Journal of Comprehensive Pharmacy

Research Article
Available Online at: www.jcponline.in

ISSN NO: 2349-5669

Formulation design and *in vitro* Evaluation of Floating tablets of an Antiulcer drug using Different Synthetic and Natural polymer

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ARTICLE INFO

Article history:

Received 21 April 2016

Accepted 26 May 2016

Available online 27 June 2016

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ABSTRACT

Famotidine is a histamine H₂-receptor antagonist and it is widely prescribed in gastric and duodenal ulcers, Zollinger- Ellison syndrome and gastroesophageal reflux disease (GERD) but susceptible to metabolism by colonic bacteria, which in turn has ramifications for drug delivery and absorption. Thus, it is logically way to improve the therapeutic efficacy of the drug if the gastric residence time of the dosage form is increased at the absorption site. Moreover, the drug is highly soluble in aqueous environment, it is necessary to reduce/control the drug release from the formulations. Therefore, the main aim of this research was to formulate controlled-release floating tablets of Famotidine in an effort to prolong its residence time in the stomach. The drug and polymer compatibility was studied by subjecting physical mixtures of drug and polymers to FTIR spectroscopy. Five batches of tablets were prepared by using HPMC K 100M and Hibiscus mucilage in different concentrations along with gas generating agent sodium bicarbonate. The Tablets were prepared by direct compression technique. The natural polymer was isolated and extracted from leaves of Hibiscus *rosa-sinensis* in our laboratory and that is used as a polymer in combination with HPMC K 100M to prepare floating tablets. The prepared floating tablets were evaluated for weight variation, hardness, thickness, friability, drug content uniformity, buoyancy lag time, total floating time and *in vitro* dissolution studies. Results were found that hardness 4-5kg/cm² and friability test was found to less than 1% in all the cases. Drug content ranging from 96.13 to 99.67% and the % drug release was in the order of F1> F2> F3> F4> F5. It reveals that increase the Hibiscus mucilage concentration decrease the release of Famotidine from floating tablets and it was showed that the Hibiscus mucilage exhibit excellent retarding effect on drug release from the floating tablets. Among the formulations studied, formulation F3 showed optimum release characteristics. The release mechanisms and the drug release rate kinetics of the tablets were examined using *in vitro* dissolution testing model. The drug release from all the formulations followed Peppas model and the 'n' value of F2, F3 and F4 was found to be between 0.5 – 1.0 indicates anomalous/non-fickian type (diffusion and erosion) of release mechanism except formulation F5 followed Zero order kinetics and showed super case II transport mechanism (i.e., n = 1.449). The 'n' value of F1 was found to be 0.36 indicates fickian type of release mechanism. Stability study was carried out for optimized formulation F3 at 40°C/75% RH for 30 days. The results of stability studies revealed no significant change in physical appearance; hardness and drug content indicating the formulation was stable.

Key words: Famotidine, Gastric retention, Hibiscus mucilage, Controlled release.

INTRODUCTION

Oral route is the most convenient and extensively utilized route for drug administration among all the routes that have been employed for systemic delivery of drugs via various pharmaceutical products of different dosage forms. Oral route of administration has been received more attention in the pharmaceutical field because of its ease of administration, patient compliance, least sterility constraints and flexible design of dosage forms [1]. Effective oral drug delivery may depend upon the factors such as gastric emptying process, gastrointestinal transit time of dosage form, drug release from the dosage form and site of absorption of drugs. Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying leading to non-uniform absorption profiles, incomplete drug release and shorter residence time of the dosage form in the stomach. This leads to incomplete absorption of drugs having absorption window especially in the upper part of the small intestine, as once the drug passes down the absorption site, the remaining quantity goes unabsorbed [2]. Conventional drug delivery systems achieve as well as maintain the drug concentration within the therapeutically effective range needed for treatment only when taken several times a day [3]. This results significant fluctuations in drug levels and also the drugs that are easily absorbed from gastro intestinal tract and have short half life are eliminated quickly from systemic circulation. These drugs require frequent dosing to achieve therapeutic activity. To avoid these limitations attempts have been made to develop many novel drug delivery systems that could revolutionize method of medication and provide a number of therapeutic benefits.

Floating drug delivery systems [4-11] or hydro dynamically balanced systems have bulk density lower than gastric fluids (1.004 g/cm^3) and therefore remain floating in the stomach without affecting the gastric emptying rate for a prolonged period. The drug is slowly released at a desired rate from the floating system and after the complete release; the residual system is expelled from the stomach. This leads to an increase in the GRT, which could be advantageous because it reduces the inter subject variability in absorption and lower probability of dose dumping by reducing frequency of dosing, and it also advantageous for local action of drugs in the stomach. Moreover, it improves the absorption of drugs with short-half life, reduces drug waste, and improves solubility of drugs that are less soluble in high pH environment.

Famotidine is a competitive & reversible inhibitor of H_2 receptor antagonist which inhibits the direct action of histamine on gastric acid secretion. It also reduces

basal acid secretion, nocturnal acid secretion and food stimulated acid secretion. The drug is susceptible to metabolism by colonic bacteria, which in turn has ramifications for drug delivery and absorption. Moreover, the drug is highly soluble in aqueous environment it is necessary to reduce/controls the drug release from the formulations.

Therefore, in this research study it was aimed to formulate controlled release floating tablets of Famotidine using HPMC K 100M and Hibiscus polysaccharide in different concentrations to prolong GRT of the drug in stomach, which may Increase the effectiveness in therapy, reduce dosing frequency, improving patient compliance and to maintain plasma concentration of drug in therapeutic range for longer time.

MATERIALS AND METHODS

Famotidine, was obtained as gift sample from Shasun pharmaceuticals Ltd, Pondicherry HPMC K100M were purchased from Taian Ruitai cellulose co., Ltd, P.R. China, Hibiscus mucilage, Microcrystalline cellulose were purchased from Mingtai chemical co., Ltd, Taiwan, Sodium bicarbonate were purchase from Central drug house Pvt. Ltd, New Delhi, Citric acid from Spectrum chemicals, Cochin Magnesium stearate, Talc from S.D. Fine – Chem. Ltd, Mumbai. The chemical reagents used were of analytical grade.

Drug – Excipient compatibility study [12]:

Drug – Excipient compatibility study by Thin Layer Chromatography

In this method drug and excipients in 1:2 ratio were mixed and analyzed for compatibility by using TLC after one, two, three and four weeks. 10 μ l of reference and test solutions were applied as spots on the dry activated plate. The solvent system was allowed to run up to desired height; the plates were removed and allowed to dry. The dry plates were then exposed to iodine vapors in a chamber to observe the spots. The plates were then removed and the R_f values calculated.

Drug – Excipient compatibility study by determination of λ_{max} :

A solution of Famotidine containing 10 μ g/ml was prepared in 0.1N HCl and scanned in the range of 200 – 400 nm using UV-Visible spectrophotometer. The same method is followed to Drug-Excipient mixture for determining λ_{max} .

Drug – Excipient compatibility study by Fourier Transform Infrared Radiation (FTIR)

FTIR spectroscopy was carried out to check the compatibility between the drug and excipients, where spectral measurements of drug alone and with

polymers were taken at ambient temperature and analyzed for major interaction. Samples and KBr were taken in 1:100 ratio in a mortar and triturated. A small amount of triturate was taken into a pellet maker and was compressed at 10 kg/cm² to form a transparent pellet using a hydraulic press. The pellet was kept in the sample holder and scanned between 4000 – 400 cm⁻¹ using FTIR spectrometer (Sipra lab Ltd). This was done qualitatively in order to assess the pattern of peaks and for comparison purpose.

Preparation of standard calibration curve of Famotidine

Famotidine showed one strong absorption peak at 242 nm in 0.1N HCl, which represents the maximum absorbance (λ_{max}) of the drug.

Procedure

Preparation of standard solution:

Primary stock solution: 100 mg of Famotidine was weighed accurately into 100 ml volumetric flask and dissolved in small quantity of 0.1N HCl, the volume was made up with the 0.1N HCl

Secondary stock solution: Pipette 10ml of the solution into another 100ml volumetric flask and the volume was made with the 0.1N HCl (i.e.: 100µg/ml in 0.1N HCl)

Preparation of working standard solution: Aliquots of standard solution 1ml, 2ml, 3ml, 4ml, 5ml were pipette into 10ml volumetric flasks. The volume made up with 0.1N HCl. The absorbance of each concentration was measured at 242 nm using Systronics 117 UV-Visible spectrophotometer against 0.1N HCl as a blank.

The absorbance data for standard calibration curve is given in Table 6. The standard calibration curve yields a straight line, which shows that the drug follows Beer's range in the concentration range of 10 – 50 µg/ml. The standard calibration curve of Famotidine is shown in Fig 1.

Formulation of floating tablets [13]

Floating tablets containing Famotidine were prepared by direct compression technique using varying concentrations of HPMC K 100M and Hibiscus mucilage with sodium bicarbonate. All the ingredients except magnesium stearate were blended in glass mortar uniformly. After sufficient mixing the powder blend was lubricated with magnesium stearate and purified talc. The tablets were compressed by using Rimek mini press 1 tablet punching machine with flat face punches & die (12mm in diameter). The compositions of tablets were shown in Table 1.

Evaluation of floating tablets

Precompression parameters

Bulk density [14]:

Density is defined as weight per unit volume. Bulk density, ρ_b , is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm³. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together.

Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 15 g powder blend introduced into a dry 100 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume was read. The bulk density was calculated using the following formula.

$$\text{bulk density} = \frac{\text{Weight of sample}}{\text{Apparent volume of powder}}$$

Tapped density [14]:

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped 500 times initially followed by an additional taps of 750 times until difference between succeeding measurement is less than 2% and then tapped volume, tapped density was measured, to the nearest graduated unit. The tapped density was calculated, in gm per ml, using the following formula.

$$\text{tapped density} = \frac{\text{Weight of sample}}{\text{tapped volume of powder}}$$

Angle of repose [14]:

The frictional force in a loose powder can be measured by the angle of repose (θ). It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle θ , is in equilibrium with the gravitational force.

The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose (θ) was calculated using the following formula:

$$\tan \theta = \frac{\text{Height of the pile}}{\text{radius of the base of the pile}}$$

Fig 1: standard calibration curve of Famotidine in 0.1 N HCl

Table 1: Composition of Famotidine floating tablets

Ingredients (mg/tablet)	F1	F2	F3	F4	F5
Famotidine	200	200	200	200	200
Hibiscus mucilage	20	25	30	35	40
HPMC K100M	40	35	30	25	20
MCC	60	60	60	60	60
Sodium bicarbonate	60	60	60	60	60
Citric acid	10	10	10	10	10
Magnesium stearate	5	5	5	5	5
Talc	5	5	5	5	5
Total weight	400	400	400	400	400

where $\theta = \tan^{-1} (h / r)$ θ = angle of repose

Carr's index (%) [14]:

The compressibility index (carr's index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater inter particle interactions and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the carr's index which is calculated using the following formulas:

$$\text{Carr's Index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Hausner's ratio [14]:

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

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

Post compression parameters [15-21]:

Tablet thickness and diameter:

Thickness and diameter of tablets were important for uniformity of tablet size. Thickness and diameter were measured using Vernier calipers.

Hardness:

This test is used to check the hardness of a tablet which may undergo chipping or breakage during storage, transportation and handling. In this five tablets were selected at random and the hardness of each tablet was measured with Pfizer hardness tester. The hardness is usually measured in terms of kg/cm².

Uniformity of weight:

This test is performed to maintain the uniformity of weight of each tablet which should be in the prescribed range, this is done by sampling and weighing 20 tablets at random and average weight is calculated. Not more than two of the individual weights deviate from the average weight by more than the percentage show in the table.

Friability test:

The friability of tablets was determined using Roche friabilator. It is expressed in percentage (%). Ten tablets were initially weighed (W_{initial}) and transferred into friabilator. The friabilator was operated at 25rpm for 4 min or run up to 100 revolutions. The tablets were weighed again (W_{final}). The % friability was then calculated by using following formula

$$F = \frac{W_{\text{initial}} - W_{\text{final}}}{W_{\text{initial}}} \times 100$$

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

Content uniformity:

Tablet containing 400mg of drug is dissolved in 100ml of 0.1N HCl taken in volumetric flask. The drug is allowed to dissolve in the solvent. The solution was filtered, 1ml of filtrate was taken in 100ml volumetric flask and diluted to mark with 0.1N HCl and analyzed spectroscopically at 242nm. The concentration of Famotidine in mg/ml was obtained by using standard calibration curve of the drug. Drug content studies were carried out in triplicate for each formulation batch.

***In vitro* floating study:**

The time taken by the tablet to emerge onto the surface of the medium after adding to the dissolution medium is called Buoyancy lag time (BLT). Duration of time by which the dosage form constantly emerges on surface of medium called Total floating time (TFT).

Both BLT & TFT were determined by placing the tablet in 900ml of simulated gastric fluid without pepsin, at pH 1.2, temperature 37±0.5°C, paddle rotation at 50rpm using stopwatch.

***In vitro* dissolution studies:**

In vitro release studies were carried out using USP dissolution testing apparatus II (paddle type). The dissolution test was performed using 900ml of simulated gastric fluid (pH 1.2), at 37±0.5°C and 75rpm. Samples of 5ml were withdrawn at predetermined time intervals, filtered and replaced with 5ml of fresh dissolution medium. The collected samples were suitably diluted with dissolution fluid and were analyzed at 242nm by using a UV spectrophotometer. Each dissolution study was performed for three times and the mean values were taken.

Dissolution kinetics [22, 23]:

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, Peppas and Hixson-Crowell model using PCP-DISSO-v3 software. Based on the r-value, the best-fit model was selected.

Zero order kinetics:

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly can be represented by the equation:

$$Q_t = K_0 t + Q_0$$

Where Q_t = amount of drug dissolved in time t.

Q_0 = initial amount of the drug in the solution and

K_0 = zero order release constant.

To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as cumulative amount of drug released *versus* time.

First order kinetics:

Assuming that the exposed surface area of a tablet decrease exponentially with time during dissolution process and suggested that drug release from most of the slow release tablets could be described adequately by apparent first order kinetics.

The release of the drug which followed first order kinetics can be expressed by the equation:

$$\log C = \log C_0 - \frac{k}{2.303} t$$

Where C_0 = initial concentration of drug,

k = first order rate constant

The data obtained are plotted as log cumulative percentage of drug remaining versus time which would yield a straight line with a slope of - k/2.303.

Higuchi model:

The first example of a mathematical model aimed to describe drug release from a matrix system was proposed by Higuchi in 1961. : It defines a linear dependence of the active fraction released per unit of surface (Q) on the surface root of time.

$$Q = K^2 t^{1/2}$$

Where, K^2 is release rate constant

The data obtained were plotted as cumulative percentage drug release versus square root of time.

Hixson-Crowell model:

Hixson and Crowell derived the equation –

$$W_0^{1/3} - W_t^{1/3} = \kappa t$$

Where W_0 = initial amount of drug

W_t = remaining amount of drug at time t

κ = constant representing surface-volume relation.

The equation describes the release from systems where there is a change in surface area and diameter of particles or tablets. To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as cube root of drug percentage remaining in matrix versus time.

Korsmeyer and Peppas release model:

In order to define a model, which would represent a better fit for the formulation dissolution data was further analyzed by Peppas & Korsmeyer equation

$$Mt \setminus M \alpha = K.t^n$$

Where Mt = amount of drug released at time t and

$M\alpha$ = amount released at Time α

K = kinetic constant and

n = diffusional exponent.

To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as log cumulative percentage drug release *versus* log time. In this model, the value of 'n' characterizes the release mechanism of drug.

Stability studies [24]:

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under influence of a variety of environmental factors such as temperature, humidity and light, and enables recommended storage conditions, re-test periods and shelf to be established. In the present study, stability studies were carried out at 40°C and 75% RH for a specific time period up to 4

weeks for optimized formulation. For stability study, the tablets were sealed in aluminium packaging coated inside with polyethylene. These sample containers were placed in desiccator maintained at 75% RH. The samples were analyzed for appearance, hardness, and drug content.

RESULTS AND DISCUSSION**Drug – Excipient compatibility study:**

This study confirmed no interaction between the drug and excipients i.e., the physical appearance of drug-excipient mixture, R_f value and λ_{max} of drug observed for 4 weeks were found to be almost similar with the initial observations. Hence, it can be concluded that the drug Famotidine was found to be compatible with the excipients used in the designed formulation. The observations of drug-excipient compatibility study are tabulated in Table 2 & 3.

Drug – Excipient compatibility study by FTIR study

Based on the FTIR interpretation results, all the major drug peaks were identified when compared with the physical mixture of drug and polymer/excipients which ensured that there was no any chemical interaction between them. The significant peaks (functional groups) and FTIR spectra of drug and drug-polymer mixture are shown in Table 4 and Fig 2, 3, 4 and 5.

Pre-compression parameters:

The values of bulk density were found to be in the range from 0.372gm/cm³ to 0.394gm/cm³ and tapped density from 0.444gm/cm³ to 0.456gm/cm³. The angle of repose values were found to be in the range from 23.45° to 28.15°. This indicates good flow property of the blend. Compressibility index value ranges between 11.65% to 17.54% indicating that the powder blend have the required flow property for direct compression. The values of Hausner's ratio were range from 1.131 to 1.212. The values are shown in Table 5.

Post-compression parameters

Tablets mean thickness were almost uniform in all the five formulations and were found to be in the range of 3.38mm to 3.41mm. The measured hardness of tablets of each batch ranged between 4.7kg/cm² to 4.8kg/cm². This ensures good handling characteristics of all batches. The % friability was less than 1% in all formulations ensuring that the tablets were mechanically stable. All the tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits of $\pm 5\%$ of the weight.

The weights of all the tablets were found to be uniform with low standard deviation. The percentage of drug content was found to be in between 96.13% to 99.67%

Table 2: Drug-Excipient compatibility study by Physical observation

Ingredients	Observations at 0 day		
	Appearance	R _f	λ _{max} (nm)
Drug	Buff	0.375	242
Drug ± HPMC K 100M	White	0.372	242
Drug ± HPMC K 15M	White	0.374	242
Drug ± Hibiscus mucilage	Light green	0.373	242
Drug ± Xanthan gum	White creamy	0.376	242
Drug ± Guar gum	Light yellow	0.375	242
Drug ± Carbopol 934P	White	0.377	242
Drug ± MCC	White	0.374	242
Drug ± Sodium bicarbonate	White	0.371	242
Drug ± Citric acid	Buff	0.368	242

Table 3: Drug-Excipient compatibility study

Ingredients	1 st week			2 nd week			3 rd week			4 th week		
	A	R _f	λ _{max}	A	R _f	λ _{max}	A	R _f	λ _{max}	A	R _f	λ _{max}
Drug	NC	0.374	NC	NC	0.374	NC	NC	0.372	NC	NC	0.371	NC
Drug + HPMC K 100M	NC	0.372	NC	NC	0.370	NC	NC	0.370	NC	NC	0.371	NC
Drug + HPMC K 15M	NC	0.374	NC	NC	0.375	NC	NC	0.373	NC	NC	0.373	NC
Drug + Hibiscus mucilage	NC	0.373	NC	NC	0.373	NC	NC	0.372	NC	NC	0.371	NC
Drug + Xanthan gum	NC	0.376	NC	NC	0.375	NC	NC	0.376	NC	NC	0.374	NC
Drug + Guar gum	NC	0.375	NC	NC	0.373	NC	NC	0.374	NC	NC	0.372	NC
Drug + Carbopol 934P	NC	0.377	NC	NC	0.375	NC	NC	0.375	NC	NC	0.374	NC
Drug + MCC	NC	0.374	NC	NC	0.374	NC	NC	0.373	NC	NC	0.372	NC
Drug + Sodium bicarbonate	NC	0.370	NC	NC	0.371	NC	NC	0.370	NC	NC	0.369	NC
Drug + Citric acid	NC	0.368	NC	NC	0.368	NC	NC	0.368	NC	NC	0.367	NC

A = Appearance, NC = No change.

Table 4: FTIR spectra - Interpretation & Comparison

Functional groups	Stretching/Deformation	FTIR significant peaks			
		Pure drug (cm ⁻¹)	Drug + HPMC K100M (cm ⁻¹)	Drug+ Hibiscus mucilage (cm ⁻¹)	Drug + All Excipients (cm ⁻¹)
C-N	Stretching	1225.65	1225.59	1225.49	1225.15
C-N	Stretching	1354.65	1354.63	1357.63	1354.01
C-NO ₂	Stretching	1391.02	1391.14	1392.87	1382.48
C-S	Stretching	691.53	691.70	692.09	692.06
C=C	Stretching	1617.56	1617.75	1618.50	1616.95
CH ₃	Stretching	2942.96	2945.27	2943.40	2943.04
CH ₃	Deformation	1436.22	1435.62	1432.20	1433.25
N-H	Deformation	1583.37	1584.15	1585.56	1586.18
CH ₃ - N	Stretching	2782.24	2779.76	2782.73	2781.95

Fig2: FTIR spectra of Famotidine

Fig 3: FTIR spectra of Famotidine and HPMC K100M

Fig 4: FTIR spectra of Famotidine and Hibiscus mucilage

Fig 5: FTIR spectra of Famotidine and All Excipients

which was within acceptable limits. The results are shown in Table 6.

***In vitro* release study:**

Dissolution apparatus USP II paddle method was used to carry out *in vitro* drug release studies on the prepared batches of floating tablets with a stirring speed of 75 rpm; at $37 \pm 0.5^\circ\text{C}$ in 900ml of (pH 1.2) simulated gastric fluid for 8hrs. The formulation F1 released 92.4% of drug within 6hr of the study indicating that the polymer combination is insufficient to control the drug release. Tablet of batch F2, F3, F4 and F5 showed 90%, 78.6%, 69.7% and 61% at the end of 8 hrs respectively. Formulation F3 containing equal amounts of HPMC K 100M & Hibiscus mucilage showed better control of drug release and able to release entire amount of drug in 12hrs than the other formulations and therefore it may be considered as the optimized formulation. It is evident from the *in vitro* dissolution data that increase in Hibiscus mucilage concentration decreased release rate of the drug. The *in vitro* dissolution profiles were shown in Fig 6, 7, 8, 9, and 10.

The results of dissolution data were fitted to various kinetic equations to analyze the release mechanism. All the formulations followed Peppas model and were found to be best fitted in all dissolution profiles having higher correlation coefficient (r value). Formulation F5 followed Zero order kinetics.

The 'n' value of formulations F2, F3, and F4 was ranges between 0.49 to 0.89 indicating that the drug release occurred via non-Fickian diffusion, which shows that the release from initially dry, hydrophilic glassy polymers that swell when added to water and become rubbery show anomalous diffusion as a result of the rearrangement of macromolecular chains. The 'n' value of formulation F1 was 0.36 indicating that the drug release followed Fickian diffusion which depends on diffusion of the drug. The 'n' value of formulation F5 was 1.44 indicating that the drug release followed super case II transport mechanism due to the erosion of the polymer. The kinetic plots are shown in Fig 11, 12, 13, and 14.

Stability studies:

Stability studies were carried out for optimized formulation F3 at $40^\circ\text{C}/75\% \text{ RH}$ for 30 days. The results of stability studies revealed no change in physical appearance, hardness and drug content indicating the formulation was stable. The results of stability study are shown in table 8.

CONCLUSION

Gastro retentive floating tablets of Famotidine was successfully formulated using HPMC K 100M and Hibiscus polysaccharide as a release retardant materials in different concentrations by direct compression technique.

Table 5: Pre-compression parameters of Famotidine powder mixture

Formulation	Bulk Density(g/cm ³)	Tapped Density(g/cm ³)	Angle of repose (θ)	Carr's index	Hausner's ratio
F1	0.380±0.020	0.444±0.026	23.45±0.010°	14.41±0.021	1.168
F2	0.372±0.019	0.452±0.030	26.76±0.021°	17.69±0.030	1.215
F3	0.381±0.021	0.451±0.028	24.58±0.015°	15.52±0.027	1.183
F4	0.394±0.025	0.446±0.032	22.19±0.030°	11.65±0.036	1.131
F5	0.376±0.026	0.456±0.036	28.15±0.028°	17.54±0.029	1.212

Table 6: Post-compression parameters of Famotidine floating tablets

Formulation	Weight variation	Hardness (kg/cm ²)	Thickness (mm)	Friability (%)	Drug content (%)
F1	0.403±0.005	4.75±0.05	3.38±0.02	0.74±0.04	98.72
F2	0.402±0.006	4.78±0.04	3.39±0.04	0.72±0.06	97.78
F3	0.402±0.005	4.82±0.03	3.40±0.05	0.45±0.02	97.07
F4	0.401±0.010	4.83±0.06	3.39±0.03	0.56±0.04	96.13
F5	0.403±0.008	4.78±0.05	3.41±0.04	0.61±0.07	99.67

Table 7: Buoyancy study of Famotidine floating tablets

Formulation code	Floating lag time (min)	Total floating time (hrs)
F1	2.02	10
F2	1.20	>12
F3	4.03	>12
F4	6.30	>12
F5	6.06	>12

Fig 6: *in vitro* dissolution study of F1

Fig 7: *in vitro* dissolution study of F2

Fig 8: *in vitro* dissolution study of F3

Fig 9: *in vitro* dissolution rate study of F4

Fig 10: *In vitro* dissolution study of F5

Fig 11: Zero order release kinetics of Famotidine floating tablets

Fig 12: First order release kinetics of Famotidine floating tablets

Fig 13: Higuchi matrix release kinetics of Famotidine floating tablets

Fig 14: Peppas release kinetics of Famotidine floating tablets

Table 8: Stability study of optimized formulation F3

Time in weeks	Formulation F3		
	Appearance	Hardness (Kg/cm ²)	Drug content (%)
0	Creamy white	4.95	99.72
1	Creamy white	4.95	99.55
2	Creamy white	4.93	99.21
3	Creamy white	4.92	98.96
4	Creamy white	4.92	98.71

Drug-Excipient study & FTIR study confirmed no physical and chemical interaction between the drug and polymer/Excipients used in the formulation. All the tablets were found to be good without any chipping and capping. Formulated tablets gave satisfactory results for various physicochemical evaluations for tablets like Tablet dimensions, Hardness, Friability, Weight variation and content uniformity. The drug content was almost uniform in all the tablets prepared. The low values of standard deviation indicate uniform distribution of drug within the matrices. It is evident from the *in vitro* dissolution data that increase in Hibiscus mucilage concentration decreased the drug release rate. The results generated in this study showed that the release profile and kinetics of drug release were function of polymer type and polymer concentration. Among all the formulations F3 with equal concentration of HPMC K100M and Hibiscus mucilage showed good controlled release and able to release entire amount of drug in 12hrs than the other formulations and therefore it may be considered as the optimized formulation. All formulations followed Korsmeyer-Peppas model except formulation F5 which followed zero order kinetics. For formulations F2, F3 and F4 the 'n' was found to be between 0.5-1.0 indicate anomalous/non-fickian type release mechanism where the drug release was controlled by both diffusion and erosion mechanism. The 'n' value for formulations F1 and F5 was found to be 0.36 and 1.44 indicate fickian and super case II type of release mechanism where the drug release was controlled only by diffusion in F1 and erosion in F5 formulations. The results of stability studies for optimized formulation F3 revealed no change in physical appearance, hardness and drug indicating the formulation was stable.

REFERENCE

- Ambale SM, Ganesh NS, Ramesh B, Deshpande KB. An overview on limitations of gastroretentive drug delivery system. *Int J Pharm Sci Rev Res*. 2011;**8(2)**:133-139.
- Jain AK. Design and Evaluation of Floating Tablets of Vitamin B₁. *Int J Res Pharm Biomed Sci*. 2011;**2(3)**:1058-1065.
- Arunachalam A, Karthikeyan M, Konam K, Prasad PH, Sethuraman S, Ashutoshkumar S, Manidipa S. Floating drug delivery systems: A review. *Int J Res Pharm Sci*. 2011;**2(1)**:76-83.
- Balagani PK, Palapati K, Katamreddy JD. Formulation design and evaluation of mucoadhesive buccal tablets of Nitroglycerin. *Int J Pharm Pharm Sci*. 2014;**6(7)**: 251-259.
- Balagani PK, Sumalatha YS. Formulation Development and Evaluation of Floating Tablets of Etodolac. *World J Pharm Pharm Sci*. 2015;**4(7)**:1516-1532.
- Chien YW. *Novel Drug Delivery Systems*. 2nd edition, Revised and expanded. NewYork: Marcel Dekker; 1992.
- Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. *Acta Pol Pharm*. 2010;**67(3)**:217-223.
- Bhowmik D, Chiranjib B, Chandira M, Jayakar B, Sampath Kumar KP. Floating Drug Delivery System-A Review. *Der Pharmacia Lettre*. 2009;**1(2)**:199-218.
- Edukondalu V, Ashok K, Jagadeesh K, Pushpalatha V, Satyanandam S, Lakshmi NV. Formulation and evaluation of oral floating tablets of Atenolol using Okra gum. *Der Pharmacia Lettre*. 2011;**3(3)**:342-349.
- Rathod H, Patel V, Modasia M. Floating drug delivery system: innovative approach of gastroretention. *Int J Pharm Sci Rev Res*. 2010;**4(3)**:184-192.
- Irisappan SC, Balagani PK, Narayanan V. Formulation and invitro evaluation of floating drug delivery system for Salbutamol Sulphate. *Int J Pharma Biomed Sc*. 2010;**1(1)**:12-15.
- Ingani HM, Timmermans J, Moes AJ. Conception and *in vivo* investigation of peroral sustained release floating dosage forms with enhanced gastrointestinal transit. *Int J Pharm*. 1987;**35(1)**:157-164.
- Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. Hollow microspheres for use as a floating controlled drug delivery system in the stomach. *J Pharm Sci*. 1992;**81(2)**:135-140.
- Manubolu S, Balagani PK. Formulation Design and Evaluation of Controlled Release Zolmitriptan Rapimelts. *J Compr Phar*. 2014;**1(4)**:119-135.
- Mayavanshi AV, Gajjar SS. Floating drug delivery systems to increase gastric retention of drugs: A Review. *Res J Pharm Tech*. 2008;**1(4)**:345-348.
- Madaka S, Sanka K, Veerareddy PR. Design and evaluation of Hydrochlorothiazide floating drug delivery system. *Asian J Pharm Sci*. 2011;**6(5)**:208-217.

17. Rahman Z, Ali M, Khar R. Design and evaluation of bilayer floating tablet of captopril. *Acta Pharm.* 2006;**56**(1):49-57.
18. Kumar NS. Aceclofenac floating tablets - a promising sustained release dosage form. *Int J Drug Dev & Res.* 2011;**3**(2):290-300.
19. Irisappan SC, Balagani PK, Jayaveera KN. Characterization of Glibenclamide loaded cellulose acetate microparticles prepared by an emulsion solvent evaporation method. *J Pharm Res.* 2013;**7**(8):766-773.
20. Shayeda, Nadigoti J. Floating Drug Delivery Systems. *Int J Pharm Sci Nanotech.* 2009;**2**(3):595-604.
21. Sheth PR, Tossounian J. The hydrodynamically balanced systems (HBSTM): a novel drug delivery system for oral use. *Drug Dev Ind Pharm.* 1984;**10**(2):313-339.
22. Sivabalan M, Vani T, Phaneendhar Reddy V, Anup Jose NG. Formulation and evaluation of gastroretentive glipizide floating tablets. *Int J Compr Pharm.* 2011;**2**(1):1-4.
23. Raju DB, Sreenivas R, Verma MM. Formulation and evaluation of floating drug delivery system of Metformin Hydrochloride. *J Chem Pharm Res* 2010;**2**(2):274-278.
24. Zaware SR, Gaikwad PD, Bankar VH, Pawar SP. A Review on Floating Drug Delivery System. *Int J Ph Sci.* 2010;**2**(3):834-847.

Cite this article as: Irisappan SC, Paleti N, Balagani PK, Palapati K. Formulation design and *in vitro* Evaluation of Floating tablets of an Antiulcer drug using Different Synthetic and Natural polymer. *J Compr Phar* 2016;3(3):99-114.