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FORMULATION DEVELOPMENT AND *IN VITRO* EVALUATION OF FLOATING TABLETS OF LAFUTIDINE BY DIRECT COMPRESSION METHOD

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ABSTRACT

In the present research work gastro retentive floating matrix formulation of Lafutidine by using various polymers were developed. Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium bicarbonate concentration was optimized. Then the formulation was developed by using different concentrations of polymers Xanthan gum, guar gum and Sodium Alginate as polymeric substances. The formulation blend was subjected to various preformualation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations Only Xanthan gum, Sodium Alginate highest concentrations (60 mg) retards the drug release upto 12 hours and the drug release 96. 25%, 95. 81% respectively. In this Xanthan gum releases the more drug release when compared to Sodium alginate. So F3 Formulation considered as optimized formulation. Optimised formulation F3 was kept for release kinetic studies. From the above graphs, it was evident that the formulation F3 was followed the Peppas release mechanism.

KEYWORDS: Lafutidine, Xanthan gum, Guar Gum and Sodium Alginate, Floating tablets.

INTRODUCTION

Oral delivery of drugs is the most preferable route of drug delivery. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient compliance and flexibility in formulation and cost-effective manufacturing process.[1]

Many of the drug delivery systems, available in the market are oral drug delivery type systems Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as:

1. 1 Controlled Drug Delivery Systems

Controlled drug delivery systems have been developed which are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of drug to a tissue.

METHODOLOGY

Analytical method development

a) Determination of absorption maxima

A solution containing the concentration 10 µg/ mL drug was prepared in 0. 1N HCL UV spectrum was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 400 nm.

b) Preparation calibration curve

10mg Lafutidine pure drug was dissolved in 10ml of methanol (stock solution1) from stock solution1 1ml of solution was taken and made up with10ml of 0. 1N HCL (100µg/ml). From this 1ml was taken and made up with 10 ml of 0. 1N HCL (10µg/ml). The above solution was subsequently diluted with 0. 1N HCL to obtain series of dilutions Containing 2, 4, 6, 8, 10 µg /ml of per ml of solution. The absorbance of the above dilutions was measured at 236 nm by using UV-Spectrophotometer taking 0. 1N HCL as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight-line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis.

Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy[11-15]

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany (Alpha T). The solid powder sample directly place on yellow crystal which was made up of ZnSe. The

spectra were recorded over the wave number of 4000 cm^{-1} to 550 cm^{-1}.

Pre formulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose[16-20]

The frictional force in a loose powder can be measured by the angle of repose. 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, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose.

Table 1: Angle of Repose values (as per USP).

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density[21-26]

Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. 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. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read.

Tapped density

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated, in gm per L, using the formula:

Measures of powder compressibility

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 interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

Table 2: Carr's index value (as per USP).

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

Formulation development of floating Tablets

For optimization of sodium bicarbonate concentration, granules were prepared by direct compression method.

Procedure for direct compression method

1) Drug and all other ingredients were individually passed through sieve no¹ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method by using 7mm punch.

Optimization of Sodium bicarbonate

Sodium bicarbonate was employed as effervescent gas generating agent. It helps the formulation to float. Various concentrations of sodium bicarbonate were employed; floating lag time and floating duration were observed. Based on the concentration of sodium bicarbonate was finalised and preceded for further formulations.

Table 3: Optimization sodium bicarbonate concentration.

Ingredients	DO1	DO2	DO3
Lafutidine	20	20	20
Xanthan Gum	60	60	60
$NaHCO_3$	5	7. 5	10
Citric Acid	7. 5	7. 5	7. 5
Mg. Stearate	3	3	3
Aerosil	3	3	3
MCC pH 102	Q. S	Q. S	Q. S
Total weight	250	250	250

All the quantities were in mg.

Based on the floating lag time and floating duration the concentration of sodium bicarbonate was optimized.

Table 4: Formulation composition for Floating tablets.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lafutidine	20	20	20	20	20	20	20	20	20
Xanthan gum	20	40	60	-	-	-	-	-	-
Guar gum	-	-	-	20	40	60	-	-	-
Sodium Alginate	-	-	-	-	-	-	20	40	60
Sodium bi Carbonate	7. 5	7. 5	7. 5	7. 5	7. 5	7. 5	7. 5	7. 5	7. 5
Citric acid	7. 5	7. 5	7. 5	7. 5	7. 5	7. 5	7. 5	7. 5	7. 5
MCC	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S
Aerosil	3	3	3	3	3	3	3	3	3
Magnesium Stearate	3	3	3	3	3	3	3	3	3
Total tablet	250	250	250	250	250	250	250	250	250

All the quantities were in mg.

Evaluation of post compression parameters for prepared Tablets

The designed compression tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage.[27-30] The mean and deviation were determined. The percent deviation was calculated using the following formula.

Table 5: Pharmacopoeial specifications for tablet weight variation.

Average weight of tablet (mg) (I. P)	Average weight of tablet (mg) (U. S. P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7. 5
More than	More than 324	5

Hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

Thickness

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Pre-weighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re- weighed, and loss in the weight of tablet is the measure of friability and is expressed in percentage as.

Determination of drug content

Both compression-coated tablets of were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of Lafutidine were accurately weighed, transferred to a 100ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

***In vitro* Buoyancy studies**

The in vitro buoyancy was determined by floating lag time, and total floating time. (As per the method described *by Rosa et al*) The tablets were placed in a 100ml beaker containing 0. 1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time (FLT) and duration of time the tablet constantly floats on the dissolution medium was noted as Total Floating Time respectively (TFT).

***In vitro* drug release studies**

- **Dissolution parameters:**
- **Apparatus** -- USP-II, Paddle Method
- **Dissolution Medium** -- 0. 1 N HCL
- **RPM** -- 50
- **Sampling intervals (hrs)** --0. 5, 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 12
- **Temperature** -- 37°C ± 0. 5°C

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

Procedure

900ml of 0. 1 HCL was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°C ± 0. 5°c. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 12 hours and then the medium 0. 1 N HCL was taken and process was continued from 0 to 12 hrs at 50 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with media and analyzed by spectrophotometrically at 236 nm using UV-spectrophotometer.

Application of Release Rate Kinetics to Dissolution Data

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics

To study the zero–order release kinetics the release rate data are fitted to the following equation.

RESULTS AND DISCUSSION[34-35]

Analytical Method

a. Determination of absorption maxima

The standard curve is based on the spectrophotometry. The maximum absorption was observed at 236 nm.

b. calibration curve

Graphs of Lafutidine was taken in 0. 1N HCl (pH 1. 2).

Table 6: Observations for graph of Lafutidine in 0. 1N HCL.

Concentration [µg/mL]	Absorbance
0	0
5	0. 162
10	0. 346
15	0. 548
20	0. 732
25	0. 926

Standard graph of Lafutidine was plotted as per the procedure in experimental method and its linearity is shown in Table and Fig. The standard graph of Lafutidine showed good linearity with R^2 of 0. 999, which indicates that it obeys "Beer- Lamberts" law.

Fig. 1: Standard graph of Lafutidine in 0. 1N HCL.

8. 2. Drug – Excipient compatibility studies

Fourier Transform-Infrared Spectroscopy

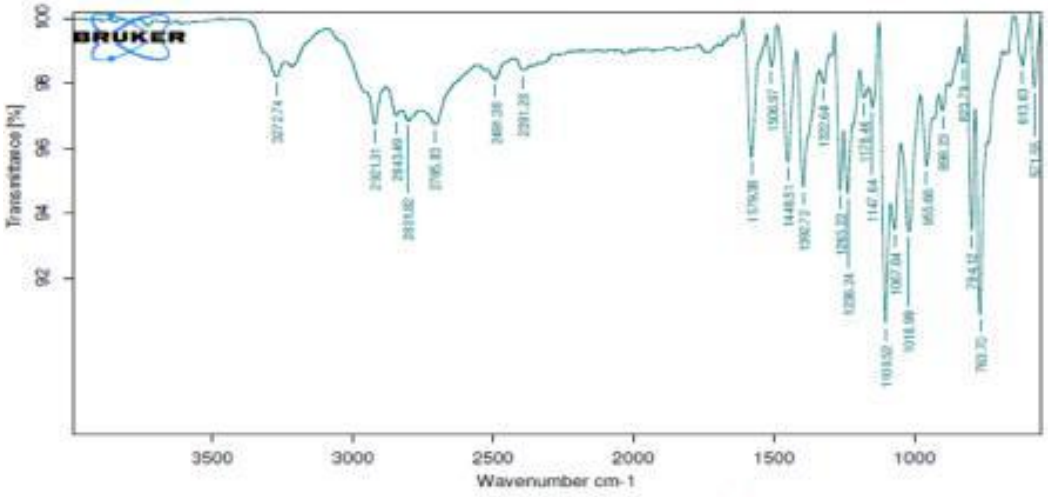

Figure 2: FTIR Spectrum of pure drug.

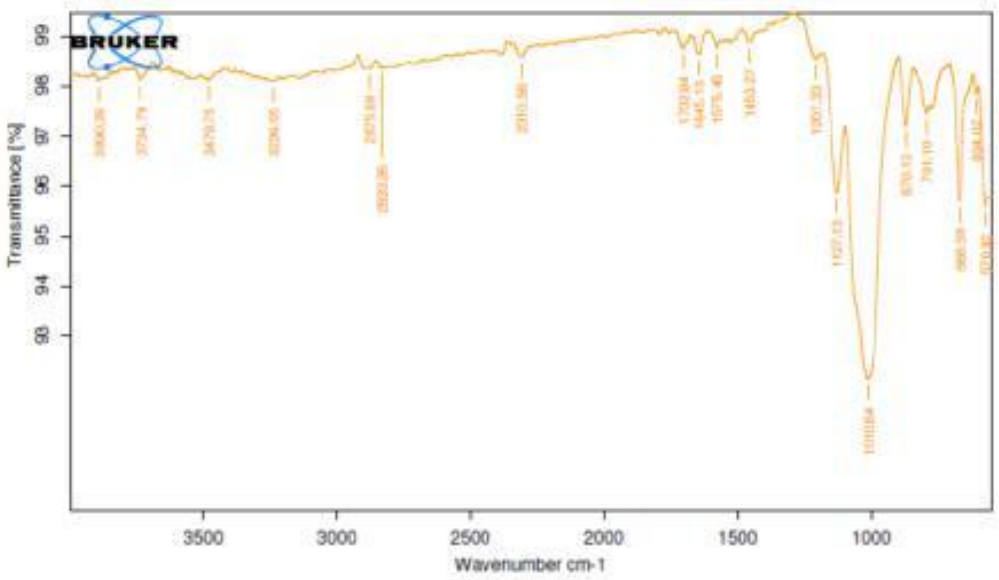

Fig. 3: FTIR Spectrum of optimized formulation.

Table 7: Pre-formulation parameters of blend.

Formulation code	Angle of repose (θ) ±SD	Bulk density (gm/cm) ±SD	Tapped density (gm/cm) ±SD	Hausner ratio (HR)±SD	Carr index (Ic) ±SD
F1	22.21±0.825	0.224±0.010	0.262±0.011	1.129±0.006	11.423±0.511
F2	21.84±0.645	0.210±0.010	0.260±0.010	1.180±0.010	15.398±0.594
F3	22.96±0.471	0.227±0.010	0.266±0.005	1.173±0.005	15.002±0328.
F4	22.85±0.520	0.230±0.010	0.270±0.010	1.173±0.010	14.827±0.550
F5	22.46±0.471	0.225±0.020	0.260±0.010	1.150±0.060	15.792±0.357
F6	22.64±0.746	0.234±0.015	0.270±0.026	1.190±0.010	16.016±0.640
F7	23.64±0.312	0.220±0.005	0.282±0.011	1.207±0.004	17.676±0.732
F8	22.85±0.665	0.230±0.011	0.260±0.010	1.124±0.005	15.399±0.592
F9	21.54±0.346	0.220±0.010	0.266±0.015	1.190±0.010	15.397±0.594
F10	22.87±0.934	0.250±0.010	0.250±0.010	1.163±0.030	11.706±0.512
F11	22.43±0.726	0.230±0.011	0.260±0.010	1.180±0.010	16.676±0.560
F12	24.06±0.556	0.230±0.011	0.300±0.010	1.199±0.009	16.015±0.640

All the values are expressed as mean ± SD. (n=3)

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

Lafutidine are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.421 to 0.561 (gm/ml) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.581 to 0.642 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 18 which shows that the powder has good flow properties. All the formulations has shown the hausners ratio ranging between 0 to 0.146 indicating the powder has good flow properties.

Optimization of sodium bicarbonate concentration

Three formulations were prepared with varying concentrations of sodium bicarbonate by direct compression method to compare the floating buoyancy in between direct compression method. The formulation containing sodium bicarbonate in 7.5 mg concentration showed less floating lag time in wet granulation method and the tablet was in floating condition for more than 12 hours.

Quality Control Parameters For tablets

Tablet quality control tests such as weight variation, hardness, and friability, thickness, Drug content and drug release studies were performed for floating tablets.

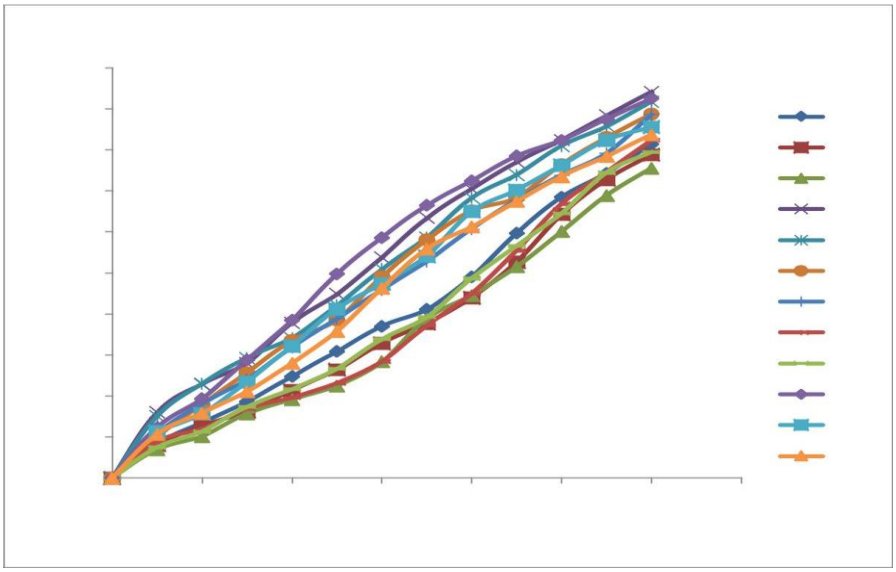

Fig. 4: Dissolution data of Lafutidine Floating tablets containing Xanthan Gum.

Table 8: *In vitro* quality control parameters.

Formulation code	Weight variation Average wt (mg)±SD	Hardness (Kg/cm2) in±SD	Diameter (mm) ±SD	in Thickness (mm) ±SD	in Friability (%)±SD	Drug content uniformity (%)±SD
F1	200.2± 0.952	4.932± 0.115	8.67± 0.577	2.129± 0.010	0.766± 0.090	96.362±0.305
F2	199.97± 0.877	4.863± 0.115	9.00± 0.000	2.239± 0.049	0.745± 0.060	98.738±0.228
F3	200.1± 0.857	4.946± 0.115	8.65± 0.577	2.253± 0.000	0.779± 0.017	98.432±0.355
F4	200.14± 0.815	4.644± 0.115	9.00± 0.000	2.204± 0.100	0.663± 0.010	94.513±0.130
F5	200.5± 0.885	4.943± 0.115	.32± 0.577	2.144± 0.066	0.592± 0.055	97.564±0.407
F6	195.6± 0.824	4.856± 0.115	9.65± 0.577	2.126± 0.055	0.759± 0.015	99.044±0.817
F7	200.15± 0.815	4.737± 0.115	8.65± 0.577	2.942± 0.057	0.663± 0.010	98.424±0.116
F8	200.04± 0.889	4.802± 0.200	8.67± 0.577	2.355± 0.100	0.782± 0.010	96.172±0.677
F9	200.12± 0.748	4.355± 0.208	9.34± 0.577	2.245± 0.057	0.756± 0.057	99.672±0.612
F10	200.2± 0.834	4.465± 0.115	8.67± 0.577	2.881± 0.052	0.769± 0.011	98.148±0.502
F11	199.58± 0.934	5.062± 0.155	9.00± 0.000	2.250± 0.000	0.671± 0.010	99.486±0.147
F12	200.3±0.833	4.801± 0.200	8.65± 0.577	2.279± 0.057	0.764± 0.011	98.592±0.391

All the parameters for tablets such as weight variation, friability, hardness, thickness, drug content was found to be within limits.

***In Vitro* Drug Release Studies**

Table- 9.

Formulation codes	Average Weight (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (Seconds)	Total Floating Time (Hrs)
F1	249. 3	5. 5	0. 43	3. 0	99. 12	25 s	>12 hrs
F2	249. 6	6. 0	0. 45	2. 9	98. 34	35 s	>10 hrs
F3	249. 7	5. 5	0. 67	3. 1	100. 12	56 s	>18 hrs
F4	248. 3	5. 5	0. 45	3. 2	101. 34	75 s	>20 hrs
F5	247. 5	6. 0	0. 78	3. 0	98. 12	60 s	>20 hrs
F6	249. 2	5. 5	0. 87	2. 9	99. 45	80 s	>24 hrs
F7	251. 6	5. 5	0. 65	3. 0	100. 43	35 s	>12 hrs
F8	250. 7	6. 0	0. 32	2. 9	101. 91	30 s	>12 hrs
F9	250. 1	5. 5	0. 74	2. 8	100. 12	38 s	>12 hrs

Table 10: *In-vitro* drug release data of Lafutidine floating tablets of Batch F7 to F12.

	% Cumulative release					
	FT7±SD	**FT8±SD**	**FT9±SD**	**FT10±SD**	**FT11±SD**	**FT12±SD**
1	10.831±0.352	8.872±0.172	7.474±0.455	12.323±0.0.447	11.322±0.219	10.625±0.532
2	16.998±0.0.266	11.997±0.328	12.328±0.412	18.331±0.437	15.622±0.397	16.824±0.742
3	24.017±0.352	18.878±0.220	17.341±0.353	28.774±0.744	24.466±0.485	21.058±0.653
4	33.898±0.393	19.618±0.306	21.623±0.307	38.457±0.524	32.158±0.353	27.949±0.698
5	38.828±0.315	23.146±0.399	25.634±0.532	49.716±0.659	43.154±0.439	35.747±0.618
6	45.856±0.353	29.388±0.347	33.853±0.534	58.581±0.656	47.343±0.448	46.248±0.661
7	55.835±0.348	37.172±0.394	39.282±0.332	69.471±0.568	54.060±0.573	55.865±0.662
8	60.689±0.308	44.951±0.353	49.630±0.367	72.428±0.632	64.934±0.513	63.201±0.746
9	67.741±0.352	55.434±0.308	56.568±0.355	78.508±0.228	73.164±0.581	67.382±0.702
10	75.842±0.306	67.828±0.351	64.488±0.397	83.304±0.402	76.211±0.397	73.515±0.747
11	79.132±0.353	74.582±0.308	75.404±0.315	87.488±0.444	82.343±0.415	78.396±0.704
12	88.621±0.414	82.356±0.306	79.521±0.423	92.354±0.864	85.624±0.367	83.731±0.537

All the values are expressed as mean ± SD. (n=3).

From the dissolution data it was evident that the formulations prepared with Guar Gum as polymer were retarded the drug release Less than 12 hours.

Whereas the formulations prepared with higher concentration of Xanthan gum retarded the drug release up to 12 hours in the concentration 60 mg. In lower concentrations, the polymer was unable to retard the drug release upto 12 hours.

Fig. 8: Zero order release kinetics.

The formulations prepared with Sodium alginate gum showed good retardation capacity of drug release (95. 81%) up to 12 hours in concentration 60 mg whereas Less concentrations (20 mg, 40 mg) not retard the drug release up to 12 hours. Hence, they were not considered.

5.8.5 Different Drug Release Kinetics Model For Lafutidine Floating Tablets

Table 11: Regression coefficients fit to different drug release kinetics models for Lafutidine floating tablets.

Formulation	Zero order	First order	Higuchi	Peppas	
code	**r2**	**r2**	**r2**	**r2**	**n**
F1	0.917	0.942	0.910	0.974	0.904
F2	0.985	0.902	0.865	0.970	0.969
F3	0.977	0.990	0.848	0.963	0.993
F4	0.994	0.916	0.952	0.990	0.780
F5	0.992	0.930	0.951	0.989	0.767
F6	0.995	0.943	0.940	0.995	0.878
F7	0.997	0.916	0.930	0.994	0.867
F8	0.960	0.857	0.818	0.928	0.956
F9	0.992	0.922	0.885	0.986	0.979
F10	0.983	0.955	0.956	0.990	0.863
F11	0.996	0.958	0.942	0.994	0.865
F12	0.995	0.959	0.922	0.978	0.910

CONCLUSION

Development of Gastro retentive floating drug delivery of Lafutidine tablets is to provide the drug action up to 12 hours. From the compatibility studies, it is concluded that, HPMC K4M, Xanthangum, HPMCK100,were compatible with drug Lafutidine and thus suitable for the formulation of Lafutidine floating tablets. Lafutidine tablets were fabricated by direct compression method. *In-vitro* buoyancy studies were performed for all the formulations, F1 to F12 by using 0.1 N HCL solution at 37^0C. Tablet containing HPMC (F4) showed good buoyancy with very short lag time and long floatation time of more than 12 hrs in 0.1 N HCL. *In-Vitro* release study is performed for 12 hrs. Optimized formula containing HPMCK100 (F4) showed better release compare to other formulations and it followed zero order kinetics. The non-Fickian diffusion was confirmed as the drug release mechanism from this formulation.From this study, it was concluded that HPMCK100 can be used in formulation of Lafutidin esustained release gastro retentive floating drug delivery system. Overall, this study concludes that viscosity of the polymer is a major factor affecting the drug release and floating properties of FDDSetentive floating system may be a suitable method for Lafutidine administration.

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CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

REFERENCES

1. Leon Lachman, Herbert a. Liberman, The Theory and Practice of Industrial Pharmacy, 293-302.
2. Robinson JR, Lee V. H. L, Controlled Drug Delivery: Fundamentals and Applications, 2nd edn. Marcel Dekker, New York, 1978; 24-36.
3. Brahmankar D. M, Jaiswal S. B, Biopharmaceutics and Pharmacokinetics a Treatise, 1st ed. Vallabh Prakashan; New Delhi, 1995; 64-70.
4. Chein Y. W, Novel Drug Delivery Systems, 2nd ed.: Marcel Dekker; New York, 1992; 4-56.
5. Ansel, Pharmaceutical Dosage Form and Drug Delivery System, Lipincott, 7th edition, 553.
6. Gennaro R. A. Remington, the Science and Practice of Pharmacy, 20th ed. New York: Lippincott Williams, 2000; 1045.
7. Banker G. S, Rhodes C. T, Modern Pharmaceutics. 3rd ed. Marcel Dekker, New York, 1996; 678-721.
8. Vyas S. P, Khar R. K, Controlled Drug Delivery: Concepts and Advances, 1st ed. Vallabh Prakashan, New Delhi, 2002; 345-376.
9. Shweta Arora, Floating Drug Delivery: A Review, AAPS Pharm Scitech., 2005; 47(11): 268-272.
10. Libo Yang, A New Intragastric Delivery System for the Treatment of H. Pylori associated with gastric ulcers, Elsevier J. Of Controlled Release., Apr 1999; 34(5): 215-222.
11. Ross and Wilson, Anatomy Physiology and Health Education. 9th ed. Churchil Livingston, 295-311.
12. Wilson K. R. W, Waugh A. Anatomy and Physiology in Health and Illness, 9th ed. Churchill Livingstone: London, 1996; 342-345.
13. Garima Chawla- A Means to address regional variability in intestinal drug absorption: Pharmtech, 2003; 234-238.
14. Chawla G, Gupta P, Koradia V, Bansal A, Gastroretention: a means to address regional variability in intestinal drug absorption, Pharm. Tech., 2003; 50-68.
15. Desai S, Bolton S. A floating controlled release system: in-vitro and in-vivo evaluation, J. Pharm. Res., 1993; 10; 1321-1325.
16. Garg S, Sharma S. Gastroretentive drug delivery systems, Pharmatech, 2003; 160-164.
17. Dr. Jose, Khalid Shah, Gastroretentive drug delivery system, business brief, Pharmtech., 2003; 165-173.
18. Deshpande A. A, Shah N. H, Rhodes C. T, development of a novel controlled release system for gastric retention, J. Pharm. Res., 1997; 14(6); 815-819.
19. Garima Chawla- A means to address regional variability in intestinal drug absorption: Pharmtech, 2003; 234-238.
20. David S. S. The effect of density on the gastric emptying on single and multiple unit dosage forms. J. Pharm Res., 1986; 3; 208-213.
21. H. g. Sivakumar, floating drug delivery system for prolonged gastric residence time: a review, Ind. J. Pharm. Edu., Oct-Dec-2004; 311-316.
22. B. N. Singh, H. Kim, Floating drug delivery system an approach to control drug delivery via gastric retention, J. Controlled Release., 2000; 63(7): 235-259.
23. B. Y. Choi, H. J. Park, Preparation of alginate beads for floating drug delivery system: effect of co2 gas forming agent. J. Controlled Release, 2000; 25(6): 488-491.
24. Ingani H. M, Timmermans J, Moes A. J, concept and in-vivo investigation of peroral sustained release floating dosage forms with enhanced gastrointestinal transit, Int. J. Pharm., 1987; 35: 157-164.
25. Bhavana V, Khopade A. J, Jain W. D, Shelly and Jain N. K, targeted oral drug delivery, Indian Drugs., 1996; 33: 365-373.
26. Roop K. Khar, controlled drug delivery, Gastroretentive system, 4th Edn., 202-203.
27. Hradman J. G, Limbrid, Goodman Gilman's, the Pharmacological Basis of Therapeutics, 10th Edn, New York, 2001; 1765.
28. Ichikawa M, Watanabe S, Miyake Y, A new multiple-unit oral floating dosage system: preparation and in-vitro evaluation of floating and sustained-release characteristics, J. Pharm. Sci., 1991; 80: 1062-1066.
29. Abubakr O. Nur and Jun S. Zhang, captopril floating and/or bioadhesive tablets: Design and Release kinetics, Taylor and Francis, 2000; 26(9): 965 – 969.
30. Menon A, Wolfgang A. R, Saks A. Development and evaluation of a monolithic floating dosage form for furosemide, J. Pharm. Sci., 1994; 83: 239-245.
31. Ozdemir N, Ordu S, Ozkan Y. Studies of floating dosage forms of furosemide: in-vitro and in vivo evaluations of bilayer tablet formulations, drug. Dev. Ind. Pharm., 2000; 857-866.
32. Xu X, Sun M, floating matrix dosage form for phenaporlaminehcl based on gas forming agent, int. J. Pharm, 2006; 25(4): 324-332.
33. Srivastava A. K, Wadwa S. Oral sustain delivery of atenolol from floating matrix tablets and invitro evaluation, drug. Dev. Ind. Pharm., 2005; 31(45): 367-374.
34. Wie J. P, Huang, preparation of the 5-fluoro uracil floating sustain release tablets for gastric retention, beijing, da Xue Xue Bao., 2004; 36(4): 493-442.
35. Streubel A, Siepmann J, Bodmeier R, floating matrix tablets based on low density foam powder: effects of formulation and processing parameters on drug release, Eur. J. Pharm. Sci., 2003; 18: 37-45.