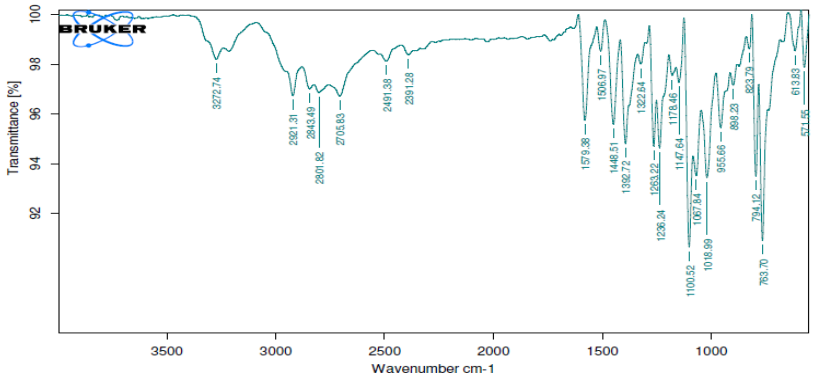

Fig 1.3: FT-IR spectra of pure drug

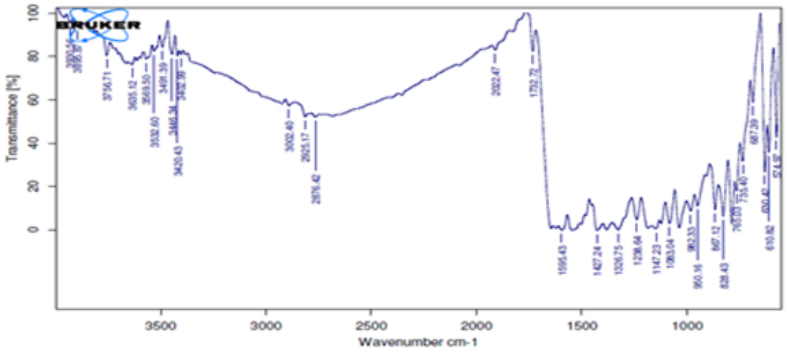

Fig 1.4: FTIR Spectra of optimized formulation

Flow Properties:

Pre compresssion parameters:

Table No 1.8: Flow properties of tablet blend.

Formulation code	Angle of repose (θ)	Tapped density (gm/ml)	Bulk density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	31.17±0.56	0.526±0.25	0.456±0.23	13.31±0.20	1.15±0.54
F2	30.16±0.14	0.539±0.44	0.461±0.43	14.47±0.43	1.17±0.17
F3	29.52±0.85	0.548±0.81	0.438±0.52	20.07±0.56	1.25±0.78
F4	30.47±0.23	0.586±0.59	0.493±0.86	15.87±0.89	1.19±0.85
F5	27.69±0.95	0.529±0.96	0.429±0.95	18.90±0.98	1.23±0.51
F6	28.53±1.05	0.514±0.65	0.415±0.68	19.26±0.65	1.24±0.98
F7	30.42±0.85	0.539±0.18	0.448±0.37	16.88±0.11	1.20±0.65
F8	33.18±0.23	0.514±0.64	0.439±0.14	14.59±0.54	1.17±0.34
F9	31.15±0.61	0.538±0.32	0.451±0.41	16.17±0.42	1.19±0.22

Post compression parameters

Table No 1.9: Evaluation of Prepared Nimodipine Superporous Hydrogel Tablets.

Formulation Code	Hardness (Kg/cm²)	Thickness (mm)	Friability%	Weight variation (%)	Drug content (%)
F1	6.6±0.18	4.2 ± 0.17	0.268±0.29	249.2±0.82	89.78±0.15
F2	6.4±0.28	3.3 ± 0.09	0.175±1.02	248.2±0.89	92.63±0.52
F3	6.8±0.56	3.0 ± 0.04	0.569±0.16	247.8±0.53	90.48±0.48
F4	6.2±0.17	3.6 ± 0.06	0.684±0.18	249.1±0.73	87.52±0.96
F5	7.2±0.53	3.2 ± 0.32	0.790±0.75	246.8±0.52	96.75±0.17
F6	6.8±0.29	3.6 ± 0.06	0.631±0.56	248.4±0.48	92.56±0.26
F7	6.9±0.17	4.3 ± 0.12	0.523±0.15	251.6±0.96	98.48±0.18
F8	6.1±0.28	3.7± 0.01	0.609±0.36	247.6±0.82	99.36±0.63
F9	6.5±0.36	3.9± 0.06	0.694± 0.84	246.8±0.96	96.15±0.45

Swelling Index:

Table No.1.10: Swelling Index of dried SPH's

Formulations	Swelling index(%)	Porosity (%)	Void fraction (ml/g)
F1	47.35 ± 0.23	40.22 ± 0.28	0.59 ± 0.03
F2	58.00 ± 0.14	62.84 ± 0.36	0.62 ± 0.04
F3	44.28 ± 0.18	58.49 ± 0.54	0.52 ± 0.01
F4	52.60 ± 0.80	52.69 ± 0.58	0.74 ± 0.03
F5	68.75 ± 0.56	71.82 ± 0.22	0.84 ± 0.02
F6	59.50 ± 0.20	69.16 ± 0.36	0.69 ± 0.04
F7	62.80 ± 0.26	64.86 ± 0.72	0.80 ± 0.03
F8	79.40 ± 0.32	80.02 ± 0.48	0.91 ± 0.01
F9	66.28 ± 0.16	72.66 ± 0.76	0.88 ± 0.03

Sem Analysis:

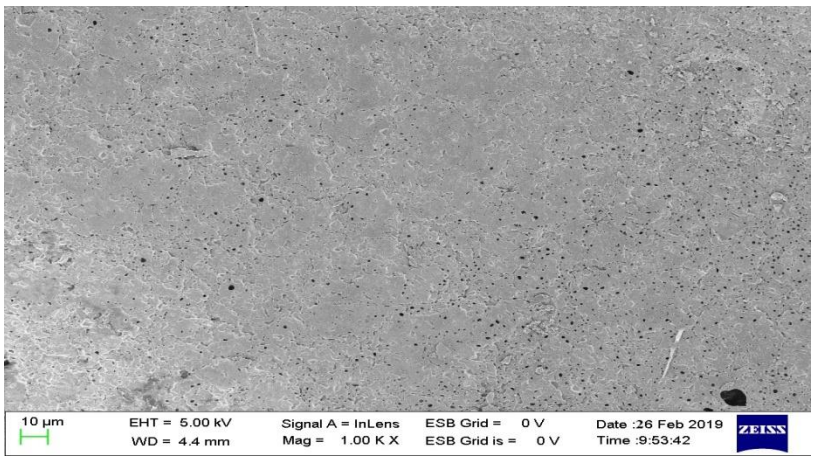

Fig.1.5: Surface morphology of the formulated hydrogel indicates the porous nature of the hydrogel showing 10µ range.

Dissolution Studies:

Table No.1.11: Cumulative % drug release profile of Nimodipine Superporous Hydrogel tablets prepared by Direct Compression Method

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	36.85±0.26	22.95±0.22	26.85±0.53	32.63±0.21	18.63±0.68	23.62±0.88	26.49±0.06	16.28±0.13	17.62±0.20
1	42.19±0.48	29.65±0.13	33.49±0.16	46.85±0.64	26.85±0.06	29.05±0.92	36.16±0.52	26.84±0.26	30.84±0.12
2	52.96±0.54	39.84±0.02	42.85±0.25	53.95±0.26	30.48±0.42	36.48±0.16	42.16±0.78	32.10±0.101	37.13±0.71
3	60.48±0.14	52.63±0.32	59.63±0.60	59.16±0.13	46.28±0.14	50.18±0.34	49.63±0.40	39.62±0.54	42.85±0.85
4	76.08±0.53	69.18±0.64	70.62±0.33	62.96±0.42	52.49±0.30	59.06±0.52	56.59±0.26	46.18±0.22	50.63±0.96
5	82.64±0.96	75.49±0.11	76.18±0.92	75.36±0.50	60.85±0.62	65.82±0.78	63.08±0.91	52.06±0.38	59.82±0.63
6	99.45±0.82	86.39±0.56	89.62±0.50	82.95±0.61	69.16±0.96	76.89±0.44	70.63±0.15	59.76±0.63	66.18±0.31
7		99.82±0.13	97.06±0.81	91.54±0.90	81.54±0.88	89.04±0.62	79.84±0.30	66.19±0.91	70.49±0.08
8			101.02±0.81	98.38±0.80	80.32±0.54	98.97±0.20	87.63±0.06	70.36±0.80	79.52±0.56
9					89.06±0.12		92.06±0.15	78.62±0.52	83.16±0.72
10					97.63±0.02		99.54±0.52	85.86±0.40	90.12±0.14
11					100.02±0.48			90.54±0.12	99.26±0.26
12								98.62±0.23	

***In-Vitro* Drug Release of F1-F9**

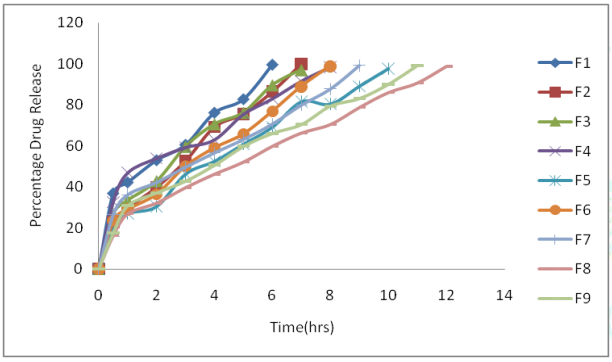

Fig.1.6: In *Vitro* Drug Release Of F1-F9

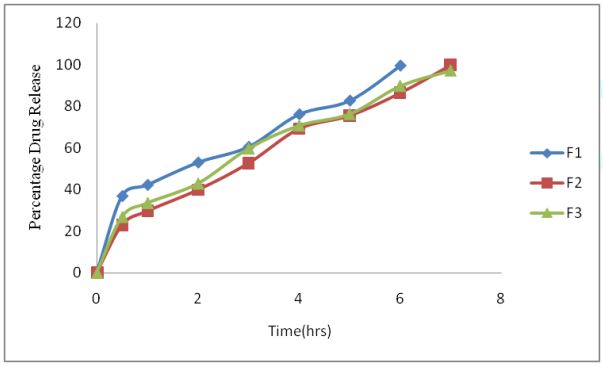

Fig.1.7: *In Vitro* Drug Release Of F1-F3

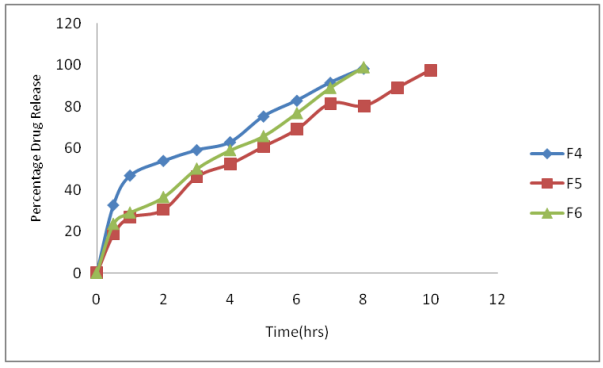

Fig.1.8: *In Vitro* Drug Release Of F4-F6

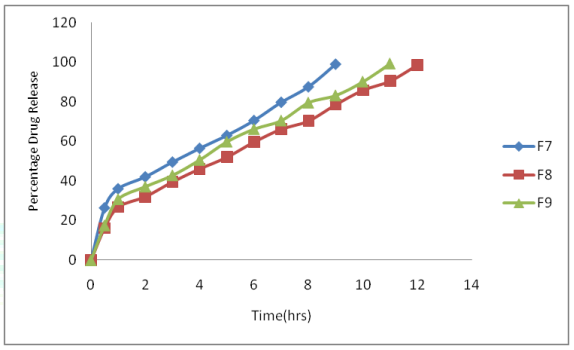

Fig.1.9: *In Vitro* Drug Release Of F7-F9

Drug Release Kinetics:

ZERO ORDER:

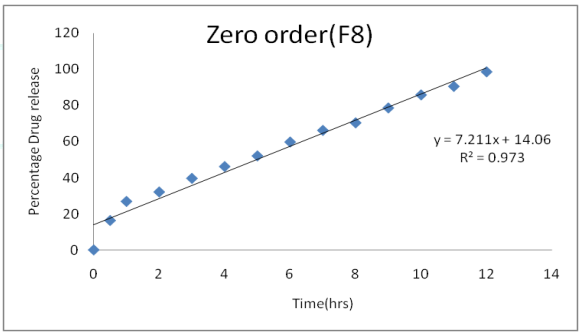

Fig.1.10: Zero order graph of optimized formulation

FIRST ORDER:

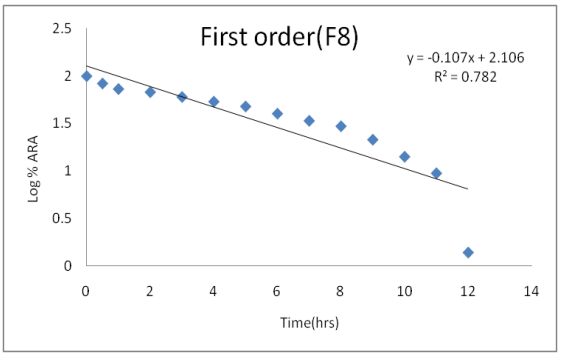

Fig.1.11: first order graph of optimized formulation

HIGUCHI:

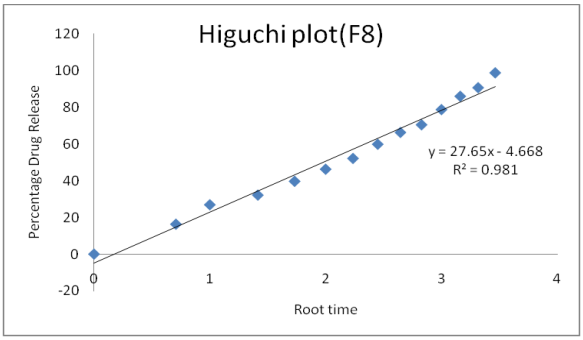

Fig.1.12: Higuchi graph of optimized formulation

PEPPAS:

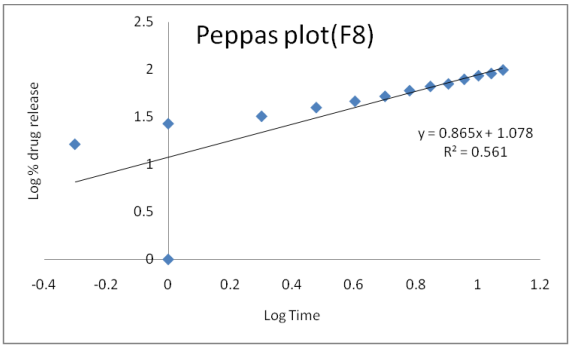

Fig.1.13: Peppas graph of optimized formulation

Table No.1.12: Drug release kinetics of optimized formulation(F8)

R^2 values					n values
Formulation	**Zero order**	**First order**	**Higuchi**	**Korsmeyer – Peppas**	**Korsmeyer-Peppas (n)**
F8	0.973	0.782	0.981	0.561	0.865

Table No.1.13: Comparision with Marketed product

Time(hrs)	Optimized Formulation(F8)	Nimotop 30mg
0	0	0
0.5	16.28±0.13	62.63±0.76
1	26.84±0.26	97.41±0.08
2	32.10±0.10	
3	39.62±0.54	
4	46.18±0.22	
5	52.06±0.38	
6	59.76±0.63	
7	66.19±0.91	
8	70.36±0.80	
9	78.62±0.52	
10	85.86±0.40	
11	90.54±0.12	
12	98.62±0.23	

CONCLUSION

The results obtained conclusively demonstrated that Superporous Hydrogel tablets of Nimodipine were effectively prepared with desired properties. Superporous Hydrogel tablets of Nimodipine were prepared by direct compression method. The directly compressed formulations exhibited better in-vitro drug release profiles. The formulation F8 prepared by direct compression containing combination of polymers (i.e., plantago ovate and carbopol)-Glyoxal 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-compressional and post compressional parameters the results revealed that the all formulations shows good precompressional properties showing better flowability, hardness is maintained in the range of 6.1-7.2kg/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 Nimodipine offer 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 time.

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