FORMULATION DEVELOPMENT AND *IN VITRO* EVALUATION OF FLOATING TABLETS OF LAFUTIDINE BY EMPLOYING EFFERVESCENT TECHNOLOGY

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RESEARCH ARTICLE

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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 optimised. 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 pre-formulation 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 optimised 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. Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.

2. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.

3. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the C_{ss} values fall or rise beyond the therapeutic range.

4. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs. (2-3)

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits.

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.

Controlled drug delivery or modified drug delivery systems are divided into four categories.

1. Delayed release

2. Sustained release

3. Site-specific targeting

4. Receptor targeting

More precisely, controlled delivery can be defined as:

1. Sustained drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects.

2. Localized drug action by spatial placement of a controlled release system adjacent to or in the diseased tissue.

3. Targeted drug action by using carriers or chemical derivatives to deliver drug to a particular target cell type.

4. Provide physiologically/therapeutically based drug release system. In other words, the amount and the rate of drug release are determined by the physiological/ therapeutic needs of the body.(4-5)

A controlled drug delivery system is usually designed to deliver the drug at particular rate. Safe and effective blood levels are maintained for a period as long as the system continues to deliver the drug (Figure 1). Controlled drug deliveries usually results in substantially constant blood levels of the active ingredient as compared to the uncontrolled fluctuations observed when multiple doses of quick releasing conventional dosage forms are administered to a patient. (6-10)

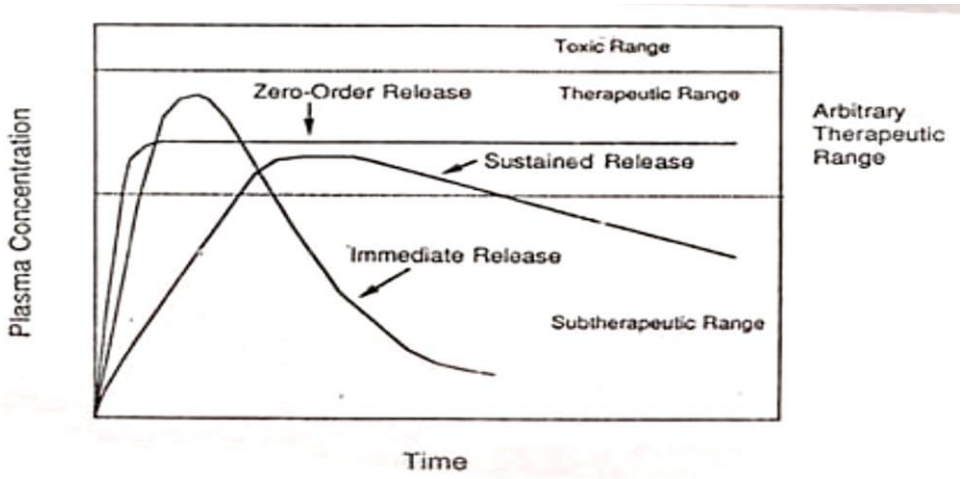


Figure 1: Drug level verses time profile showing differences between zero order, controlled releases, slow first order sustained release and release from conventional tablet

Oral drug delivery systems have progressed from immediate release to site-specific delivery over a period of time. Every patient would always like to have a ideal drug delivery system possessing the two main properties that are single dose or less frequent dosing for the whole duration of treatment and the dosage form must release active drug directly at the site of action.

Thus the objective of the pharmacist is to develop systems that can be as ideal system as possible. Attempts to develop a single- dose therapy for the whole duration of treatment have focused attention on controlled or sustained release drug delivery systems. Attention has been focused particularly on orally administered sustained drug delivery systems because of the ease of the administration via the oral route as well as the ease and economy of manufacture of oral dosage forms. Sustained release describes the delivery of drug from the dosage forms over an extended period of time. It also implies delayed therapeutic action and sustained duration of therapeutic effect. Sustained release means not only prolonged duration of drug delivery and prolonged release, but also implies predictability and reproducibility of drug release kinetics. A number of different oral sustained drug delivery systems are based on different modes of operation and have been variously

named, for example, as dissolution controlled systems, diffusion controlled systems, ion-exchange resins, osomotically controlled systems, erodible matrix systems, pH-independent formulations, swelling controlled systems, and the like.

An orally administered controlled drug delivery system encounters a wide range of highly variable conditions, such as pH, agitation intensity, and composition of the gastrointestinal fluids as it passes down the G.I tract. Considerable efforts have been made to design oral controlled drug delivery systems that produce more predictable and increased bioavailability of drugs. However, the development process is precluded by several physiological difficulties, like inability to retain and localize the drug delivery system within desired regions of the G.I tract and highly variable nature of the gastric emptying process. An important factor, which may adversely affect the performance of an oral controlled drug delivery system, is the G.I transit time. The time for absorption in the G.I transit in humans, estimated to be 8-10 hr from mouth to colon, is relatively brief with considerable fluctuation. G.I transit times vary widely between individuals, and depend up on the physical properties of the object ingested and the physiological conditions of the gut. This variability may lead to predictable bioavaialability and times to achieve peak plasma levels. One of the important determinants of G.I transit is the residence time in the stomach.

Majority of the drugs are well absorbed from all the regions of the G.I tract while some are absorbed only from specific areas, principally due to their low permeability or solubility in the intestinal tract, their chemical instability, the binding of the drug to the gut contents, as well as to the degradation of the drug by the microorganisms present in the colon. Therefore, in instances where the drug is not absorbed uniformly over the G.I tract, the rate of drug absorption may not be constant in spite of the drug delivery system delivering the drugs at a constant rate into the G.I fluids. More particularly, in instances where a drug has a clear cut absorption window, i.e., the drug is absorbed only from specific regions of the stomach or upper parts of the small intestine; it may not be completely absorbed when administered in the form of a typical oral controlled drug delivery system. It is due to the relatively brief gastric emptying in humans, which normally averages 2-3 hrs through the major absorption zone. It may cause incomplete drug release from the dosage form at absorption sites leading to diminished efficacy of the administered dose. It is apparent that for a drug having such an absorption window, an effective oral controlled drug delivery system should be designed not only to deliver the drug at a controlled rate, but also to retain the drug in the stomach for a long period of time. For this drug, increased or more predictable availability would result if controlled release systems could be retained in the stomach for extended periods of time.

It is suggested that compounding narrow absorption window drugs in a unique pharmaceutical dosage form with gastro retentive properties would enable an extended absorption phase of these drugs. After oral administration, such a dosage form would be retained in the stomach and release the drug there in a controlled and prolonged manner, so that the drug could be supplied continuously to its absorption sites in the upper gastrointestinal tract. This mode of administration would best achieve the known pharmacokinetic and pharmacodynamic advantages of controlled release dosage form for these drugs.

Incorporation of the drug in a controlled release gastroretentive dosage form (CRGRDF) can yield significant therapeutic advantages due to a variety of pharmacokinetic and pharmacodynamic factors.

Controlled release or Extended-release dosage forms with prolonged residence times in the stomach are highly desirable for drugs. which are:

- Administered two or more time a day.
- Only absorbed in the upper GI regions.
- Insoluble in water.
- Targeted at sites in the upper GI tract.
- Bioavailable through active transport mechanisms.
- Irritating to the mucosa.

- Misbalancing, irritating, or unsafe in the lower GI region.
- More effective when plasma levels are more constant.
- That is locally active in the stomach.
- That has an absorption window in the stomach or in the upper small intestine.
- That is unstable in the intestinal or colonic environment or degrades in colon.
- Have low solubility at high pH values.

DRUG PROFILE

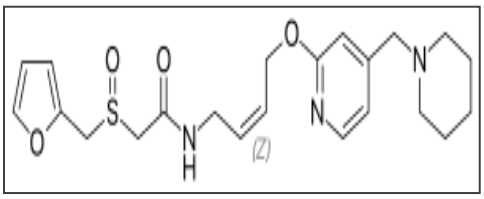
Drug: Lafutidine

Synonym: Protecadin

Drug category: Histamine H_2-receptor antagonist

Treatment of peptic ulcer and gastro-oesophageal reflux disease (GORD)

Structure



Chemical name/Nomenclature/IUPAC Name :2-(furan-2-ylmethylsulfinyl)-N-[(Z)-4-[4-(piperidin-1-ylmethyl)pyridin-2-yl]oxybut-2-enyl]acetamide

Molecular Formula: $C_{22}H_{29}N_3O_4S$

Molecular Weight: 431.54 gm/mole

PHYSICOCHEMICAL PROPERTIES

Storage Conditions: Store at room temperature

Dosage: 10 mg of Lafutidine, twice daily,

PHARMACOKINETIC PROPERTIES

Half-life: 1.92 ± 0.94 hrs

Absorption: Absorbed after oral administration. rapidly absorbed in the GIT.

Protein binding: 88 %

Metabolism: Hepatic by CYP2D6 and CYP3A4 enzymes

Excretion: Excreted through urine

Adverse effects/Side effects

Adverse events observed during clinical trials included constipation, diarrhoea, drug rash, nausea, vomiting and dizziness

The gastroretentive drug delivery systems can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability.

Lafutidine, an anti-histamine drug, is prescribed for the treatment and management of peptic ulcer and gastro-oesophageal reflux disease (GERD).

In the present investigation floating tablets of Lafutidine were prepared by direct compression using Effervescent Technology.

Plan of Work

1. Literature Survey

2. Selection and Procurement of suitable Drug candidate and Excipients

3. Preparation of standard graph of Lafutidine in 0.1 N HCL

4. Drug and Excipient compatibility studies using FTIR

5. Formulation of floating tablets of Lafutidine
A. Optimisation of sodium bicarbonate Concentration

B. Formulation development of Lafutidine floating tablets

6. Pre-compression studies of Formulation blend of F1 - F9
A. Angle of repose
B. Bulk density
C. Tapped density
D. Carr's index
E. Hausner's ratio

7. Preparation of the Floating tablets of Lafutidine

8. Post Compression Evaluation of prepared floating tablets of Lafutidine
A. Weight variation
B. Tablet Thickness
C. Tablet Hardness
D. Friability
E. Assay
F. *In vitro* buoyancy studies
i. Floating lag time
ii. Total Floating time
G. *In vitro* release studies

9. Selection of optimised formulation

10. Kinetic analysis of Optimised dissolution data

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. 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 was calculated using the following formula:

$\tan \theta = h / r$ $\tan \theta$ = Angle of repose

h = Height of the cone, r = Radius of the cone base

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.

The bulk density was calculated using the formula:

Bulk Density = M / V_o

Where, M = weight of sample

V_o = apparent volume of powder

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:

Tap = M / V

Where, Tap= Tapped Density

M = Weight of sample

V= Tapped volume of powder

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:

Carr's Index = [(tap - b) / tap] × 100

Where, b = Bulk Density

Tap = Tapped Density

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

- Drug and all other ingredients were individually passed through sieve no 60.
- All the ingredients were mixed thoroughly by triturating up to 15 min.
- The powder mixture was lubricated with talc.
- The tablets were prepared by using direct compression method by using 7mm punch.

Optimisation 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 optimised.

FORMULATION OF FLOATING TABLETS

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.

% Deviation = (Individual weight – Average weight / Average weight) × 100

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

$$\% \text{ Friability} = [(W1-W2) / W1] \times 100$$

Where, W1 = Initial weight of tablets

W2 = Weight of the tablets after testing

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 100 ml 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 $\pm$ 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: 900 mL 0f 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.

$$F = K_o t$$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

$$\text{Log } (100\text{-}F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$$F = k\ t1/2$$

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$M_t/ M_\infty = K\ t^n$$

Where, M_t/ M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n > 1. In this model, a plot of log (M_t/ M_∞) versus log (time) is linear.

RESULTS AND DISCUSSION (31-32)

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

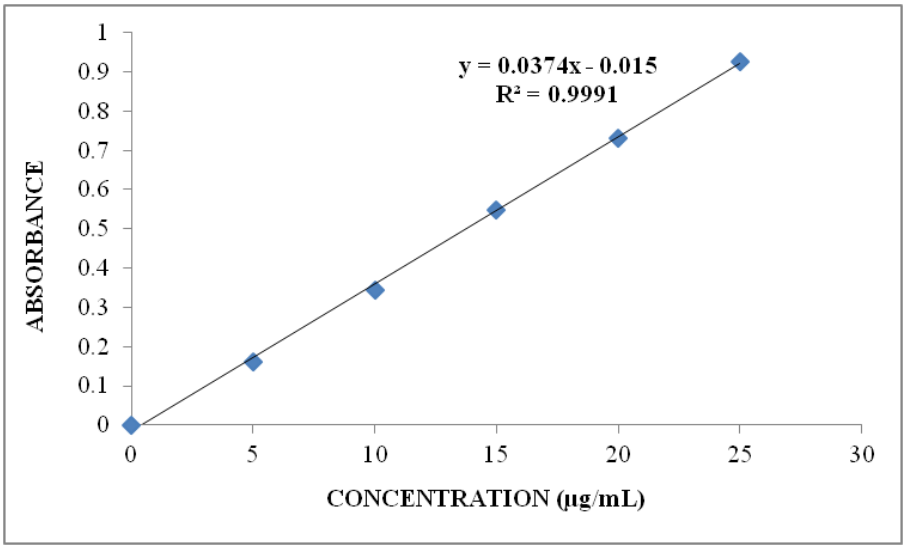


Figure 1: Standard graph of Lafutidine in 0.1N HCL

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.

Drug – Excipient compatability studies

Fourier Transform-Infrared Spectroscopy

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 show 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.

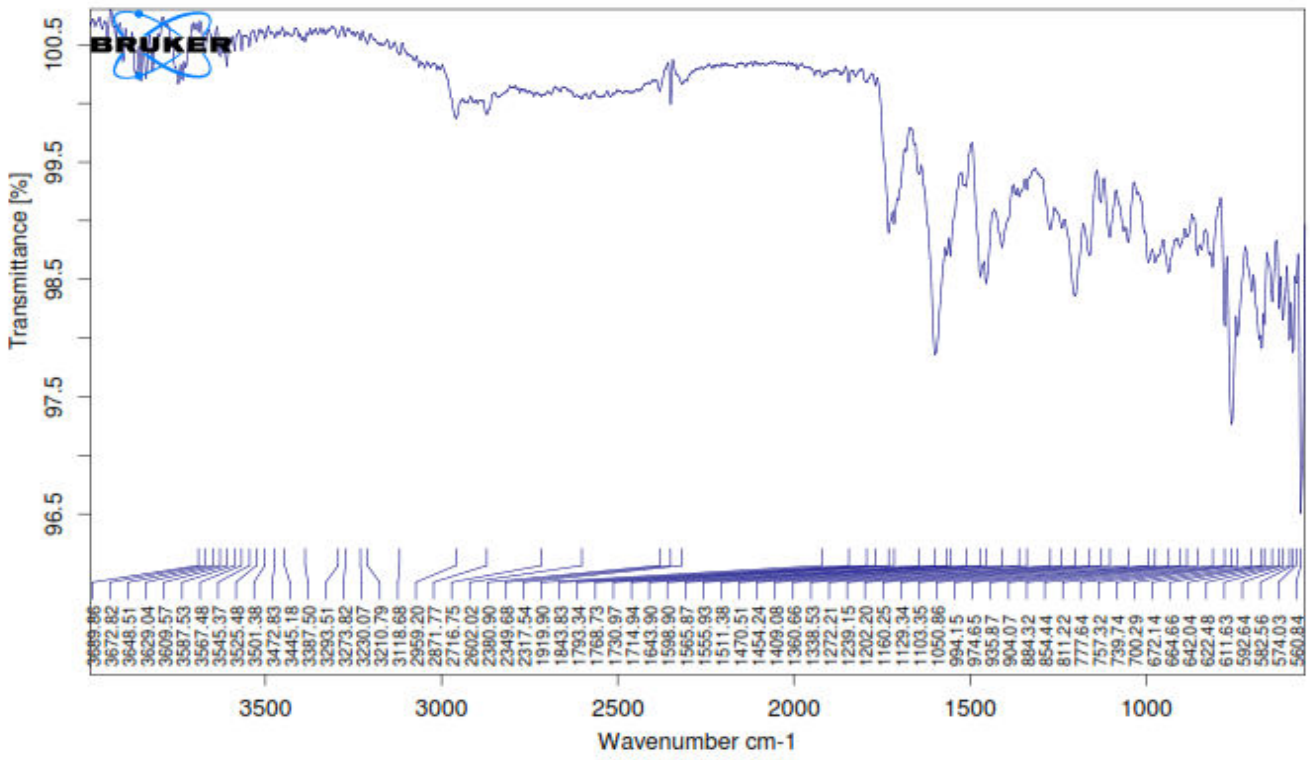


Figure 2: FTIR Spectrum of pure drug

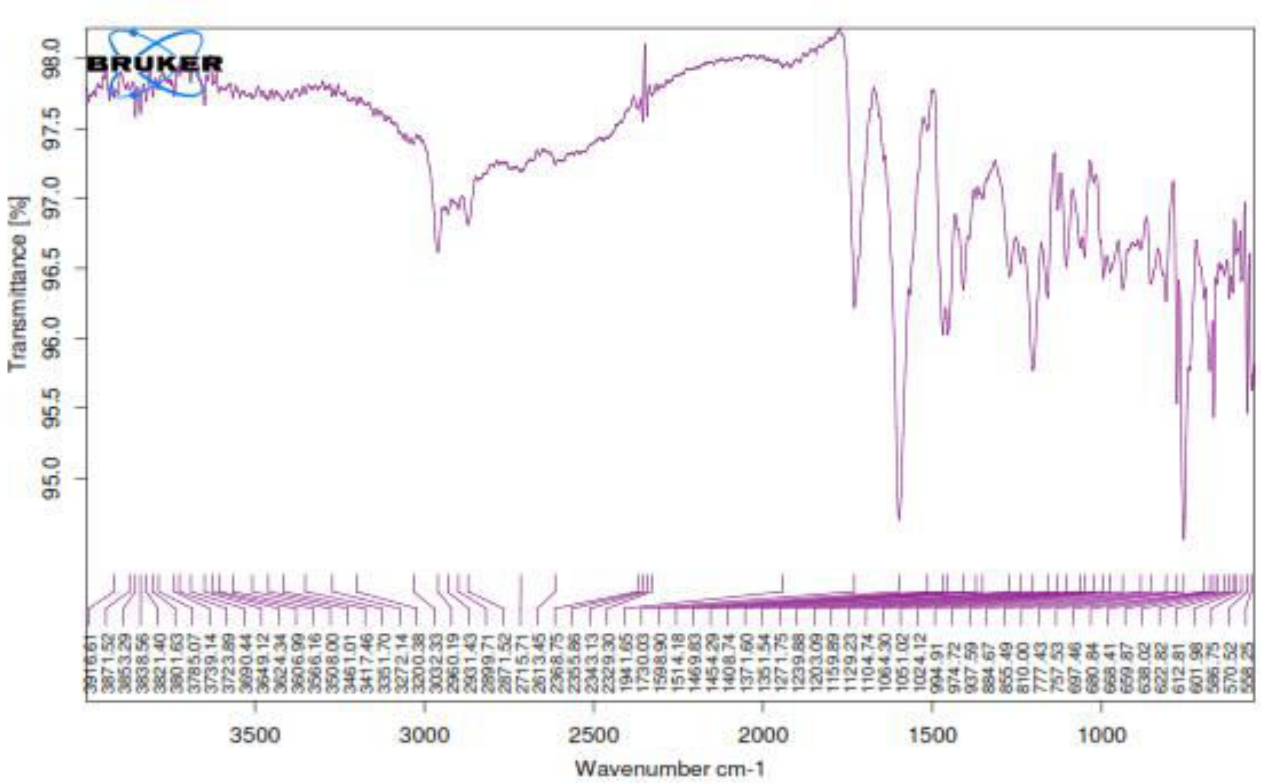


Figure 3: FTIR Spectrum of optimized formulation

Pre-formulation parameters of powder blend

Table 7: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/mL)	Tapped density (gm/mL)	Carr's index (%)	Hausner's Ratio
F1	24.58 o	0.510	0.610	21.32	0.112
F2	29.67o	0.421	0.621	28.26	0.056
F3	30.90o	0.458	0.581	25.90	0.078
F4	28.15o	0.561	0.632	21.78	0.141
F5	23.13o	0.541	0.642	18.45	0.098
F6	25.41o	0.483	0.587	26.53	0.088
F7	30.89o	0.463	0.591	24.67	0.110
F8	31.23o	0.437	0.623	28.78	0.121
F9	24.34o	0.521	0.632	17.32	0.146

Table 8: *In vitro* quality control parameters

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

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

In Vitro Drug Release Studies

Table 9: Dissolution data of Floating Tablets

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	20.28	19.31	18.57	21.26	20.38	22.24	19.16	18.18	19.83
1	39.34	37.85	35.85	38.32	38.46	36.84	21.32	29.26	21.31
2	54.52	46.32	41.31	44.24	50.15	46.23	36.44	33.23	26.92
3	76.38	59.51	54.32	51.76	62.43	53.58	44.33	39.68	34.39
4	92.62	63.62	65.71	58.82	79.32	64.32	57.67	48.95	46.41
5	96.78	78.91	68.92	80.42	85.16	82.27	67.52	50.36	51.75
6	99.86	84.89	73.53	92.72	89.11	96.32	70.14	60.32	63.81
7		90.32	77.21	98.22	94.74	97.92	75.56	76.41	74.57
8		93.57	82.31		99.21		83.54	83.23	78.81
9		98.18	84.85				99.83	86.18	83.75
10			90.67					98.69	87.32
11			94.31						93.05
12			96.25						95.81

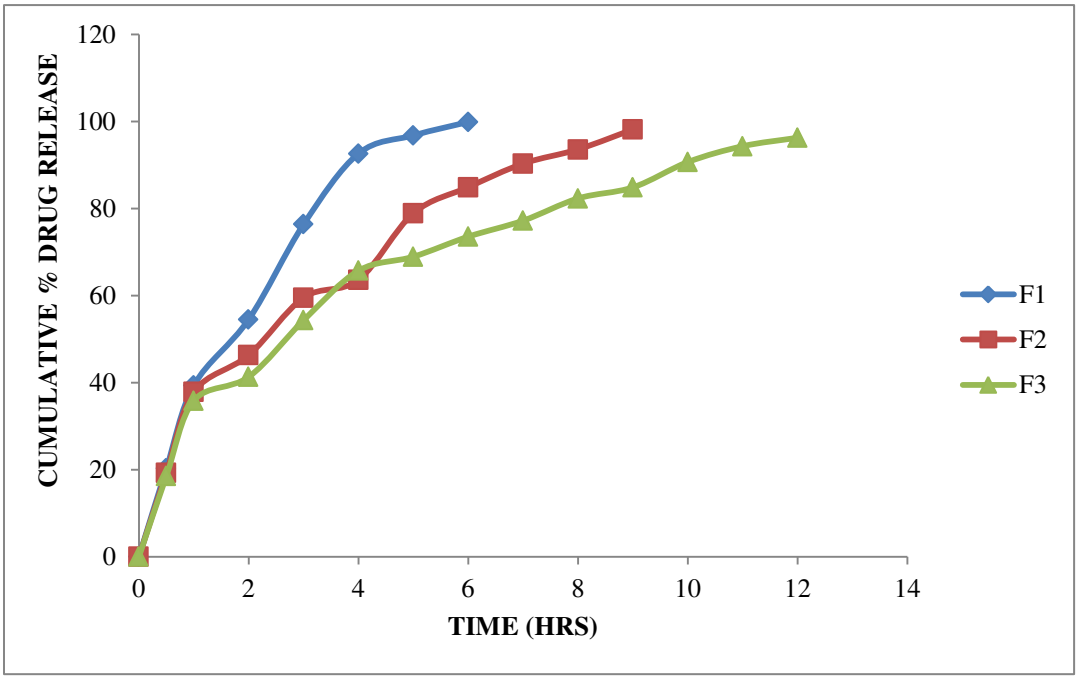


Figure 4: Dissolution data of Lafutidine Floating tablets containing Xanthan Gum

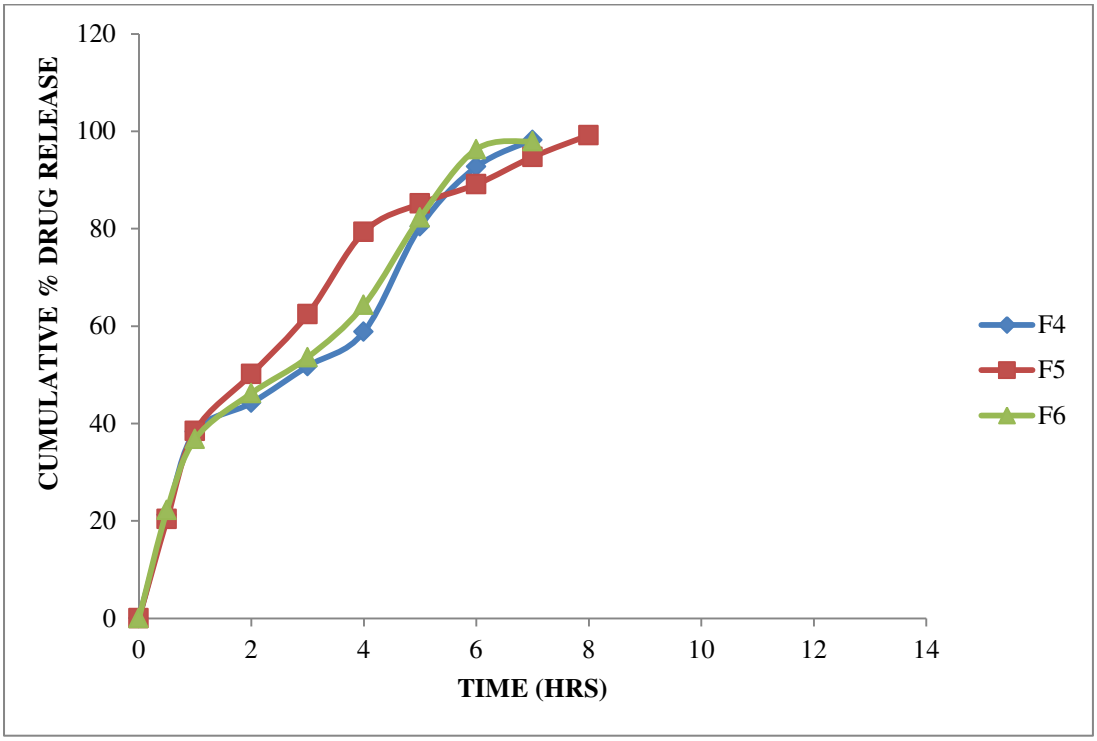


Figure 5: Dissolution data of Lafutidine Floating tablets containing Guar Gum

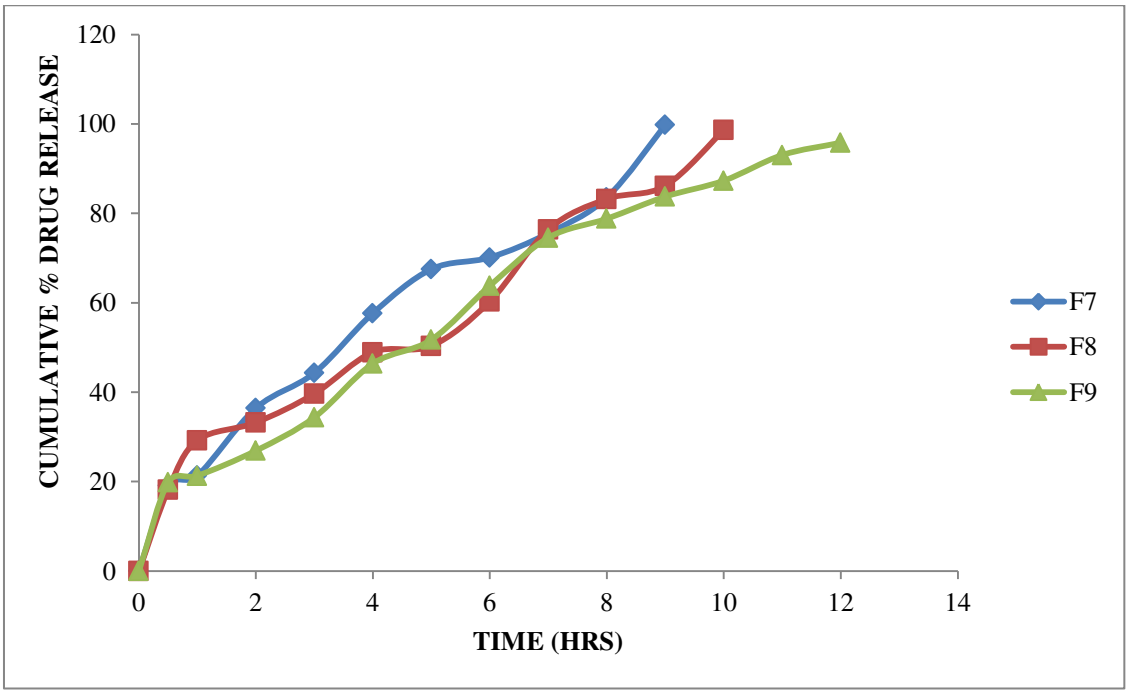


Figure 6: Dissolution data of Lafutidine Floating tablets containing Sodium Alginate

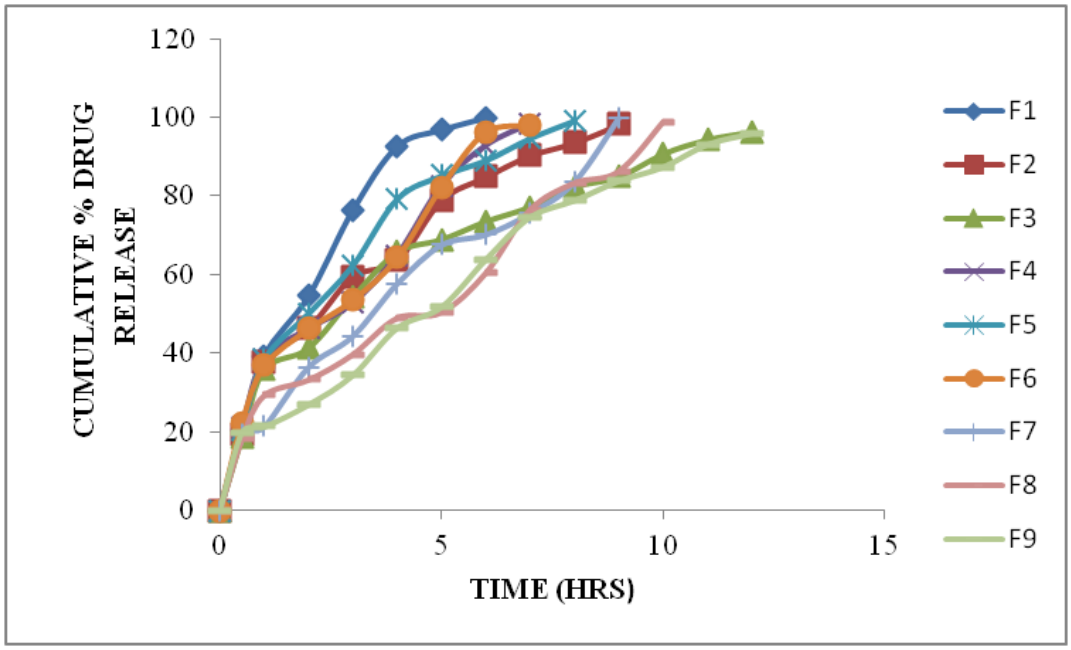


Figure 7: Dissolution data of Lafutidine Floating tablets All Formulations (F1-F9)

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.

The formulations prepared with Sodium alginate gum showed good retardation capacity of drug release (95.81%) upto 12 hours in concentration 60 mg whereas Less concentrations (20 mg, 40 mg) not retard the drug release upto 12 hours. Hence they were not considered.

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 optimised formulation.

Hence from the above dissolution data it was concluded that F3 formulation was considered as optimised formulation because good drug release (96.25%) in 12 hours.

Application of Release Rate Kinetics to Dissolution Data for optimised formulation:

Table 10: Application kinetics for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE(CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
18.57	0.5	0.707	1.269	0.301	1.911	37.140	0.0539	0.731	81.43	4.642	4.334	0.307
35.85	1	1.000	1.554	0.000	1.807	35.850	0.0279	0.446	64.15	4.642	4.003	0.638
41.31	2	1.414	1.616	0.301	1.769	20.655	0.0242	-0.384	58.69	4.642	3.886	0.755
54.32	3	1.732	1.735	0.477	1.660	18.107	0.0184	-0.265	45.68	4.642	3.575	1.067
65.71	4	2.000	1.818	0.602	1.535	16.428	0.0152	-0.182	34.29	4.642	3.249	1.393
68.92	5	2.236	1.838	0.699	1.492	13.784	0.0145	-0.162	31.08	4.642	3.144	1.498
73.53	6	2.449	1.866	0.778	1.423	12.255	0.0136	-0.134	26.47	4.642	2.980	1.661
77.21	7	2.646	1.888	0.845	1.358	11.030	0.0130	-0.112	22.79	4.642	2.835	1.806

82.31	8	2.828	1.915	0.903	1.248	10.289	0.0121	-0.085	17.69	4.642	2.606	2.036
84.85	9	3.000	1.929	0.954	1.180	9.428	0.0118	-0.071	15.15	4.642	2.474	2.167
90.67	10	3.162	1.957	1.000	0.970	9.067	0.0110	-0.043	9.33	4.642	2.105	2.536
94.31	11	3.317	1.975	1.041	0.755	8.574	0.0106	-0.025	5.69	4.642	1.785	2.856
96.25	12	3.464	1.983	1.079	0.574	8.021	0.0104	-0.017	3.75	4.642	1.554	3.088

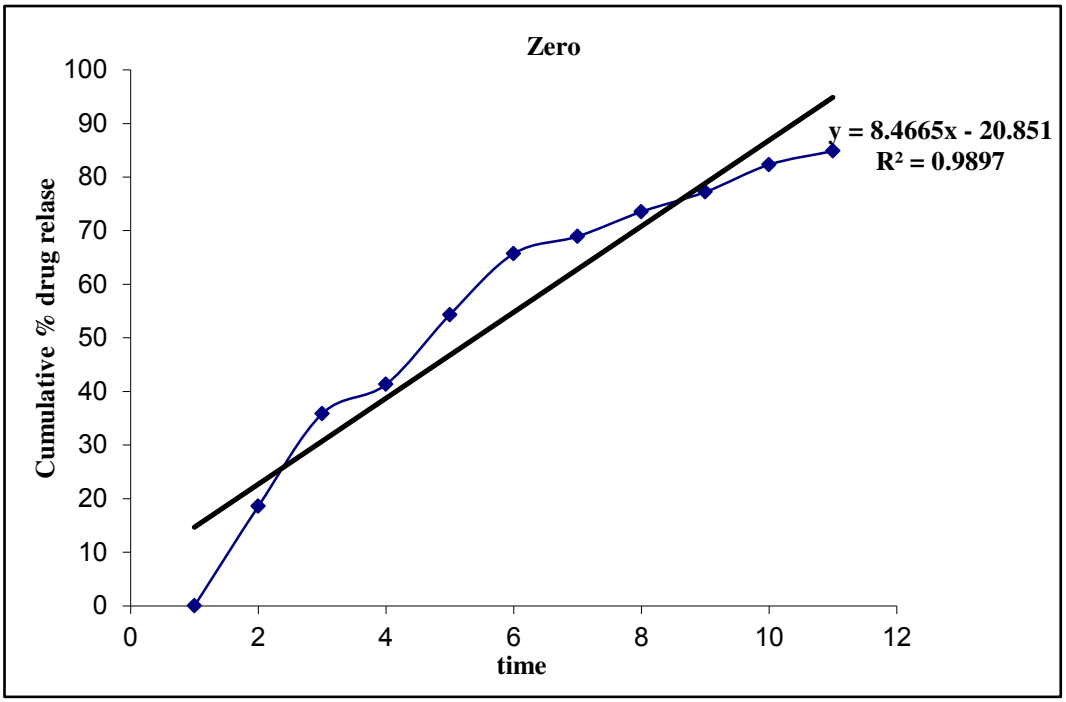


Figure 8: Zero order release kinetics

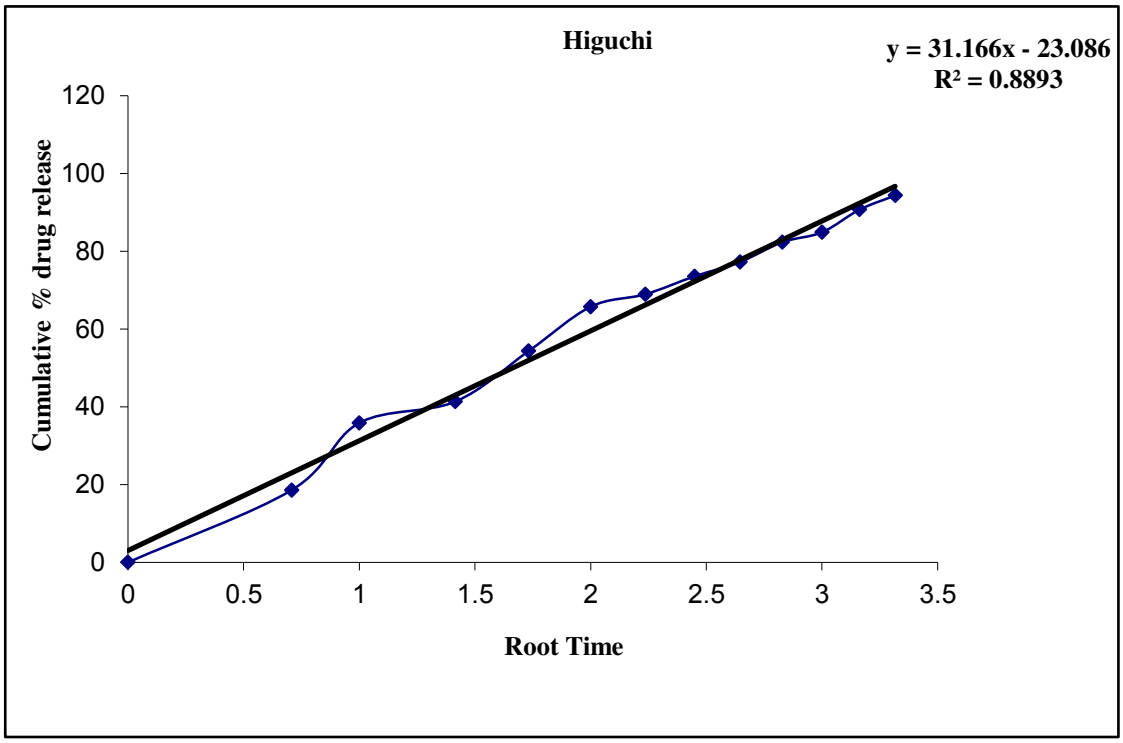


Figure 9: Higuchi release kinetics

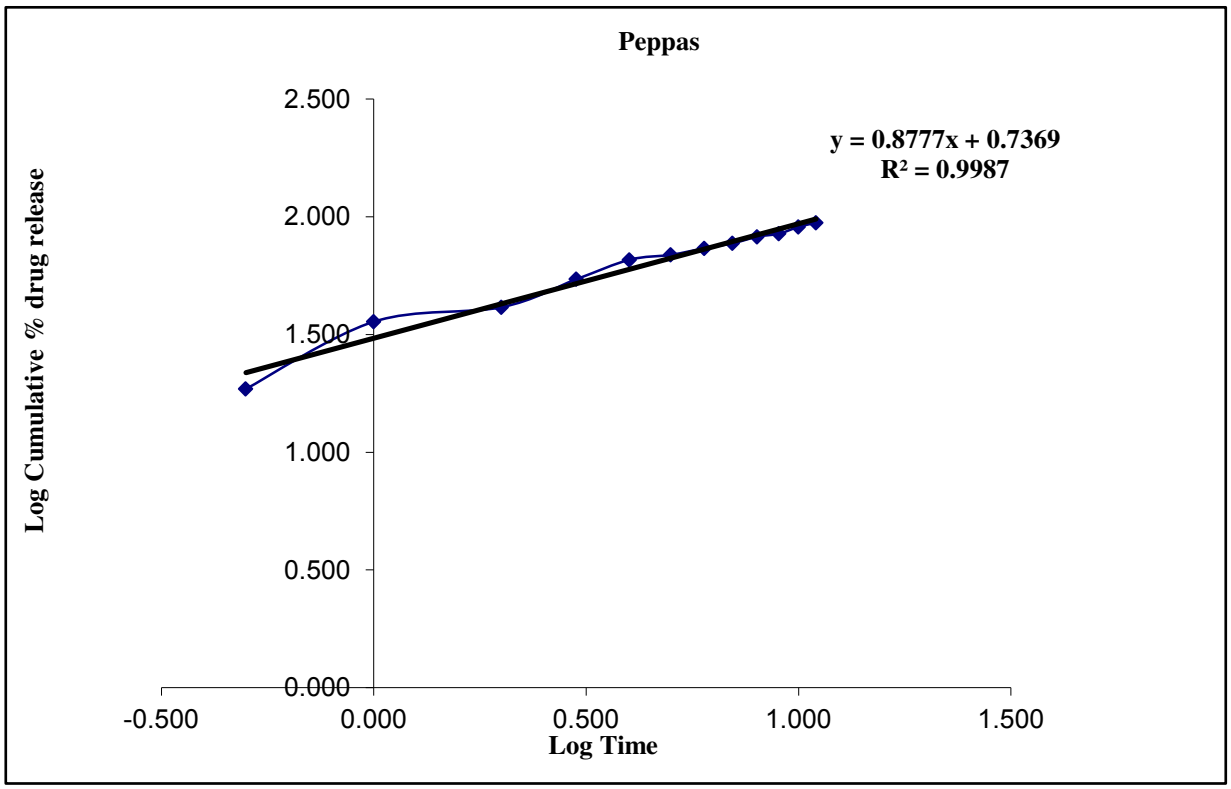


Figure 10: Kors mayer peppas release kinetics

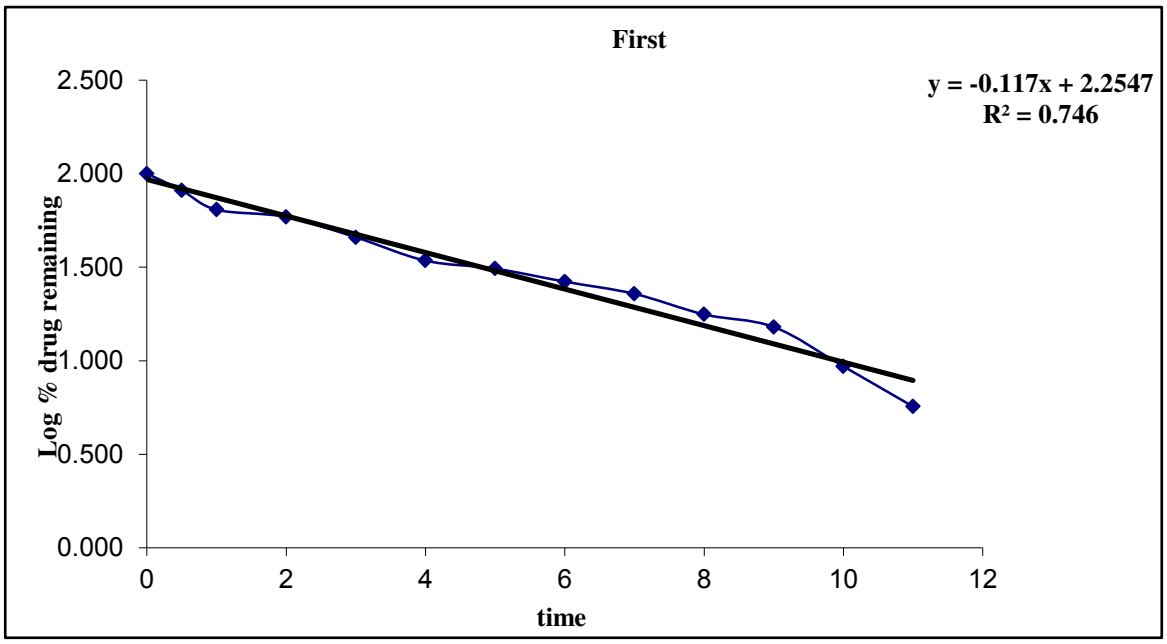


Figure 11: First order release kinetics

Optimised formulation F3 was kept for release kinetic studies. From the above graphs it was evident that the formulation F3 was followed Peppas release mechanism.

CONCLUSION

Development of Gastro retentive floating drug delivery of Lafutidine tablets is to provide the drug action up to 12 hours. Gastro retentive floating tablets were prepared by direct compression method using various polymers like Xanthan gum, guar gum and Sodium Alginate. The formulated gastro retentive floating tablets were evaluated for different

parameters such as drug Excipient compatability studies, weight variation, thickness, hardness, content uniformity, *In vitro* Buoyancy studies, *In vitro* drug release studies performed in 0.1N HCL for 12 hrs and the data was subjected to zero order, first order, Higuchi release kinetics and karsmayer peppas graph. FTIR studies concluded that there was no interaction between drug and Excipients. The physico-chemical properties of all the formulations prepared with different polymers Xanthan gum, guar gum and Sodium Alginate were shown to be within limits. Quality control parameters for tablets such as weight variation, Hardness, Friability, thickness, drug content and floating lag time were found to be within limits. *In-vitro* drug release studies were carried out for all prepared formulation and from that concluded F3 formulation has shown good results. Finally concluded release kinetics to optimised formulation (F3) has followed Peppas release kinetics. Present study concludes that gastro retentive 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.

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