Research Article

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FORMULATION AND EVALUATION OF FLOATING TABLETS OF NIZATIDINE

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ABSTRACT

The present investigation is concerned with formulation and evaluation of floating tablet of Nizatidine using the hydrophilic polymer hydroxypropyl methylcellulose and gas generating agent sodium bicarbonate and citric acid by wet granulation method. Nizatidine is H_2 receptor antagonist and antiulcer having dose 150 mg twice daily. The drug-excipient compatibility studies were conducted by using FTIR, DSC and visual observations. The granules were prepared by wet granulation method and evaluated for their granules properties. A 3^2 factorial design was applied to systematically optimize the drug release profile. The amount of citric acid (X1) and concentration of polymer HPMC K100M (X2) were selected as independent variables. The % drug release at 6 hour (Q6) and drug release at 12 hour (Q12), and t_{50} % were selected as dependent variables. The results of factorial design indicated that low level of HPMC K100M favors the preparation of floating controlled release of Nizatidine tablets. The tablets were compressed by tablet compression machine and evaluated with different parameter like thickness, hardness and weight variation, *in-vitro* buoyancy study swelling index, drug content uniformity, and *in-vitro* drug release. Effect of hardness on floating tablet revealed that increase in hardness affect buoyancy lag time due to reduction in porosity of compact mass. Formulations of NFT7 provided sustain release of Nizatidine over the period of 12 h.

Keywords: Floating tablets, Gastric retention, Nizatidine, Factorial design, H_2 antagonist.

INTRODUCTION

Oral delivery of the drug is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in the formulations. It is evident from the recent scientific and patented literature that an increased interest in novel dosage forms that are retained in the stomach for prolong and predictable period of time exist today in academic and industrial research groups. This technology benefits drugs that have a narrow window of absorption in the stomach and upper GI tract. Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment.[1,2] Floating drug delivery systems (FDDS) also known as hydrodynamically balanced systems (HBS). Various approaches have been pursued to increase the retention of an oral dosage form in the stomach including floating systems, swelling and expanding systems, polymeric bio adhesive systems, modified-shape systems, high-density systems[5,6] and other delayed Gastric emptying devices. Multiple unit FDDS avoid "all-or-nothing" gastric emptying nature of single unit systems. Sustained release in the stomach is also useful for therapeutic agents that the stomach does not readily absorb, since sustained release prolongs the contact time of the agent in the stomach or in the upper part of the small intestine, which is where absorption occurs and contact time is limited. Under normal or average conditions, for example, material passes through the small intestine in as little as 1-3 h.[3,4]

Objective

- To develop and evaluate floating tablets of Nizatidine that will,

A. Remain floating on stomach contents.
B. Provide slow drug release for prolonged period.

- To delivers the drug at controlled rate such that the drug is delivered over a period of time and increased gastric residence time.
- To evaluate the *in-vitro* buoyancy study of the formulations developed.
- To investigate the effect of citric acid and HPMC K100M on the formulation by using factorial design.

MATERIALS AND METHODS

Nizatidine was obtained as a gift sample from Dr. Reddys Pharmaceutical, Hyderabad, India. HPMC K15M were purchased from Colorcon Asia, Goa. Ltd. All other chemicals were of analytical grade.

Drug Authentication

The sample of Nizatidine was evaluated for its physical state, odor and color.

Pre formulation Studies of Nizatidine

Pre formulation studies were performed on the drug, which included melting point determination, solubility and compatibility studies.

Solubility of Nizatidine

Solubility of Nizatidine was determined as slightly soluble in water, soluble in alcohol, practically insoluble in fatty oils.

Melting Point

Variation in the melting point gives idea about its purity. Melting point of Nizatidine was determined by open capillary tube method.

UV Spectroscopy
Preparation of 0.1N HCl

0.1N HCl was prepared according to IP 1996. A quantity of 8.5 ml of HCl was diluted with fresh distilled water to produce 1000 ml.

Standard Curve of Nizatidine

Nizatidine has been quantitatively analyzed by various techniques. In present studies, Nizatidine was estimated by UV Spectrophotometry method.

Preparation of Stock Solution

The drug (10 mg) was dissolved in 100 ml of 0.1 N HCl in the volumetric flask. From the stock solution volume of solution of various concentrations i.e. 5, 10, 15, 20, 25 µg/ml were prepared using 0.1 N HCl to make the volume of 10 ml in a volumetric flask. The absorbance was measured at analytical wavelength and a standard curve of Beer's law was plotted. Absorbance of these solutions was measured against pH 0.1 N HCl as blank at 313 nm using Shimadzu 1800 UV/Vis double beam spectrophotometer.

Infrared spectra analysis

Infrared spectrum of Nizatidine was determined on Fourier Transform Infrared Spectrophotometer (FTIR-4100s) using KBr dispersion method.

Differential scanning calorimetry

The Differential Scanning Calorimetric analysis was carried out using METTLER TOLEDO Star SW 9.01(Model –DSC 823e).

Formulation Development
Formulation Design

Formulation Design study is important for selection of appropriate excipients for preparation tablets. The three grades of HPMC namely HPMC K 4M, HPMC K15K, HPMC K100M were used for trial preparation of tablets.

Preparation of Nizatidine Floating Tablet

Floating tablets containing Nizatidine were prepared by wet granulation technique using varying concentrations of polymer with sodium bicarbonate. Polymer and Nizatidine were mixed homogeneously using glass mortar and pestle. Isopropyl alcohol was used as granulating agent. Granules were prepared by passing the wet coherent mass through a # 16 sieve. The granules were dried in hot air oven at a temperature of 45^0C. Dried granules were sieved through # 40 sieves and lubricated with magnesium stearate and talc just 4-5 minutes before compression. Lubricated granules were compressed into tablet compression machine (Karnavati Mini press I) using 13 mm flat round punches to obtain tablets of desired specifications.[5-7]

Formulation Design
Pre-Compression Evaluation Parameters
Angle of Repose

The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.[8-10]

$$\tan\theta = h/r$$

Where, h = height of the powder cone and r = radius of the powder cone

Bulk density and Tapped density

A quantity of 2 g of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced in to 10 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at definite intervals. LBD and TDB were calculated using the following equations.

LBD = Weight of powder blend / Untapped volume of the packing

TBD = Weight of powder blend / Tapped volume of the packing

Compressibility index

It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down. The formula for Carr's Index is as below:

$$\text{Carr's index} = \text{TBD} - \text{LBD} \times 100 / \text{TBD}$$

Hausner ratio (HR)

This was calculated as the ratio of tapped density to bulk density of the sample

HR = Tapped Density / Bulk Density

Post-compression evaluation of Nizatidine Floating Tablets

Weight variation test

Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation.[11,12]

Percentage Deviation (PD) = Wavg – Winitial / Wavg

Where, Wavg = average weight and Winitial = initial weight

Uniformity of drug content

The powder equivalent to average weight of tablets was weighed and drug was extracted in 0.1N HCl, the drug content was determined measuring the absorbance at 313 nm after suitable dilution using a Shimadzu UV- Visible double beam spectrophotometer 1800.

Hardness

The hardness of the tablets was determined using Precision dial type hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets was determined.

Thickness

The thickness of the tablets was determined by using Vernier calipers. Five tablets were used, and average value was calculated.

Friability Test

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Twenty tablets were initially weighed and transferred into Friabilator. The Friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again. The % friability was then calculated by the following formula.

Percentage Friability = W – W0 × 100 / W

Where, W0 = initially weight W = weight after friability

Percentages Friability of tablets less than 1 % are considered acceptable.

***In-vitro* buoyancy studies**

The *in vitro* buoyancy was determined by floating lag time method described by Dave B.S. The tablets were placed in 100 ml beaker containing 0.1 N HCl. The time required for the tablets to rise to the surface and float was determined as floating lag time. The time between introduction of dosage form and its buoyancy in 0.1 N HCl and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).[13-15]

***In-Vitro* drug release studies**

The release rate of from floating tablets was determined using The United States Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1 N HCl, at 37 ± 0.5°C and 75 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly for 12 h and the samples were replaced with fresh dissolution medium. The samples diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 313 nm using a Shimadzu UV-Vis double beam spectrophotometer 1800. Cumulative percentage of drug release was calculated using the equation obtained from a standard curve. Graph plotted as % drug release vs. time (h).[16-18]

Swelling index of Nizatidine floating tablets

The swelling index of tablets was determined by using 0.1 N HCl (pH 1.2) at room temperature. The swelling index was calculated by the following equation.[18-21]

Swelling index (SI) = Wt – W0 × 100 / W0

Where, Wt = Weight of tablet at time t, W0 = Initial weight of tablet

Drug release kinetics of Nizatidine floating tablets

a. Zero-Order release kinetics

To studies the zero-order releases kinetics the release rate data are fitted to the following equation.

F = k.t…… (1)

Where, 'F' is the fraction of drug release, 'K' is the release rate constant and 't' is the release time

b. First – order release kinetics

To study the first-order release kinetics the release rate data are fitted to the following equation.

$F= 100\times (1-e^{-kt})$…… (2)

Where, 'F' is the fraction of drug release, 'K' is the release rate constant, 'e' is exponent coefficient and 't' is the release time

c. Higuchi release model

To study the Higuchi release model the release rate data are fitted to the following equation.

$F= K.t^{1/2}$…… (3)

Where, F' is the fraction of drug release and 'K' is the release rate constant

d. Korsmeyer and Peppas release model

To study the Korsmeyer and Peppas release model the release rate data are fitted to the following equation.

$M_t / M_\infty = K. t^n$……(4)

Where, Mt/M∞ is the fraction of drug release, 'n' is the diffusional exponent for the drug release that is dependent on the shape of the matrix dosage form.[20-22]

RESULTS AND DISCUSSION

Results for selected study are represented in Table 1 – 10 and Figures 1 – 10.

In the present study, FDDS of Nizatidine were prepared by using polymer hydroxypropylmethyl cellulose (HPMC K100M) and using sodium bicarbonate as gas generating agent and PVPk30 as binder. FDDS tablets were prepared by wet granulation technique.

Pre formulation Studies
Melting Point Determination

The melting point of Nizatidine was found to be in the range 131-134^{0}C (133^{0}C), which complied with BP standards, indicating purity of the drug sample.

Solubility

Nizatidine was found to be sparingly soluble in water, soluble in methanol, practically insoluble in fatty oils.

Calibration Curve of Nizatidine

The λ max was found to be at 313 nm. The calibration curve was linear between 05-25 µg/ml concentration ranges. The standard calibration curve of Nizatidine was determined in 0.1N HCl, by plotting absorbance against concentration at 313 nm.

Compatibility studies
IR study

Compatibility studies were performed using IR spectrophotometer. FTIR techniques have been used here to study the physical and chemical interaction between drug and excipients used. In the present study, it has been observed that there is no chemical interaction between Nizatidine and the polymer used.

DSC (Differential Scanning Colorimetry) study

By DSC study of physical transformations like melting, freezing volatilization, changes in crystallinity and specific heat, absorption and desorption as well as chemical changes. DSC thermo gram of Nizatidine show endothermic peak at 133.94°C and exothermic peak 228^{0}C. And it shows melting point at 133^{0}C thermo gram of nizatidine and HPMC K100M shows endothermic peak at 134^{0}C and exothermic peak at 238^{0}C. While the optimized batch also shows the endothermic peak at 151°C and 188°C. In the present study, it has been observed that there is no chemical interaction between Nizatidine and the polymers used.

Pre-compression Evaluation Parameter
Angle of Repose (θ)

It concludes all the formulations blend was found to be in the range 25^0 44' to 30^0 12'.

Bulk density and Tapped density

The density decreased due to this expansion and upward force of CO_2 gas generation. This plays an important role in ensuring the floating capability of the dosage form. To provide good floating behavior in the stomach, the density of the tablets should be less than that of the gastric contents (1.004 g/cm^3). For formulation F1-F9 density were found to be less than that of the gastric content.

Compressibility Index

Carr's index below 15 % usually shows good flow characteristics, but above 25 % indicate poor flowability. Compressibility index was carried out, it was found between 10.90 % and 21.88 % indicating the powder blend has the required flow property for compression.

Hausner's Ratio

Low range was observed for Hausner's ratio that indicates good flow ability. Many different types of angular properties have been employed to assess flow ability. The Hausner's ratio was found between 1.05 and 1.27.

Evaluation of Nizatidine floating tablets
Hardness and friability

The hardness of the prepared GFDDS of Nizatidine floating tablet was found to be in the range of 5.3 to 5.8 kg/cm^2. The friability of all the tablets was to be less than 1 % i.e. in the range of 0.701 to 0.935 %.

Uniformity of weight

The percent deviation from the average weight was found to be within the prescribed official limits.

Uniformity of drug content

All the batches of tablets were found to comply with uniformity of content test. Drug content was in range of 97.33 ± 1.15 to 95.66 ± 2.08 in the prepared formulation.

In vitro Buoyancy study

All the factorial design batches showed good *in-vitro* buoyancy, also the tablet remained buoyant for 12 hours, but the tablet actually floated throughout the study. The photograph (Figure 6) of *in vitro* buoyancy study the optimized batch NFT7 tablet at initial 0 min seen at the bottom of beaker, at the 10 sec the tablet was seen at center of the beaker that is the floating lag time and at 1 min the tablet was seen at surface of the beaker.

***In vitro* dissolution study**

The results obtaining *in-vitro* release studies were plotted in different model of data treatment as follows: (Figure 7 - 10)

- Cumulative percent drug released vs. time (zero order kinetics)
- Log Cumulative percent drug retained vs. time (First order rate kinetics)
- Log Cumulative percent drug released vs. square root of time (Higuchi's classical diffusion equation)
- Log Cumulative percent drug released vs. log time (Peppas Exponential equation)

From the dissolution study it was concluded that release from the matrix is largely dependent on the polymer swelling and drug diffusion. It was observed that all the tablets ascended to the upper one third of the dissolution vessels within a short time and remained floated until the complete of release studies. The drug release study was carried out up to 12 h. The percentage drug release from batch NFT1 to NFT9 vary from 87.879 to79.147% because of increase in concentration of polymer (HPMC K100M). High drug release is observed in NFT7 batch because of low concentration of polymer (HPMC K100M). Large concentration of high viscosity polymer induces the formation of strong viscous gel layer that slowed down the rate of water diffusion into the tablet matrix, which may result in decreases the drug release. Being water soluble polymers, they dissolve and form pores filled liquid in which drug can there after diffuse in dissolution medium. All the formulations were designed as dosage form for 12 h. From the dissolution study it was concluded that release from the matrix is largely dependent on the polymer swelling and drug diffusion.

Kinetic study

The three parameters were used to study the release mechanism, n- Release exponent, k- Release rate constant and r- Correlation coefficient. Linear regression analysis and model fitting showed that as these formulation followed zero order, Korsmeyer and Peppas model, first order model, which has higher values of correlation coefficient. Thus, the release of Nizatidine is controlled by zero order mechanism.

$$\text{Log \% R} = \log K + n \log t$$

Where, % R is percentage drug release; K is release ratio constant and n- is the diffusion release exponent that could be used to characterize the different release mechanism

The value of exponent n can be used to characterize the release mechanism of controlled release matrix tablet. The mean diffusion exponent values (n) ranged from 0.3318 to 0.3885 indicating that all these formulations presented a dissolution behavior controlled by anomalous transport. While the kinetic constant (k) ranged from 0.2737 to 23.307 indicating that Nizatidine release from hydrophilic binder matrices followed Fickian diffusion. The correlation coefficient revealed that Peppas model was better applicable to release data for the maximum of the batches (NFT3 - NFT7) where NFT1, NFT2, NFT8 and NFT9 show the matrix model.

Table 1: Composition of Nizatidine floating tablet

Ingredients(mg.)	NFT1	NFT2	NFT3	NFT4	NFT5	NFT6	NFT7	NFT8	NFT9
Nizatidine	150	150	150	150	150	150	150	150	150
HPMC K100M	80	100	120	80	100	120	80	100	120
Sod. Bicarbonate	80	80	80	80	80	80	80	80	80
Citric Acid	10	10	10	20	20	20	30	30	30
PVP K30	30	30	30	30	30	30	30	30	30
Magnesium stearate	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5
Total Wt.(mg)	365	385	405	375	395	415	385	405	425

Table 2: Standard values of angle of repose

Angle of repose	Flow property
$>25^0$	Excellent
25^0-30^0	Good
37^0-40^0	Fair
Beyond 40^0	Poor

Table 3: Standards for uniformity of weight as per I.P .

Avg. wt. of tablet	% Deviation
80 mg or < 80 mg	10
> 80 mg to < 250 mg	7.5
> 250 mg or more	5

Table 4: Calibration Curve of Nizatidine in 0.1 N HCl

S. No.	Concentration (µg/ml)	Absorbance at 313 nm
1.	0	0
2.	5	0.204
3.	10	0.409
4.	15	0.613
5.	20	0.818
6.	25	1.004

Table 5: Flow properties of granules prepared by different techniques

Batch Code	Angle of repose (θ)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Hausner's ratio (HR)	Carr index (CI)
NFT1	$27^0$32	0.523 ± 0.062	0.680 ± 0.014	1.27 ± 0.034	16.77 ± 0.04
NFT2	$28^0$00	0.458 ± 0.052	0.652 ± 0.053	1.05 ± 0.073	17.50 ± 0.51
NFT3	$27^0$50	0.474 ± 0.053	0.524 ± 0.062	1.08 ± 0.033	21.88 ± 0.65
NFT4	$30^0$12	0.464 ± 0.017	0.565 ± 0.017	1.13 ± 0.061	16.82 ± 0.56
NFT5	$29^0$56	0.443 ± 0.014	0.456 ± 0.023	1.26 ± 0.045	19.01 ± 0.42
NFT6	$28^0$21	0.525 ± 0.031	0.552 ± 0.031	1.12 ± 0.034	21.85 ± 0.09
NFT7	$27^0$71	0.558 ± 0.012	0.487 ± 0.019	1.18 ± 0.055	10.90 ± 0.23
NFT8	$25^0$44	0.448 ± 0.018	0.488 ± 0.073	1.07 ± 0.029	13.77 ± 0.45
NFT9	$26^0$38	0.430 ± 0.018	0.0545 ± 0.054	1.10 ± 0.026	12.56 ± 0.24

Table 6: Evaluation of physical parameters of Nizatidine floating tablets

Batch Code	Weight variation Average wt in (mg) ± SD	Hardness (kg/cm^2) ± SD	Thickness (mm) ± SD	Friability (%)	Drug Content Uniformity (%) ± SD
NFT1	365 ± 2.64	5.3 ± 0.20	4.2 ± 0.11	0.719	97.33 ± 1.15
NFT2	385 ± 2.51	5.4 ± 0.20	5.2 ± 0.12	0.833	96.00 ± 1.73
NFT3	405 ± 1.00	5.8 ± 0.10	6.2 ± 0.17	0.805	97.00 ± 1.00
NFT4	375 ± 2.00	5.7 ± 0.15	5.3 ± 0.20	0.851	97.00 ± 1.00
NFT5	395 ± 2.51	5.8 ± 0.11	6.0 ± 0.18	0.821	97.00 ± 1.73
NFT6	435 ± 4.72	5.8 ± 0.05	6.4 ± 0.10	0.935	97.00 ± 2.64
NFT7	385 ± 4.16	5.6 ± 0.17	5.4 ± 0.13	0.701	96.33 ± 1.15
NFT8	405 ± 4.04	5.7 ± 0.20	6.2 ± 0.15	0.814	97.66 ± 2.30
NFT9	425 ± 3.60	5.7 ± 0.17	6.7 ± 0.19	0.916	95.66 ± 2.08

Table 7: Floating Properties of Nizatidine Floating tablets

Formulation	Floating Lag Time (seconds)	Matrix Integrity	Floating Duration (hours)
NFT1	14	✓	> 12
NFT2	17	✓	> 12
NFT3	16	✓	> 12
NFT4	15	✓	> 12
NFT5	18	✓	> 12
NFT6	15	✓	> 12
NFT7	10	✓	> 12
NFT8	15	✓	> 12
NFT9	16	✓	> 12

Table 8: *In-Vitro* Drug Release Data of Nizatidine batch NFT1-NFT9

Time (h)	NFT1	NFT2	NFT3	NFT4	NFT5	NFT6	NFT7	NFT8	NFT9
0	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
1	38.098	20.585	9.245	58.411	30.204	13.655	54.184	33.620	30.662
2	44.284	25.338	15.163	62.605	36.132	19.905	57.936	39.810	35.101
3	50.031	31.458	21.092	65.722	42.477	27.237	60.439	43.681	41.109
4	53.854	37.035	27.855	69.940	46.955	32.753	68.008	51.771	48.026
5	55.562	43.666	35.156	72.067	52.051	38.410	70.373	56.047	49.883
6	58.516	46.147	40.550	73.668	56.722	42.894	73.861	62.054	51.661
7	63.332	51.213	47.107	80.568	62.712	46.472	77.103	65.282	59.403
8	69.527	54.746	51.233	83.095	65.787	52.431	83.811	71.176	61.362
9	73.094	61.275	56.148	87.405	69.602	54.621	85.559	74.368	65.309
10	78.253	64.014	62.118	91.073	70.903	62.245	89.482	78.642	69.725
11	82.430	66.648	67.983	93.012	71.258	68.370	93.108	84.615	74.582
12	87.879	71.742	72.281	94.598	73.923	73.246	99.461	88.893	79.147

Table 9: Release kinetics for Korsmeyer- Peppas Model

Formulations	n	k	r	Best fit model
NFT1	0.3318	9.0500	0.9401	Matrix
NFT2	0.5274	2.2115	0.9926	Matrix
NFT3	0.8511	0.2737	0.9973	Peppas
NFT4	0.2067	23.307	0.9587	Peppas
NFT5	0.3874	5.8499	0.9926	Peppas
NFT6	0.6752	0.8175	0.9975	Peppas
NFT7	0.2511	17.808	0.9630	Peppas
NFT8	0.4053	5.8056	0.9856	Matrix
NFT9	0.3885	5.7085	0.9835	Matrix

Table 10: Kinetic data of Nizatidine floating tablet

Formulations	Zero order (R)	First order (R)	Matrix model (R)	Hix-Crowel Model (R)
NFT1	0.6973	0.9471	0.9724	0.9185
NFT2	0.9112	0.9874	0.9937	0.9740
NFT3	0.9935	0.9877	0.9524	0.9960
NFT4	0.8290	-	0.9385	-
NFT5	0.7278	0.9396	0.9864	0.8923
NFT6	0.9910	-	0.9851	-
NFT7	0.3469	-	0.9256	0.8909
NFT8	0.8103	0.9752	0.9922	0.9607
NFT9	0.7865	0.9621	0.9881	0.9305

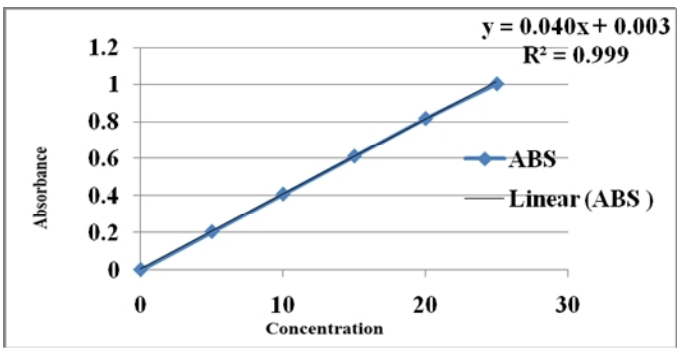

Figure 1: Standard curve of Nizatidine in 0.1 N HCl

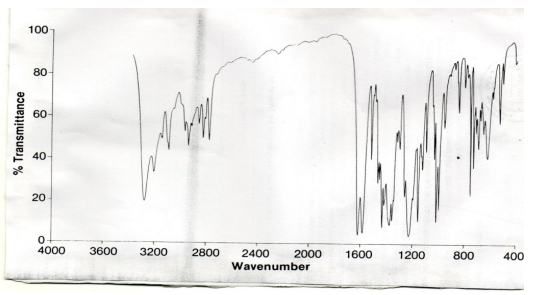

Figure 2: FTIR Spectra of Nizatidine

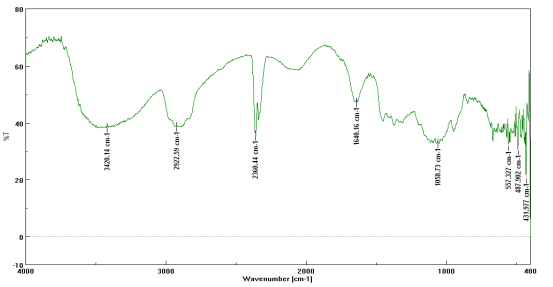

Figure 3: FTIR spectral analysis of HPMC K100M

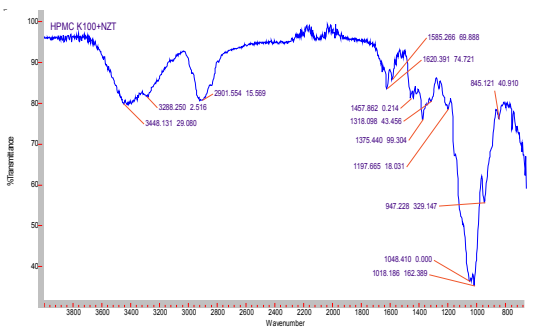

Figure 4: FTIR of Nizatidine + HPMC K100M

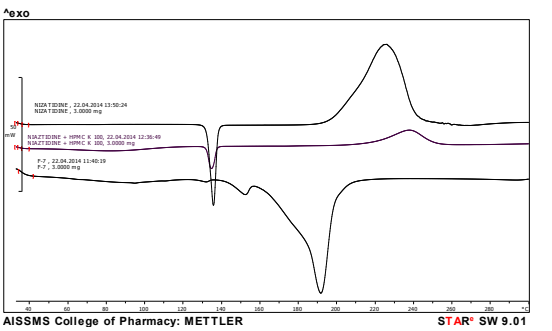

Figure 5: Overlain DSC thermo gram of Nizatidine, HPMC K100M and NFT7 Optimized formulation

NFT7 after 0 sec NFT7 after 10sec NFT7 after 1 min

Figure 6: Photograph of *in vitro* buoyancy study of NFT7 batch

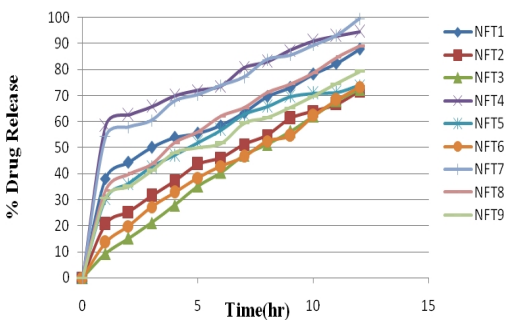

Figure 7: *In-vitro* Release Profile of Nizatidine NFT1-NFT9 Formulations

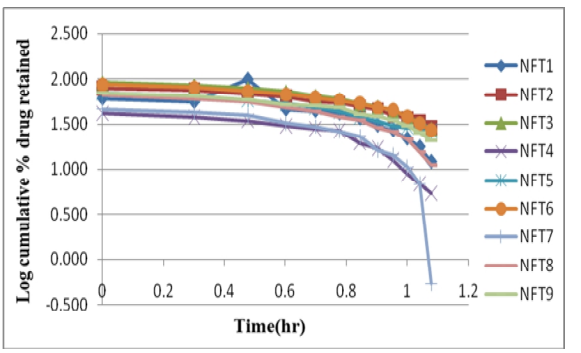

Figure 8: Comparative *In vitro* Release Profile of Nizatidine floating tablet According to first order kinetics for formulations NFT1-NFT9

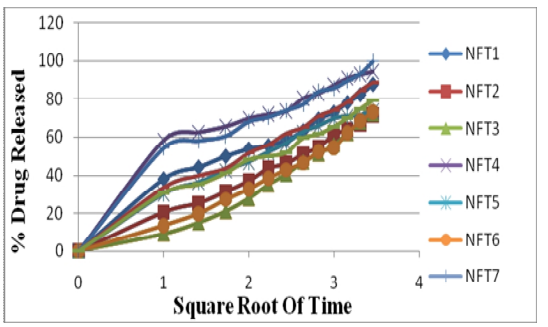

Figure 9: Comparative *In vitro* Release Profile of Nizatidine floating tablet According to Higuchi Matrix kinetics for formulations NFT1-NFT9

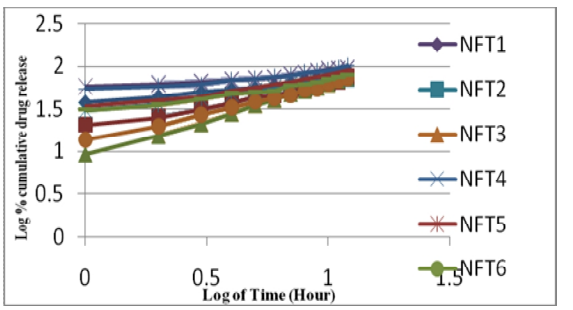

Figure 10: Comparative *In vitro* Release Profile of Nizatidine floating tablet According to Korsmeyer Peppas kinetics for formulations NFT1-NFT9

CONCLUSION

Nizatidine floating drug delivery systems with shorter lag time can be prepared by wet granulation method using HPMC K100M as a polymer and sodium bicarbonate and citric acid as gas generating agent. All the prepared tablet formulations were found to be good without capping and chipping. The present investigation described the influence of concentration of polymer (HPMC K100M) and citric acid on floating tablet of Nizatidine release using 3^2 full factorial designs. Result of multiple regression analysis indicated that both factors X_1, and X_2 significantly affect the t_{50} % and percentage drug release at 6 (Q_6) and 12 (Q_{12}) hour and should be used to manufacture the tablet formulation with desired *in-vitro* dissolution. The *in vitro* dissolution profiles of all the prepared Nizatidine floating drug delivery system formulations were found to extend the drug release over a period of 10 to 12 hours and the drug release rate decreased with increase in polymer concentration. IR spectroscopic and DSC studies indicate no drug-excipients interaction and physicochemical changes in the prepared formulations. Comparing the all formulations, NFT7 was considered as an ideal formulation which exhibited 99.461 % of drug release in 12 hours and floating lag time of 10 seconds with a total floating time of 12 hours. From the result it was observed that drug and polymer ratio influence the *in vitro* drug release and *in vitro* buoyancy of Nizatidine floating tablets. Hence, the floating system of Nizatidine is expected to provide

clinician with a new choice of safe and more bioavailable formulation in the management of GERD-Gastroesophageal reflux disease. The study reveals satisfactory results with a further scope of pharmacokinetic and pharmacodynamics evaluation.

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REFERENCES

1. Arora S, Ali J, Ahuja A, Khar RK. Floating drug delivery systems. AAPS Pharm Sci Tech 2005; 6(3): E372- E390. http://dx.doi.org/10.1208/pt060347
2. Mathur P, Saroha K, Syan n *et al*. floating drug delivery system: An innovative acceptable approach in Gastro-retentive drug delivery. Sch Res Lib 2010; 2(2): 257-270.
3. Sheth NS, Mistry RB. Formulation and evaluation of floating drug delivery system. Int J Pharma Bio Sci 2011; 2(1): 571-580.
4. Narang N. An updated review on floating drug delivery system, Int J Pharma 2011; 3(1): 1-7.
5. Zaware SR, Gaikwad PD, Bankar VH *et al*. A Review on floating drug delivery system. Int J Pharm Sci 2010; 2(3): 834–847.
6. Singh LP. A Review article on effervescent tablet. J Pharma Bio Sci 2011; 5(11): 1-6.
7. Prajapati S, Dharamasi A. Floating drug delivery for prolonging gastric retention of dosage form. Indian J Novel Drug deliv 2013; 5(1): 15-27.
8. Doshi SM, Tank HM. Gastro Retention - An Innovation over Conventional Poorly Soluble Drugs: A Review. Int J Pharma Chem Sci 2012; 1(2): 859-866.
9. Punitha S, Sabihta G, Kala V *et al*, Floating drug delivery system – Chrono-therapeutic Approach. Int. Res. J. Pharm 2011; 2(4): 38-45.
10. Sharma N, Agarwal D, Gupta MK *et al*. A Comprehensive review on floating drug delivery system, Int. J Res Pharma Bio Sci 2011; 2(2):4 28-441.
11. Reddy GJ, Potu AR, Reddy VP *et al*. Development and *in vitro-in vivo* behavior of Nizatidine floating tablets. Sch Res Lib. 2011; 3(1): 454-465.
12. Motukuri R, Nagesh P, Venisetty RK. Development and evaluation of gastric retentive floating tablets of Nizatidine. Int J Pharma Res Bio Sci 2014; 3(1): 252-276.
13. Chandra AS. Formulation and *in vitro* evaluation of effervescent floating matrix tablet of Nizatidine using natural and semisynthetic polymers. Int. Res. J. Pharma 2012; 3(12): 109-117.
14. Roy Chowdhury S, Verma P. Floating Drug delivery system- A new era in novel drug delivery system. Int J Pharma Res Bci Sci 2012; 1(5): 91-107.
15. Ware M, Tiwari SP, Roy A *et al*. New insights into gastro-retentive floating drug delivery systems. World J Pharma Sci 2013; 3(1): 252-270.
16. Patel R. Formulation and optimization of floating matrix tablet of ranitidine hydrochloride. Pharm Glob Int J Comprehensive Pharm 2011; 5 (08): 1-5.
17. Nagaraju K *et al*. Design and characterization of ranitidine hydrochloride floating tablets by wet granulation method. Int J Pharma Controlled Release 2012; 4(4): 77-80.
18. Patil VS, Gaikwad PD, Bankar VH *et al*. Formulation and evaluation of floating matrix tablet of locally acting H_2-antagonist. Int J Pharma Tech 2010; 528-540.
19. Bhoyar PK. Overview of a gastro-retentive floating drug delivery system. World J Pharma Res 2012; 1(2): 22-40.
20. Gastroesophageal reflux disease. http://www.medicinenet.com
21. Government of India. Ministry of Health Welfare. The Indian Pharmacopoeia.Vol -II, the Controller of Publication; New Delhi; 2007. p. 550.
22. Garg R, Gupta GD. Progress in controlled Gastro-retentive delivery system. Trop J Pharm Res 2008; 7(3): 1055-1066. http://dx.doi.org/10.4314/tjpr.v7i3.14691

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