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FORMULATION AND IN VITRO EVALUATION OF HYDROGEL NIZATIDINE TABLETS

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ABSTRACT

Hydrogels 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 Nizatidine as hydrogel tablets, their applications and various evaluation technique. The aim of this study is to prepare Gastro retentive dosage form based on SPH using a model drug Nizatidine for swelling & prolonged drug release characteristics in acidic pH. The formulation is based on preparation of third generation hydrogels with three different polymers, such as, Sodium alginate, Hydroxy ethyl cellulose, Chitosan, PVPK30. were used with different concentrations by cross linking technique to get the desired sustained release profile over a period of time. The characterization studies for hydrogels, were performed by measurement of apparent density, porosity, swelling studies, mechanical strength, and FT-IR. All formulations were evaluated for stability, drug content and kinetic drug release & in-vitro drug release profile.

KEYWORDS: Gastro retentive dosage forms, hydrogels, chitosan, swelling, Nizatidine.

INTRODUCTION

In recent years, gastric retentive drug delivery systems are more effective drug delivery system. When, some of the drugs were formulated as controlled release dosage forms they can't attain the sufficient bioavailability and effective plasma level due to its less gastro

intestinal transit time.[1] By retention of such drugs in the stomach, we can prolong the overall gastrointestinal transit time and increase the bioavailability. This would be particularly valuable for the drugs that exhibit an absorption window in the upper part of the small intestine.[2] There are a number of approaches that can be used to prolong gastric retention time, such as floating drug delivery systems, swelling and expanding systems, polymeric bio-adhesive systems, and modified shape systems, high density systems and other delayed gastric emptying devices. From the formulation considerations, FDDS appears to be the most flexible and potent approach to prolong gastric residence time of drug.[3]

Nizatidine [N-[2-[[[2-(dimethylamino) methyl]-4-thiazolyl] methyl thio] ethyl]-N'-methyl-2-nitro-1, 1-ethenediamine] is competitive, reversible inhibitor of the histamine H_2 receptors of the gastric acid secreting cells.[4] It is also used for the treatment of acid-reflux disorders (GERD), peptic ulcer disease, active benign gastric ulcer and active duodenal ulcers.

It has a very short biological half-life 1-2 hours and low absolute oral bioavailability. It does not have any demonstrable anti-androgenic effects and drug interactions compared to any other class of H_2- receptor antagonists.[5] It also finds applications in the field of local delivery of drug to the stomach and proximal small intestine and importantly in treating microorganisms (Helicobacter pylori), which colonize the stomach because the major factors governing reduced luminal drug delivery are gastric acidity, gastric emptying and the epithelial mucus layer and therefore it helps to provide better availability of new products with new therapeutic possibilities and increased patient compliance.[6]

Aim

The aim is to design, develop & characterise a desired gastroretentive hydrogel formulations containing Nizatidine drug as an antacid and duodenal ulcers drug.

Objective

Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. To avoid this limitation, the development of oral sustained-controlled release formulations is an approach to release the drug slowly into the gastrointestinal tract (GIT) and maintain an effective drug concentration in the systemic circulation for a long time.

To formulate a site-specific orally administered controlled release dosage form, it is desirable to achieve a prolonged gastric residence time by the drug delivery. Prolonged gastric retention improves bioavailability, increases the duration of drug release, reduces drug waste, and improves the drug solubility that are less soluble in alkaline pH environment. Gastro retentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastro retentive dosage forms can remain in the gastric region for long period and hence significantly prolong the gastric retention time (GRT) of drugs.

One of the novel approaches in Gastro retentive drug delivery is swellable systems (hydrogels) which differ sufficiently from the conventional types to warrant separate The aim of the present study is to design and evaluate the effervescent floating tablets of Nizatidine by using different polymers like Chitosan, HPMC and Carbopol940 and gas generating agents like sodium bicarbonate and calcium carbonate.

Plan of work

To develop a desired gastro retentive hydrogel formulations containing Nizatidine drug as an antacid drug.

The experimental study was framed as follows

1. Carry out a literature review for gastro retentive hydrogel and drug.
2. Characterization of drug substances and other excipients for their physical and chemical behavior.
3. Construction of calibration curves for Nizatidine in pH 1.2 buffer solution
4. Polymers like Sodium alginate, Hydroxy ethyl cellulose, Chitosan, PVPK30. were used with different concentrations by crosslinking technique
5. Evaluation for the pre compression parameters.
6. Formulation development of gastro retentive hydrogels of Nizatidine by direct compression technique.
7. Evaluation of the compressed tablets.
8. Selection of optimized formula based on the invitro dissolution profile and other parameters.
9. Stability study of optimized formulation as per ICH guidelines.

To achieve the above aim and objectives the experimental work was framed as below

Preparation of standard curve for drug.

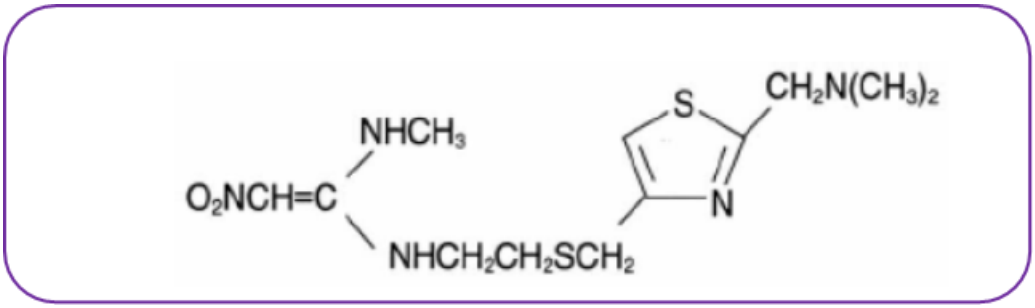
Compatibility study of drug with polymers by FT-IR.

To design and develop hydrogel tablets of a Antacid drug by direct compression.

Drug profile: Nizatidine

Description: A histamine H2 receptor antagonist with low toxicity that inhibits gastric acid secretion. The drug is used for the treatment of duodenal ulcers. [PubChem]

Structure



Iupacname

dimethyl[(4-{[(2-{[(E)-1-(methylamino)2nitroethenyl]amino}ethyl)sulfanyl]methyl}-1,3-thiazol-2-yl)methyl]amine.

Half Life: 1-2 hours

Chemical Formula: C12H21N5O2S2

Molecular Weight; 331.457

Indication: For the treatment of acid-reflux disorders (GERD), peptic ulcer disease, active benign gastric ulcer, and active duodenal ulcer.

Mechanisam of Action: Nizatidine competes with histamine for binding at the H2-receptors on the gastric basolateral membrane of parietal cells. Competitive inhibition results in reduction of basal and nocturnal gastric acid secretions. The drug also decreases the gastric acid response to stimuli such as food, caffeine, insulin, betazole, or pentagastrin.

Pharmaco dynamics: Nizatidine is a competitive, reversible inhibitor of histamine at the histamine H2-receptors, particularly those in the gastric parietal cells. By inhibiting the action of histamine on stomach cells, nizatidine reduces stomach acid production. Nizatidine had no

demonstrable antiandrogenic action. Full-dose therapy for the problems treated by nizatidine lasts no longer than 8 weeks.

Applications in pharmaceutical formulation or technology

Magnesium stearate is widely used in cosmetics, foods and pharmaceutical formulations.

It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25% and 5.0% w/w.

It is also used in barrier creams.

Preformulation studies

Prior to the development of tablet dosage form, it is essential that certain fundamental physical and chemical properties of the drug molecule alone and when combined with excipients are determined. This first learning phase is known as preformutation. The overall objective of the preformulation is to generate information useful to the formulator in developing stable and bioavailable dosage forms which can be mass produced.

The goals of preformulation studies are

To establish the necessary physicochemical characteristics of a drug substance, and

To establish its compatibility with different excipients.

Spectroscopic study

Identification of pure drug: Identification of Nizatidine was carried out by Infra Red Absorption Spectroscopy.

Determination of absorption maximum (λmax)

The wavelength at which maximum absorption of radiation takes place is called as λmax. This λmax is characteristic or unique for every substance and useful in identifying the substance. For accurate analytical work, it is important to determine the absorption maxima of the substance under study. Most drugs absorb radiation in ultraviolet region (190-390nm), as they are aromatic or contain double bonds.

Accurately weighed 100mg of Nizatidine was dissolved in 0.1N Hcl (pH 1.2) taken in a clean 100ml volumetric flask. The volume was made up to 100ml with 0.1N Hcl which will give stock solution-I with concentration 1000µg/ml. From the stock solution-I, 5ml was pipette out in 50ml volumetric flask. The volume was made up to 50ml 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 of nizatidine

a) Preparation of 0.1N HCl: 0.1N HCl was prepared according to IP 1996.Dissolved 2gm of sodium chloride and 7ml of hydrochloric acid in 1000 ml of volumetric flask and diluted with distilled water.

b) Standard calibration curve of nizatidine in buffer pH 1.2.

Standard solution: Accurately weighed 10mg of Nizatidine was dissolved in ethanol taken in a clean 10ml volumetric flask. The volume was made up to 10ml with ethanol 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, 3 and 3.5 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 315nm.

Drug excipient compatibility study

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. 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).

Flow properties (precompression parameters)

The flow properties of powders are critical for an efficient tableting operation. A good flow of powder or granulation is necessary to assure efficient mixing and acceptable weight uniformity of the compressed tablets. If a drug is identified to be "poorly flowable" at the pre- formulation stage, the problem can be solved by selecting appropriate excipients. In some cases, drug powders may have to be pre-compressed or granulated to improve their flow properties. During pre-formulation, evaluation of drug substance and its flow characteristics should be studied, especially when the anticipated dose of the drug is large.

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.

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

Preparation of sustained release superporous hydrogel tablets of nizatidine

Method

The main goal of this study was to prepare superporous hydrogel tablets of nizatidine by using direct compression method with chitosan and different polymers like sodium alginate, hydroxy ethyl cellulose, PVP k-30 in different ratios in combination with microcrystalline cellulose.

Procedure for the preparation of superporous hydrogel tablets

The superporous hydrogel tablets of nizatidine was formulated by incorporating prepared polymers like chitosan and different polymers like Sodium alginate, Hydroxy ethyl cellulose, PVP k-30 in different ratios in combination with microcrystalline cellulose.

Further more microcrystalline cellulose was utilized as diluents whereas magnesium stearate functioned as glidant and lubricant respectively.

The ingredients 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 nizatadine equivalent to 300mg were compressed by using suitable diameter, spherical tablet and adjusting thickness and hardness accordingly punches on a 16 station rotary compression machine. The content of each tablet is listed in Table. no. 4.6.

Table No. 4.6: Formulations of nizatidine tablets prepared by direct compression method

S.NO.	Ingredients (in mgs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	Nizatidine	150	150	150	150	150	150	150	150	150
2	Sodium alginate	20	40	60	_	_	_	_	_	_
3	Hydroxyl ethyl cellulose	_	_	_	20	40	60			
4	Chitosan	_	_	_	_	_	_	20	40	60
5	PVP k-30	4	4	4	4	4	4	4	4	4
6	Micro crystalline cellulose	122	102	92	122	102	92	122	102	92
7	Magnesium stearate	4	4	4	4	4	4	4	4	4
8	Tablet weight	300	300	300	300	300	300	300	300	300

* All quantities in mg per tablet, F=formulation codes

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 + 0.5oC using 50 rpm. One Nizatadine tablet was placed in each paddle of dissolution apparatus. The apparatus was allowed to run for 8hours. Samples measuring 5 ml were withdrawn at regular intervals upto 8 hours using 5 ml syringe. The fresh dissolution medium (37oC) was replaced every time with the same quantity (5ml) of dissolution medium. Collected samples were suitably diluted with 0.1N Hcl and analyzed at 315 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.

Details of parameters set: Paddle rpm: 50rpm Stirrer depth: 25mm

Dissolution medium: 1.2 PH buffer Media volume: 900ml Temperature: 37±0.5ºC

Sampling intervals: 1, 2, 3, 4, 5, 6, 7, 8, 9,10,11,12 hrs.

To ascertain the order and mechanism of drug release the in vitro release data was subjected to various kinetic equations.

Kinetic models

Treatment of dissolution data with diferent 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

Zero order kinetics

A zero-order release would be predicted by the following equation. dQ/dt = K0

Where, Q = Drug released at time ‘t K0= 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 K0.

First order kinetics

To study the first order release rate kinetics, the release rate data were fitted to the following equation, dQ/dt = K1Q

Where, Q = Amount of drug remained at time‘t’ K1 = 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.

Higuchi model

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 t1/2

Where, Qt = amount of drug released in time t, KH = Higuchi dissolution constant

Korsmeyer and Peppas model

The release rate from sustained release polymeric matrices can be described by the equation proposed by korsmeyer et al.

Q = Kkp tn

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

KKP = 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.

Accelerated stability study

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

1. 400C± 20C/ 75%RH ±5% RH
2. 250C±20C/60% RH ± 5% RH
3. 300C±20C/65% RH ± 5% RH

RESULTS AND DISCUSSIONS

RESULTS

Determination of absorption maximum (λmax)

Determination of Nizatidine λmax was done in 1.2 pH dissolution medium for accurate quantitative assessment of drug dissolution rate. The λmax was found to be 315nm.

Calibration curve of Nizatidine using 0.1 N Hcl (pH 1.2)

Nizatadine has the λmax at 315 nm. Standard graph of Nizatidine in ethanol and buffer solution was plotted and a good correlation was obtained with R2 value of 0.9990.

Table no. 5.1: Standard graph of Nizatadine1.2 pH.

S.No.	Concentration (µg/ml)	Absorbance
1	0	0
2	5	0.064
3	10	0.140
4	15	0.221
5	20	0.266
6	25	0.347
7	30	0.414

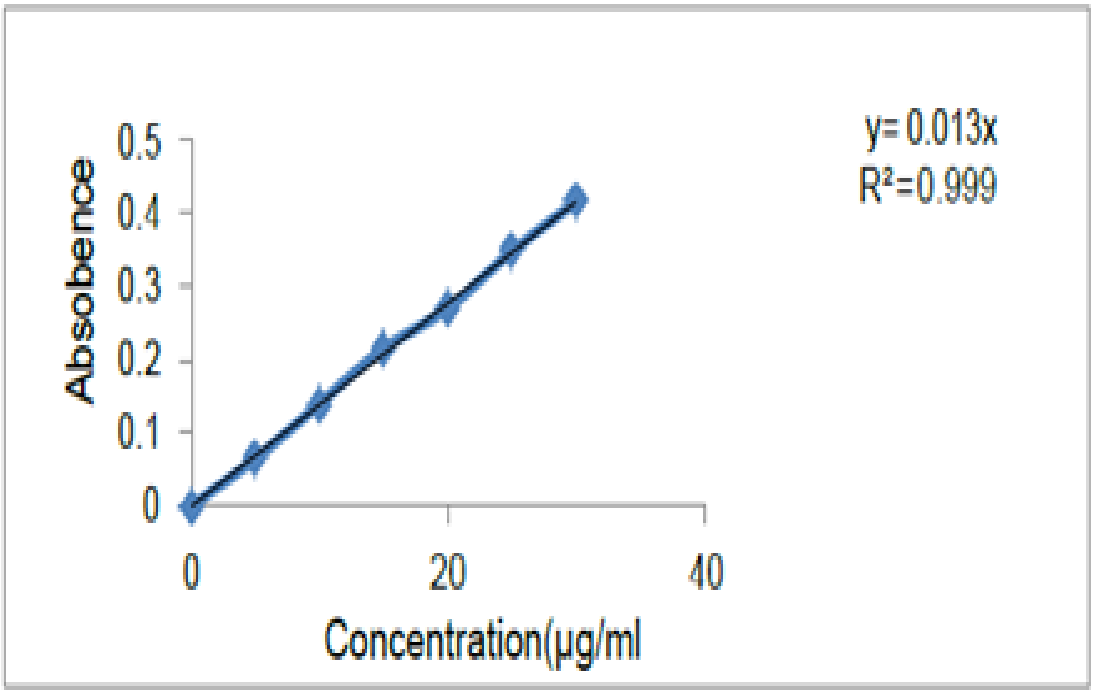


Fig. 1: calibration curve in O.1N Hcl (pH. 1.2).

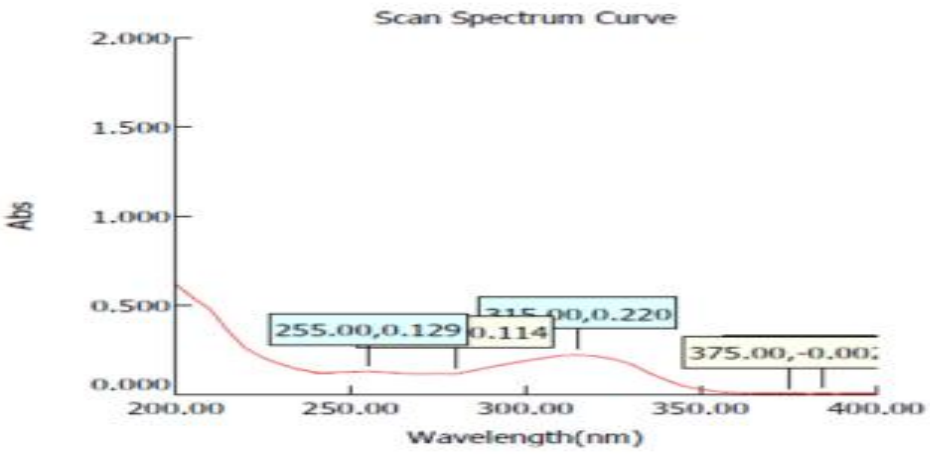


Fig. 3: Absorption spectrum.

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.

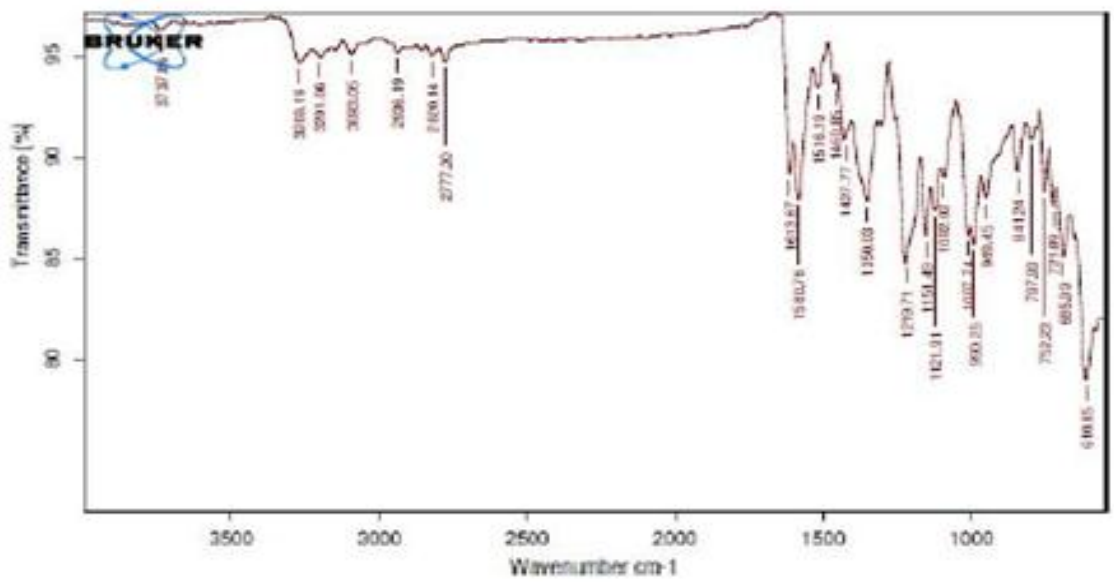


Fig. 4: FT-IR Spectrum of pure drug of nizatidine.

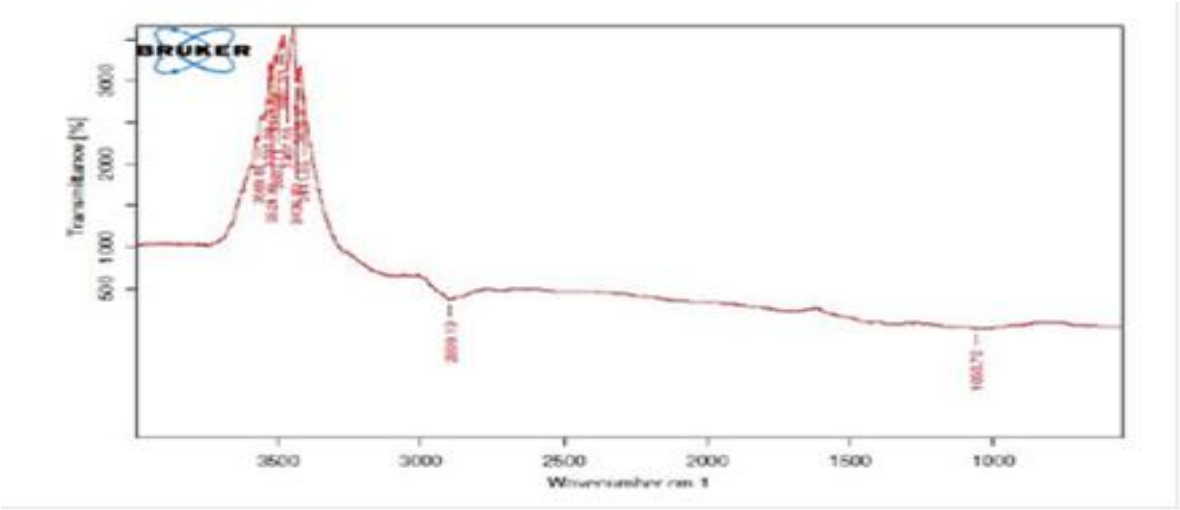


Fig. 5: FT-IR Spectrum of MCC.

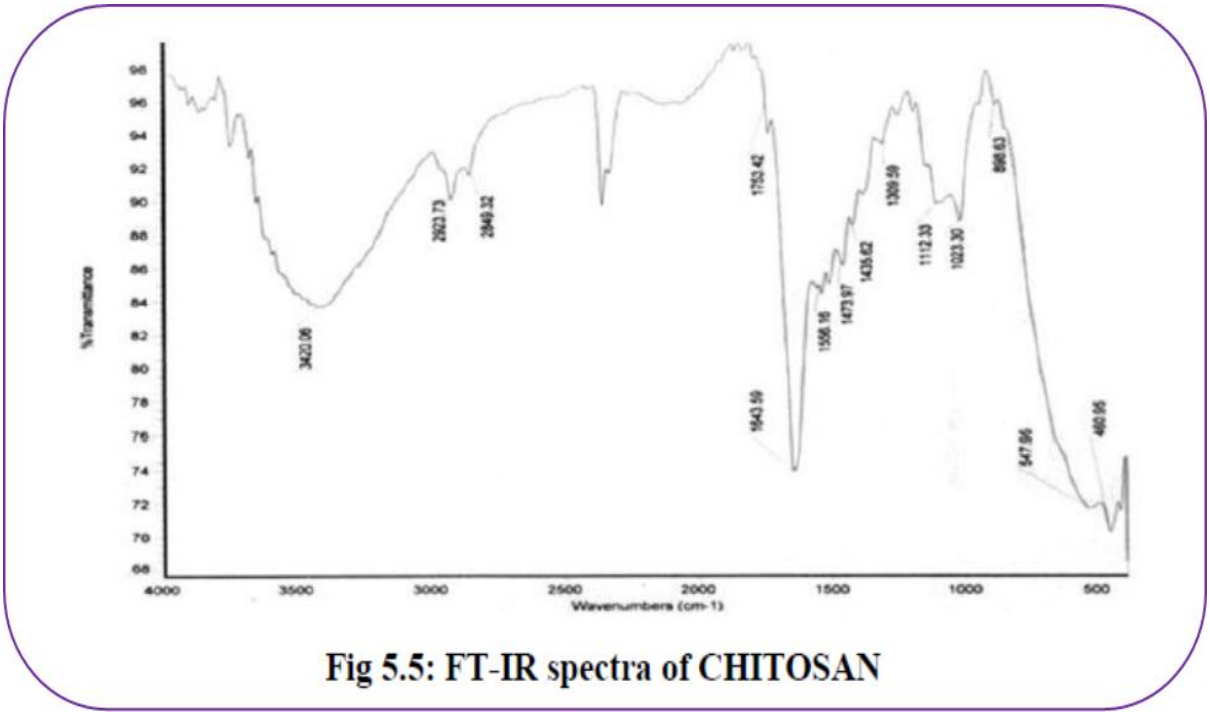


Fig 5.5: FT-IR spectra of CHITOSAN

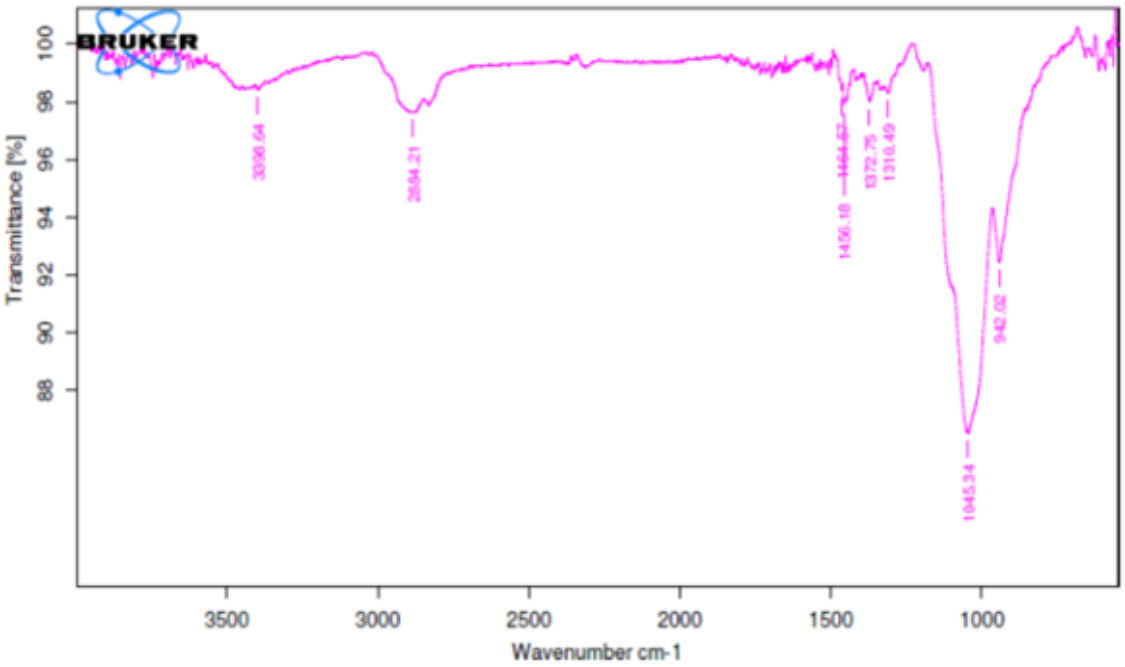


Fig. 6: FT-IR Spectrum of Sodium aliginate.

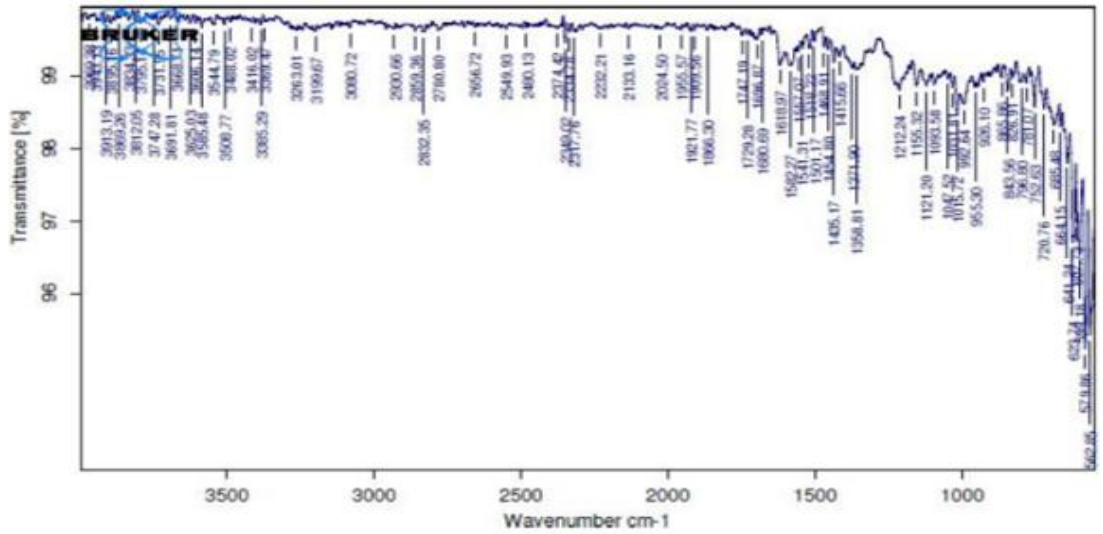


Fig. 07: FT-IR Spectrum of PVP-K-30.

Evaluation of dry mixed powder blend for pre-compressional parameters

The granulation characteristics are the most important interest to formulation scientist and therefore most universally measured. These basic measurements of the granulation have been used to develop and monitor the manufacture of many successful pharmaceutical dosage forms. Table 5.2. depicts the powder blend properties of Nizatadine tablets. Bulk density may influence compressibility, tablet porosity, dissolution and other properties and depends on the particle size, shape and tendency of particles to adhere 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 ± 0.73 to 0.471 ± 0.33. This indicates good packing capacity of powder blend. Carr's index evaluated inter particulate 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 behavior. 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 1.13 ± 0.11 to 1.18 ± 0.02.Many different types of angular properties have been employed to assess flow ability. Angle of repose is suited for particles >150 m. Values of angle of repose ≤300 generally indicate the free flowing material and angle of ≥400 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 31.16o±0.622 to 34.36o±0.629 i.e. granules were of good flow properties.

Table 3: Flow properties of tablet blend.

Formulation code	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	32.31° ±0.512	0.533±0.03	0.407 ±0.013	14.18±0.19	1.16±0.11
F2	33.39° ±0.731	0.537±0.01	0.418 ±0.017	14.13±0.41	1.16±0.45
F3	34.36° ±0.629	0.541±0.03	0.454 ±0.021	14.11 ±0.32	1.17 ±0.19
F4	32.28° ±0.321	0.532±0.03	0.399 ±0.073	15.03±0.84	1.18±0.02
F5	33.07° ±0.631	0.539±0.08	0.407 ±0.066	14.05±0.71	1.16 ±0.07
F6	31.38° ±1.731	0.559±0.02	0.471±0.033	13.50 ±1.21	1.13 ±0.12
F7	31.16° ±0.622	0.554±0.08	0.399 ±0.091	14.93 ±0.78	1.17±0.03
F8	32.35° ±0.55	0.538±0.02	0.422 ±0.038	13.05 ±1.21	1.16±0.12
F9	33.19° ±0.621	0.554±0.08	0.443 ±0.031	14.28 ±0.23	1.18±0.02

Table 4: Evaluation of prepared nizatidine superporous hydrogel tablets.

Formulation Code	Hardness (Kg/cm²)	Thickness (mm)	Friability %	Weight variation (%)	Drug content (%)
F1	4.6 ±0.13	3.0 ± 0.02	0.501±0.04	300±2.5	98.97±0.88
F2	4.6±0.19	2.8 ± 0.02	0.504±1.15	299±3.2	100.1±0.83
F3	4.1±0.21	2.6 ± 0.07	0.603±0.03	297±2.7	99.72±0.87
F4	4.5 ±0.11	2.7 ± 0.05	0.571±0.04	299±2.5	100.8±0.64
F5	4.0 ±0.63	3.0 ± 0.03	0.521±0.04	296±3.2	99.42±0.58
F6	4.4±0.30	2.7 ± 0.07	0.460±0.06	298±3.5	99.98±0.8
F7	4.9 ±0.16	2.0 ± 0.05	0.502±0.04	299±3.2	99.8±0.42
F8	3.4±0.26	3.0 ± 0.24	0.602±0.03	248±3.5	99.9±0.5
F9	3.5±0.18	2.7± 0.05	0.704± 0.35	247±3.2	98.85±0.68

Table no. 5: Swelling index and density of dried SPH'S.

Formuletion	Swelling index
F1	47.35 ± 0.23
F2	58.00 ± 0.14
F3	40.00 ± 0.12
F4	72.60 ± 0.80
F5	52.75 ± 0.56
F6	74.50 ± 0.20
F7	48.80 ± 0.26
F8	69.40 ± 0.32
F9	68.50 ± 0.16

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 74.50 ± 0.20. F6 tablet formulation having higher swelling index. This could be the reason for more moisture uptake by tablets from F4, F8 and F9 and moisture uptake values are given in Table.

Table no. 6: Porosity, void fraction, penetration pressures and water retention of superporous hydrogel formulations.

Formulations	Porosity (%)	Void fraction (ml/g)	Penetration pressure (g/cm_2)	Water retention
F1	36.3 ± 2.2	1.42 ± 0.03	50 ± 3	0.63467
F2	58.3 ± 3.1	1.25 ± 0.04	78 ± 5	0.77566
F3	66.4 ± 2.5	1.15 ± 0.01	103 ± 6	0.52869
F4	73.2 ± 4.2	0.93 ± 0.03	121 ± 8	0.97423
F5	44.2 ± 3.3	1.33 ± 0.02	60 ± 3	0.70495
F6	79.2 ± 1.5	0.85 ± 0.04	165 ± 11	0.70945
F7	89.2 ± 2.1	0.72 ± 0.03	202 ± 12	0.65385
F8	68.4 ± 2.5	1.15 ± 0.01	105 ± 6	0.93083
F9	74.2 ± 4.2	0.95 ± 0.03	126 ± 8	0.91964

Dissolution study of tablets

The formulation Fl, F2, F3 prepared with Sodium alginate based showed tablet swelling in the range of 7±6min to 720±110 min respectively. The releases of Nizatidine from all the formulations were found to be 100.1, 96.5% and 88.7%, at the end of 8hrs. The formulations F4, F5, F6, which are prepared by using Hydroxy ethyl cellulose based releases Nizatidine from all the formulations were in the range of 99.3 to 88.3% at the end of 8hrs. The formulations F7, F8, F9, which are prepared by using chitosan based releases drug from all formulations were in the range of 100.4 to94.3% at the end of 8hrs. The detailed in- vitro release data of all the formulations were given in Table 5.6.at the end of 8hrs.

Table no. 6: Cumulative % drug release profile of nizatidine superporous hydrogel tablets prepared by direct compression method.

Time (hours)	Cumulative % drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	59.40	67.22	41	61.22	68.34	54.10	38.2	43.11	39.8
2	70.16	68.74	51	69.85	70.25	64.13	42.4	47.62	46.1
3	72.55	72.71	55.91	70.38	71.96	71.12	58.32	59.55	62.5
4	75.44	74.42	64.32	72.79	74.12	73.91	66.62	72.37	68.2
5	76.22	76.93	69.9	734	77.44	78.22	79.21	78.46	74.12
6	79.11	78.25	71.63	74.41	77.85	78.35	84.4	86.88	82.45
7	91.42	88.46	73.62	84.22	80.92	80.44	97.12	92.32	89.12
8	100.11	96.54	88.71	99.33	88.31	92.91	-	100.41	94.35
9		96.72	91.62		100	98.22	-	-	101.2
10			93.71			100.01	-	-	-
11			96.72				-	-	-
12			99.98				-	-	-

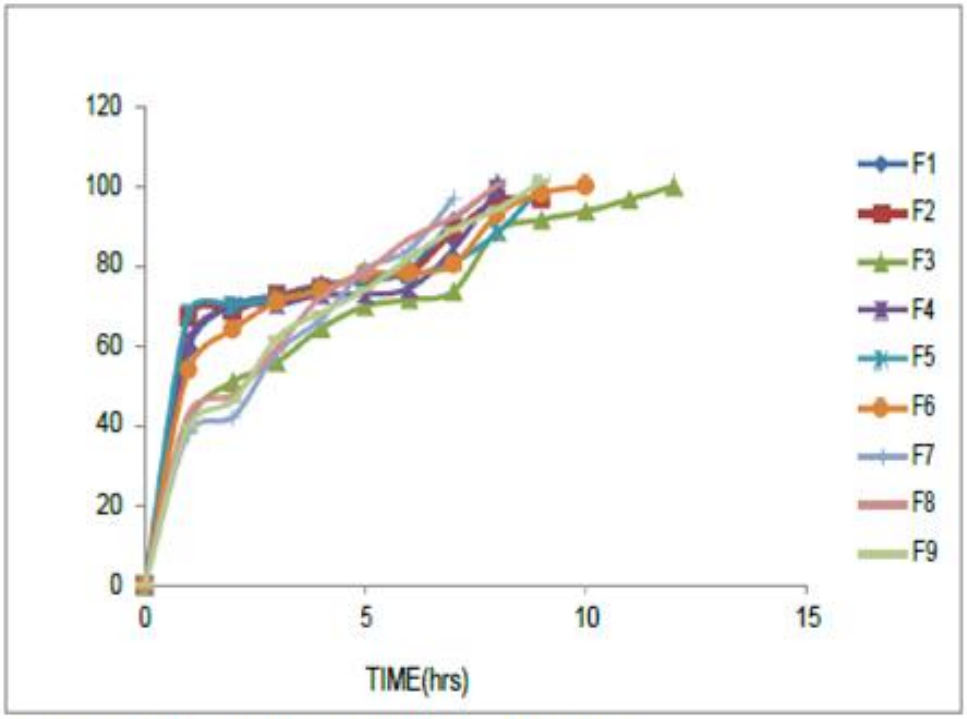


Fig no: 5.6: Cumulative %drug release (F1-F9.)

F1, F2, F3.The detailed in-vitro data were plotted for percentage drug released Vs time as shown in Fig1

Fig-1: Cumulative percent drug released Vs Time plots (zero-order) of formulation of

Table no 5.8 : Log% Cdr analysis for F3 formulations

Time(hr)	√T	LOG TIME	LOG%CDR	Cumulative %CDR
0	0	0	0	0
1	1.000	0	0	41.12
2	1.414	0.301	0.150	51.23
3	1.732	0.477	0.238	55.9
4	2.000	0.602	0.301	64.3
5	2.236	0.698	0.349	69.9
6	2.449	0.778	0.388	71.6
7	2.645	0.845	0.422	73.6
8	2.828	0.903	0.451	88.7
9	3.000	0.954	0.477	91.6
10	3.162	1.000	0.499	93.7
11	3.316	1.041	0.520	96.7
12	3.464	1.079	0.539	100

Cumulative percent drug released Vs Time plots (zero-order) of formulation of F3

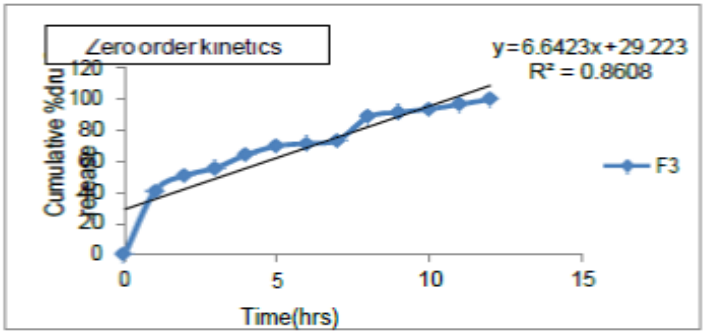


Table 5.10. Drug Content Data Stability for Formulation F3

Sl. No.	Trial No.	1st Day(%	30th Day (%)	60th Day (	90th Day (%
1.	I	99.97	99.89	99.85	99.83
2.	II	99.94	99.89	99.87	99.85
3.	III	99. 53	99.32	99.41	99. 43
4.	Mean	99.81	99.50	99.75	99.74

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.

CONCLUSION AND SUMMARY

The results conclusively demonstrated that Superporous Hydrogel tablets of Nizatadine were effectively prepared with desired properties. Superporous Hydrogel tablets of Nizatadine were prepared by direct compression method. The directly compressed formulations exhibited better in-vitro drug release profiles. The formulation F3 prepared by direct compression containing sodium alginate, PVP k-30 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 pre-compressional properties showing better flowability, hardness is maintained in the range of 3.4-4.9kg/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 Nizatadine 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. Therefore the prepared tablet shows improved bioavailability with increased drug release.

Nizatadine is a histamine H2 receptor antagonist and the site of action is systemic/site specific, the present work was aimed to formulate Superporous Nizatadine Hydrogel tablets of using an effervescent approach for gastro retentive drug delivery system to improve its bioavailability by preparing polymers to improve its localized action and sustain drug release. The tablets were formulated using polymers like chitosan Sodium alginate, pvpk- 30, Hyydroxy ethyl cellulose, along with suitable excipients. All the formulations were prepared by direct compression method. The prepared tablets of all the formulations were evaluated for physical characters, assay, in-vitro drug release, swelling index, hardness and friability. The main aim was to optimize the formulation for F1-F9 upto 12 hours in-vitro release. Optimized formulation F3 containing 60 mg Sodium alginate was consider as the best product with respect to in vitro drug release for 12 hours release action and improved

site-specific action. The results showed that the drug release rate was sustained release up to 12 hours.

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Conflict

Not interested.

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