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Formulation and evaluation of lafutidine floating tablet

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ABSTRACT

Purpose

Lafutidine is H2-receptor antagonist. The prepared tablets of various formulations were evaluated for a total floating time, buoyancy lag time, and percentage drug released. Guar gum is an efficient matrix forming agent in floating tablets by generating gas. Drug release from the prepared tablets was slowed over more 12 h and depended on the composition of guar gum and sodium bicarbonate. Lafutidine release was diffusion controlled and follows zero order kinetics. In case of F3 formulation non-fickian diffusion was the drug release mechanism from the prepared lafutidine floating tablets.

Methods

Floating tablets containing 10 mg of lafutidine could be prepared by direct compression technique employing guar gum of different grades as floating polymer and release retardant, methocel K-4, methocel K15M as floating enhancers and sodium bicarbonate as a gas generating agent.

Results

The influence of various process parameters on physic-chemical properties and drug release potential have been studied. Different formulation ratios of blend affect the physical appearance of the tablets and micromeritic properties were observed. The measured tapped density was 0.501 to 0.643(g/cm3), bulk density 0.421 to 0.540 (g/cm3), thickness 4.33 to 4.38(mm), hardness 4.26 to 5.06 (Kg/cm2), friability 0.24 to 0.46(%) were well within the limits, which indicates good flow potential of the prepared tablets. Angle of repose (θ) values for the granules was in the range 24.19 to 26.950 indicating good flow potential for the tablets.

Conclusion

The formulations with guar gum were able to float for more than 12 h. Resultant tablets blend did not have any incompatibilities showed in FT-IR studies.

Keywords: Floating drug delivery system, In vitro, Lafutidine and Controlled release.

INTRODUCTION

The design of floating drug delivery system (FDDS) should be aimed that to achieve more predictable and increased bioavailability of drugs [1]. Floating drug delivery is one of the approaches for gastroretention. FDDS or hydrodynamically balanced system shave a bulk density lower than gastric fluids and thus, remain buoyant in the stomach without

affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, drug is released slowly at a predetermined rate [2]. Lafutidine possesses a potent and long lasting gastric antisecretory effect mediated by H2- receptor blockade in animals. Lafutidine has a receptor binding affinity which is 2-80 times higher than other representative H2-receptor antagonists (e.g. famotidine, ranitidine, and cimetidine). In addition, lafutidine exerts gastroprotective effects independent of its antisecretory action. Lafutidine is freely soluble in acetic acid, slightly soluble in methanol, very slightly soluble in diethyl ether and practically insoluble in water. When 10 mg of lafutidine is orally administered to normal adult males, fasting plasma concentration of unchanged drug observed as Tmax: 0.8±0.1 h; Cmax: 174±20 ng/ml; T1/2: 3.30 h. The total execration rate of lafutidine in urine is approximately 20% of given dose. Lafutidine is absorbed in the small intestine, reaches gastric cells via the systemic circulation, and rapidly binds to gastric cell H2 receptors, resulting in immediate inhibition of gastric acid secretion [3]. In the present study an attempt will be made to formulate and evaluate hydrodynamically balanced drug delivery system of lafutidine for the treatment of ulcer, which attempts to increase the gastric retention time of lafutidine. The present research work is with lafutidine along with polymer, i.e. guar gum, which attempts to increase the gastric retention time of the lafutidine and developed for the controlled release.

MATERIALS AND METHODS

Lafutidine, Guar gum, methocel K-4, methocel K 15, PVP-K-30, Sodium bicarbonate, Citric acid were purchased from chandras lab, Hyderabad.

Preparation of Standard Solution

Lafutidine (100mg) was dissolved in ethanol in 100 ml of volumetric flask and diluted quantitatively with ethanol to obtain a solution having a known concentration of 1000 µg/ml.

Procedure

From the standard solution of lafutidine 1ml was pipetted out into a 10ml volumetric flask and subsequently diluted with ethanol to obtain a series of dilutions containing 0.02,0.04,0.06, 0.08 µg of lafutidine per ml of solution. The absorbance of these solutions was measured in analytical technologies Limited, UV-Visible Spectrophotometer at 286 nm using etanol as blank.

Preparation of lafutidine floating tablets

Lafutidine tablets were prepared by direct compression method, polymer as guar gum and drug along with excipients like poly vinyl pyrrolidone k-30, sodium bicarbonate, lactose, talc, magnesium sterate, citric acid were thoroughly blended and compressed in the first three formulaions and mithocel k-4, methocel k-15M were used different formulations different formulations for next six formulation.

Evaluation of lafutidine floating tablets

The various physical properties of tablet blend like bulk density, tapped density, compressibility index and angle of repose were determined [4].

Bulk and tapped density

Bulk and tapped densities were measured by using 10 ml of graduated cylinder. The sample poured in cylinder was tapped mechanically for 100 times, then tapped volume was noted down and bulk density and tapped density were calculated.

Tapped density = Mass of formulation/tapped volume

Hausner ratio

Tapped density and bulk density were measured and the Hausner ratio was calculated using the formula,

Hausner ratio = ρt / ρo Where, ρt = tapped density, ρo = bulk density

Compressibility Index

The bulk density and tapped density was measured and Compressibility index was calculated using the formula, % Compressibility index (C.I.) = {(ρt- ρo)/ρt} × 100 Where, ρt = tapped density, ρo = bulk density

Angle of repose (θ)

Angle of repose has been defined as the maximum angle possible between the surface of pile of powder and horizontal plane. Angle of repose of different formulations was measured according to fixed funnel standing method (n = 3). The granules mass was allowed to flow out of the funnel orifice on a plane paper kept on the horizontal surface. This forms a pile of granules on the paper. The angle of repose was calculated by substituting the values of base radius ‘r’ and pile height ‘h’ in the following

equation, where, θ is the angle of repose, h is the height and r is the radius Tan θ = h/r.

Floating lag time

In vitro buoyancy was determined by floating time as per the method described by Dave B.S.et al [5]. The randomly selected tablets from each formulation were kept in a 250 ml beaker containing 150 ml simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). The time interval between the introduction of the tablet into the dissolution medium and its buoyancy to the top of dissolution medium was taken as floating lag time.

Floating time

The floating behavior of the formulated floating controlled release tablet of lafutidine was studied. The floating time was determined using a USP XXIV type II (paddle) apparatus at 37 ± 0.5 0 C containing 900 ml of 0.1N HCl and at 50 rpm. The time for which the tablet remains a float on the surface of the medium was measured as total floating time (TFT).

In-vitro dissolution rate studies

The release rate of lafutidine from floating tablets was determined using USP dissolution testing apparatus II (paddle type). The dissolution test was performed using 900 ml at 37±0.5 0 C at 50 rpm in 0.1N HCl. Aliquot volume was withdrawn from the dissolution apparatus at the time intervals of 1 to 24 h and the samples were replaced with fresh dissolution medium. After filtration, the amount of drug released was determined from the standard calibration curve of pure drug.

RESULTS

Table1: Preparation of lafutidine floating tablets

Ingredients (mg/tablet	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Lafutidine	10	10	10	10	10	10	10	10	10
Guar gum	30	60	90	_	_	_	_	_	_
Methocel k-4	_	_	_	30	90	90	_	_	_
Methocel k-15	_	_	_	_	_	_			
							30	60	90
Pvp k-30	10	10	10	10	10	10	10	10	10
Sodium bicarbonate	30	30	30	30	30	30	30	30	30
Lactose	113	83	53	113	83	53	113	83	53
Talc	6	6	6	6	6	6	6	6	6
Magnesium sterate	6	6	6	6	6	6	5	5	5
Citric acid	5	5	5	5	5	5	5	5	5

The Lafutidine floating tablets were prepared by using guar gum, methocel K4 and methocel K15M. Guar gum is an efficient matrix forming agent for floating tablets by generating gas. The lafutidine floating tablets were prepared by wet-granulation technique employing guar gum of different grades as floating polymer and release retardant, methocel K4, methocel K15M as a floating enhancer and sodium bicarbonate as gas generating agent.

Physical Properties

Different formulation ratios of blend affects the physical appearance of the tablets and micromeritic properties were observed. The measured tapped density was 0.501 to 0.643 (g/cm3), bulk density 0.421 to 0.540 (g/cm3), thickness 4.33 to 4.38(mm), hardness 4.26 to 5.06 (Kg/cm2), friability 0.24 to 0.46(%) were well within the limits, which indicates good flow potential for the prepared tablets. Angle of repose (θ) values for the granules was in the range 24.19 to 26.95° indicating good flow potential for the tablets

Table 2: Physical properties of prepared blend

Formulation	Tapped density (g/cm3)	Bulk density (g/cm3)	Compressibility index (%)	Angle of repose (θ)
F1	0.520±0.023	0.479±0.071	15.78±1.50	25.10±0.29
F2	0.638±0.037	0.526±0.034	18.02±1.85	26.55±0.82
F3	0.643±0.039	0.534±0.016	23.04±3.16	27.22±1.35
F4	0.513±0.016	0.443±0.012	15.29±1.72	24.36±0.23
F5	0.614±0.025	0.514±0.065	15.96±1.49	26.02±0.34
F6	0.638±0.038	0.540±0.028	19.34±1.32	26.95±1.06
F7	0.501±0.0018	0.421±0.020	10.884±1.63	24.19±0.23
F8	0.576±0.034	0.491±0.076	15.79±1.68	25.46±0.34
F9	0.627±0.035	0.517±0.089	16.90±1.44	26.39±0.42

Table 3: Thickness, Hardness, Friability, Drug content, Buoyancy Lag time and Total floating time of lafutidine floating tablets.

Formulation	Thickness in (mm)	Hardness (Kg/cm2) ± S.D	Friability (%) ± S.D	Drug content (mg/tab) ± S.D	Buoyancy lag time (sec)	Total floating time (h)
F1	4.35±0.083	5.0 ± 0.01	0.31± 0.011	98.34± 0.12	18 ± 11	15 ± 0.011
F2	4.36±0.012	5.03 ± 0.02	0.24± 0.012	99.21± 0.47	19 ± 10	20 ± 0.021
F3	4.38±0.026	5.06 ± 0.04	0.24± 0.015	99.97± 0.08	19 ± 20	24 ± 0.052
F4	4.34±0.109	4.89 ± 0.41	0.34± 0.014	98.17± 0.45	18 ± 09	13± 0.451
F5	4.35±0.134	4.76± 0.33	0.28± 0.018	98.86± 0.23	15 ± 40	18 ± 0.014
F6	4.38±0.016	4.91± 0.32	0.24± 0.018	99.92± 0.69	13± 03	22 ± 0.051
F7	4.33±0.095	4.26± 0.34	0.46 ± 0.01	97.42 ± 0.7	15± 30	09 ± 0.024
F8	4.35±0.081	4.55 ± 0.46	0.29± 0.013	98.54± 0.71	16± 07	16 ± 0.077
F9	4.36±0.116	4.82± 0.22	0.25± 0.016	99.91± 0.43	12± 40	19 ± 0.085

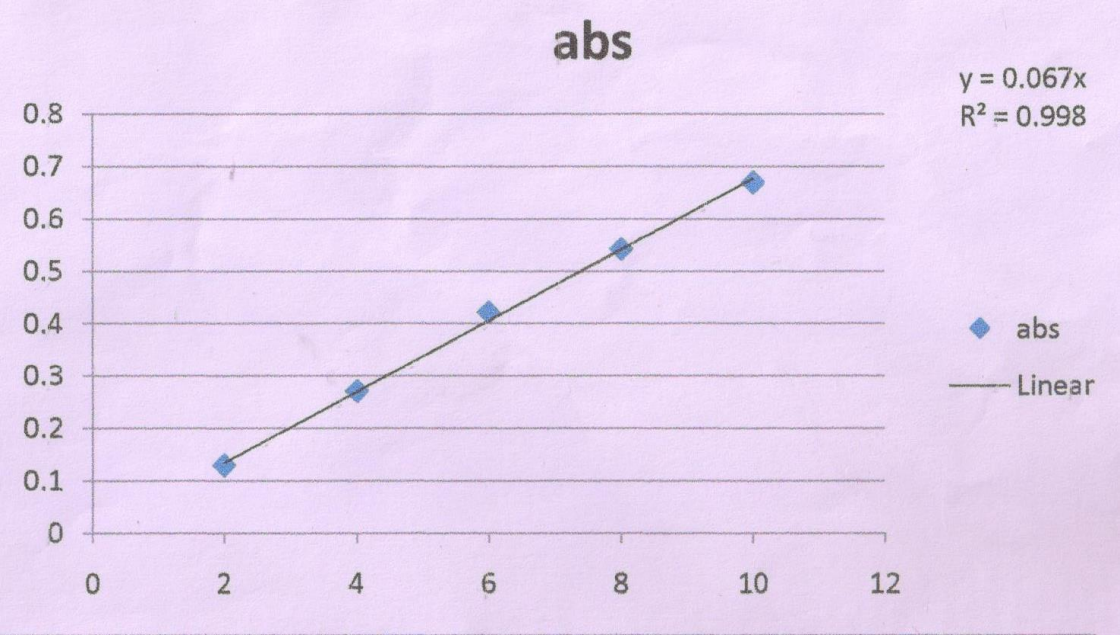

Figure 1. Calibration curve for the estimation of lafutidine

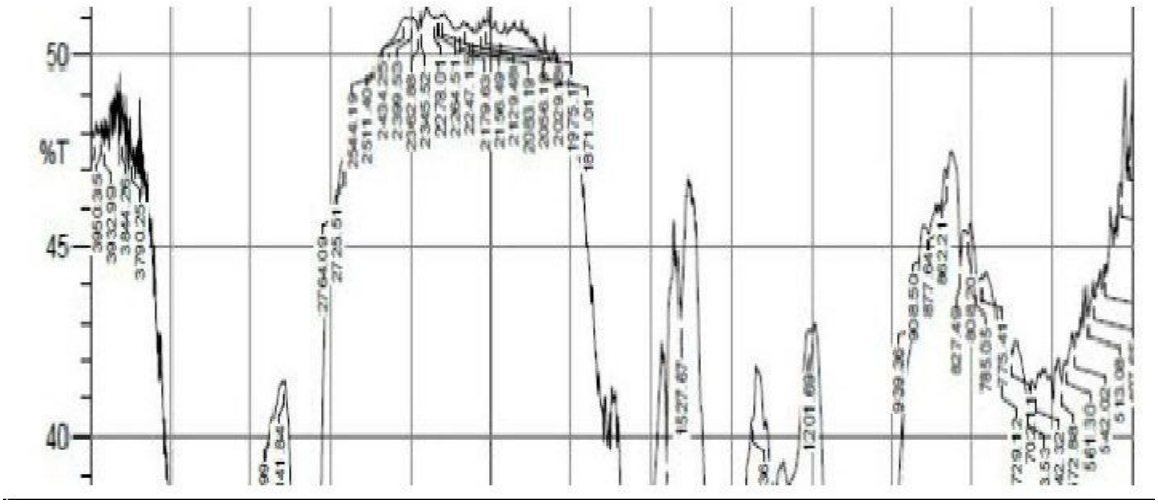

Figure 2: FT-IR spectra of lafutidine

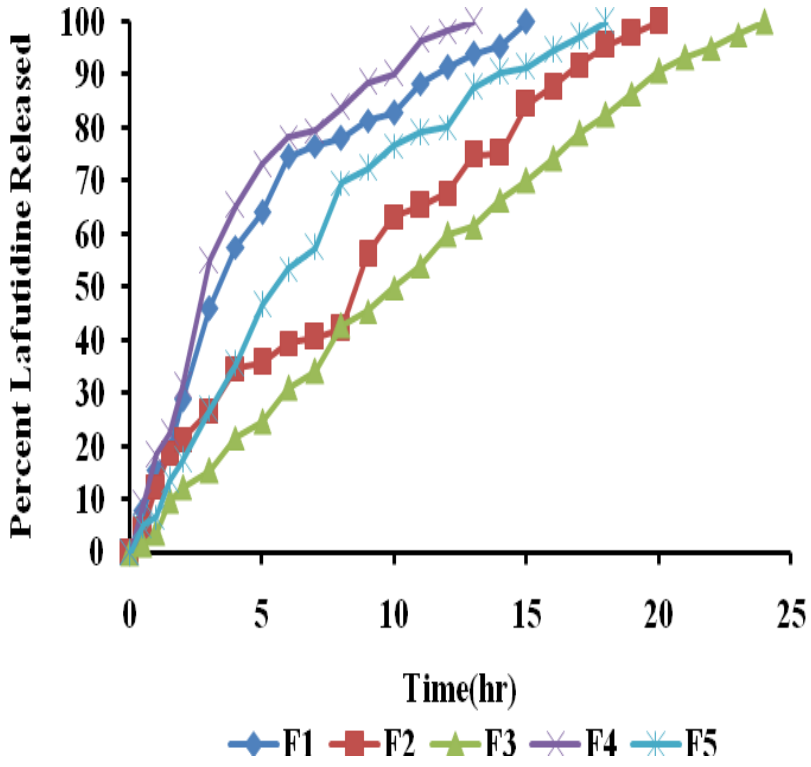

Figure 3: Release profiles of lafutidine floating tablets (F1-F5)

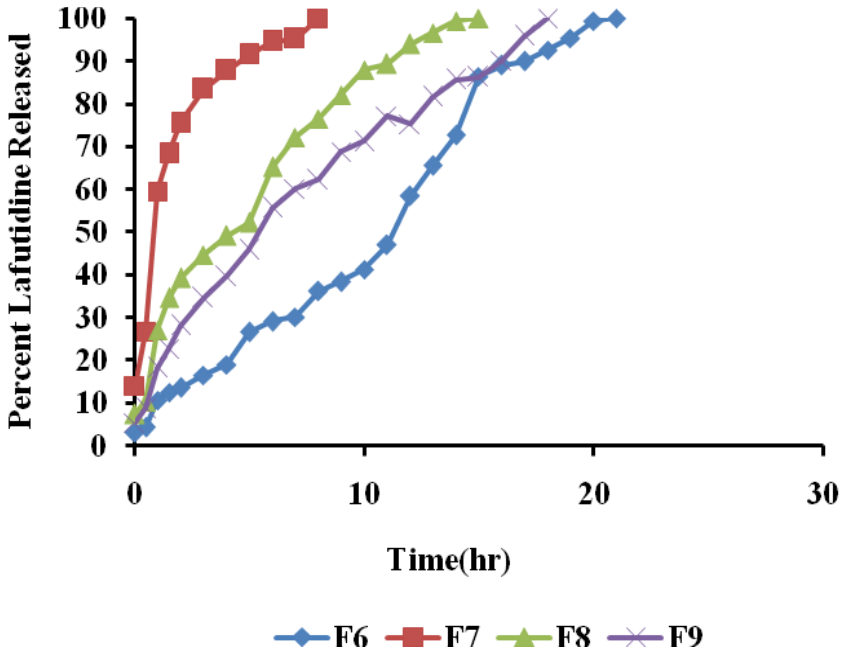

Figure 4: Release profiles of lafutidine floating tablets (F6-F9)

CONCLUSION

The evaluation results for *in-vitro* drug release showed that guar gum was able to retard the drug release more than 12 h. All the floating tablets prepared contained lafutidine within 100 ± 5% of the labeled claim. As such the prepared floating tablets were of good quality with regard to drug content, angle of repose, bulk density and tapped density. In the *in-vitro* buoyancy study varieties were observed in the floating lag time and floating time. In the *in-vitro* buoyancy study varieties were observed in the floating lag time and floating time of ideal formula F3.Lafutidine release from floating tablets was shown and spread over 12h depended on the composition of the matrix it concentration of guar gum, methocelK-4, methocelK15M, sodium bicarbonate and PVP-K-30. The dissolution data of tablets F1 to F9 was fitted to zero order, first order, korsmeyer and peppas and Higuchi models. The results of correlation coefficient (R2) were used to select the most appropriate model. The release profiles of formulations F3 fitted best to zero order model. Percent drug released verses square root time were found to be linear indicates that the drug release from the floating tablets prepared was diffusion controlled. The release data was also analyzed by the korsmeyer and peppas equation shown below in order to assess the release mechanism.

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