Preparation & Examination of Gastro Retentive Floating Drug Delivery System of Lafutidine by Using Euryale Ferox Seeds

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Abstract **Lafutidine a newly developed histamine H2 receptor antagonist was retained in the stomach and assist in improving the oral sustained delivery of drugs in the gastrointestinal tract. A floating drug delivery system (FDDS) was developed using Floating agents such as Euryale ferox seeds such as hydroxyl propyl methyl cellulose (HPMCK 4M, and xanthum gum. The prepared tablets of various formulations were evaluated for a total floating time, buoyancy lag time, and percentage drug released. The formulation code F5 having HPMCK4M showed better results it may be useful for prolonged drug release in the stomach to improve the bioavailability. Non Fickians release transport was confirmed as the drug release mechanism from the optimized formulation by KorsmeyerPeppas. Optimized floating tablets showed no significant changes in the physical appearance, drug content, total buoyancy time, and also in vitro dissolution pattern.**

Key words: Floating drug delivery system, in vitro and in vivo study, Lafutidine, sustained release, Euryale ferox seeds (EFSP).

INTRODUCTION

Gastrointestinal retention

Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.

To successfully modulate the gastrointestinal transit time of a drug delivery system through floating drug delivery system (FDDS) For maximal gastrointestinal absorption of drugs and site-specific delivery, one needs to have a good fundamental understanding of the anatomic and physiological characteristics of the human GIT.

Stomach anatomy

The main function of the stomach is to process and transport food. It serves as a short-term storage reservoir, allowing a rather large meal to be consumed quickly. Substantial enzymatic digestion is initiated in stomach, particularly of proteins. Vigorous contractions of gastric smooth muscle mix and grind foodstuffs with gastric secretions, resulting in liquefaction of food. As food is liquefied in the stomach, it isslowly released into the small intestine for furtherprocessing.

Anatomically the stomach is divided into 3 regions: fund us, body and ant rum (pylorus). Theproximal part made of fund us and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propellingactions.

It has been reported that the mean value of pH in fasted healthy subjects is 1.1± 0.15. But when food comes into the stomach, the Ph may rise to levels in the 3.0 to 4.0 level due to the buffering capacity of proteins. However, in fasted state, basal gastric secretion in women is slightlylower than that of men.

MATERIALS AND METHODS

Preparation of floating tablets of Lafutidine

Lafutidine and other excipient were blendedfor 10 min. Constant amount of magnesium stearate was added as lubricant and blended for another 2 min. Tablets were prepared by direct compression using 9-mm flat-faced punch on a 16-station

Drug-Excipient compatibility studyFTIR studies

The successful formulation of a suitable and effective solid dosage form depends upon the careful selection of the excipient. Excipients are added to facilitate administration, promote the consistent release and bioavailability of drug. It's necessary to study the compatibility of excipient with drug. Here IR spectroscopy was used to investigate and predict any physicochemical interaction between components in a formulation and to the selection of suitable compatible Excipient. FTIR studies were conducted and the spectrum was recorded in the wavelength regionof 4000 to 400 cm−1. The procedure consisted of, dispersing a sample (drug alone, and mixture of drug and polymers in KBr and compressing into discs by applying a pressure of 7 tons for 5 min in a KBr press. The pellet was placed in the light path and the spectrum was obtained.

Bulk density (Db)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve # 20) into a measuring cylinder and the initial volume was noted. The initial volume is called the bulk volume. From this, bulk density is calculated by using the following formula. It isexpressed in g/cc and is given by

Db)Bulk density = (M) mass of powder

(Vb) bulk volume of powder

Tapped density (Dt)

The tapped density was obtained by dividing the mass of powder by tapped volume of the powder. Tapped volume was measured by tapping the sample contained in the graduated measuringcylinder. It is calculated by using the following formula. It is expressed in g/cc and is given by –Bulk density

Dt = M mass of the powder / Vt Tapped volume of the powder

Carr's index

It is the simple test to evaluate the bulk density and tapped density of a powder and the rate at which it packed down. It is expressed by the given formula,

Carr's Index (%) =

[(Tapped density – Bulk density) × 100]

tapped density

Hausner's Ratio: It is the ratio of tapped density to the bulk density.

Hausner's Ratio = Tapped density

Bulk density

Angle of repose (θ)

This is the maximum angle possible betweenthe surface of the pile of the powder or granulesand the horizontal plane. The powder mixture wasallowed to pass through the funnel fixed to a standat definite height. The angle of repose was then calculated by measuring the height and radius ofthe heap of the powder formed.

Tan θ = h / rθ = angle of repose,

h = height of the heap,r = radius of the heap

Table-1: Formulation of Lafutidine Floating tablets

Composition (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Lafutidine	50	50	50	50	50	50	50	50	50	50
HPMCK 4M	25	50	75	75	75	-	-	-	-	-
Xanthum gum	-	-	-	-	-	25	50	75	75	90
Euryaleferox seeds	25	25	25	50	75	25	25	25	75	90
Microcrystalline ceulose	210	185	160	135	115	210	185	160	110	80
PVP-k-30	30	30	30	30	30	30	30	30	30	30
Talc	5	5	5	5	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5	5	5	5	5
Total	350	350	350	350	350	350	350	350	350	350

Post compression parameters

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

The hardness of the tablet is also known as crushing strength. The hardness of the tablet is defined as the compressional force required to break or fracture the tablet. The tablet is required to possess sufficient hardness to prevent its chipping, its breakage encountered during the transport or storage. The hardness was measured with Monsanto hardness tester. The hardness is usually measured in terms of Kg/cm2. Three tablets randomly selected from each formulation and the average hardness was noted.

Weight variation test

Twenty tablets were selected at random and weighed individually. The average weight (WA) of 20 tablets was calculated. Individual weights of the tablets were

compared with average weight.Not more than two of the individual weights deviate from the average weight by more than the percentage show in the following table.

% Weight variation = 100 X (WA-W)

WA

Friability test

This test is performed to know the effects of friction and shocks. The friability of the tablets was measured in a Roche friabilator. Pre-weighed sample of 10 tablets were placed in the friabilator (Electrolab, India) and rotated at 25 rpm for 4 minutes. The dusted tablets were de-dusted and Reweighed. The percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1%

Friability = [(Initial weight- Final weight)

(Initial weight)] x 100

RESULTS AND DISCUSSION

FOURIER TRANSFORMATION- INFRARED SPECTROSCOPY (FTIR)

Drug-excipient interactions play a vital role respect to release of drug from the formulation among other. FTIR techniques have been used here to study the physical &chemical interaction between drug and exicipient used. In the present study, it has been observed that the no chemical interaction between lafutidine and the polymers used. Infrared absorption spectroscopy (IR) of lafutidine showed sharp band at 1598,1173,3159 due to c=n stretch.s=o, sulfinyl stretch, N-H amide stretch. From the figure it was observed that there were no changes in these main peaks in IR Spectra of mixture of drug and polymers, which shown there were no physical interactions because of some bond formation between drug and polymers.

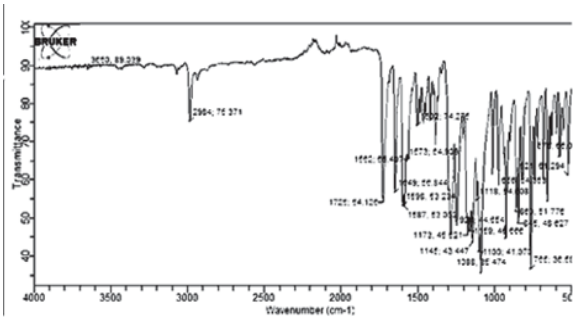

Fig - FT-IR STUDIES LAFUTIDINE

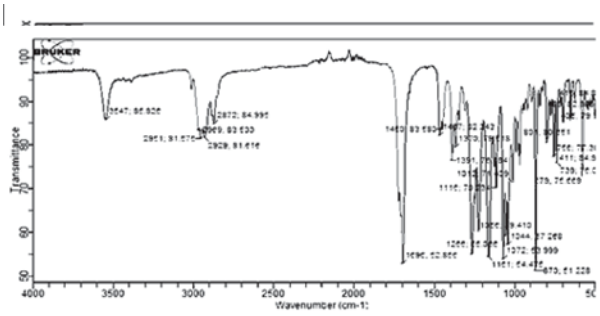

Fig-FT-IR STUDIES LAFUTIDINE AND EXCIPIENTS

Evaluation of floating tablets of lafutidine Pre-compression parameters and Carr's index of the formulations were found to be within the range that the formulations had good flow property.

Table-2 Precompression Parameters

Powder Blend	Angle of Repose (θ)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's Ratio
F1	32.31	0.533	0.407	14.18	1.16
F2	33.39	0.537	0.418	14.13	1.16
F3	34.36	0.541	0.454	14.11	1.17
F4	32.28	0.532	0.399	14.03	1.18
F5	29.24	0.539	0.407	14.05	1.16
F6	31.38	0.559	0.471	13.50	1.16
F7	31.39	0.557	0.438	14.18	1.16
F8	31.36	0.531	0.424	14.21	1.17
F9	32.28	0.522	0.389	15.13	1.18
F10	29.26	0.529	0.407	14.25	1.16

Table-3 Post comprssion parameters

Formulation Code	Thickness (mm)	Wt variation (%)	Hardness (kg/cm^2)	Friability (%)	Drug content(%)
F1	3.0	351±2.5	4.8±0.13	0.50	98.97
F2	3.2	350±3.2	4.8±0.19	0.50	100.1
F3	3.1	351±2.7	4.2±0.21	0.60	99.72
F4	3.3	350±2.5	4.5±0.11	0.57	100.8
F5	3.2	350±3.2	4.0±0.63	0.52	99.42
F6	3.0	352±3.5	4.8±0.30	0.46	99.98
F7	3.1	351±2.7	4.2±0.21	0.60	99.32
F8	4.5	349±2.5	4.5±0.11	0.57	100.2
F9	4.0	351±3.2	4.0±0.63	0.52	99.22
F10	4.8	350±3.5	4.8±0.30	0.46	99.88

Table 4: Floating characteristics of formulations

Formulation	Floating lag time (sec)	Floating time (hr)
F1	130	>6
F2	122	>8
F3	92	>10
F4	34	>11
F5	0	>12
F6	SINK	0
F7	160	5
F8	140	8
F9	74	>10
F10	2	>12

Table-6: Swelling Index

Formulations	Swelling Index
F1	1.251 ± 0.23
F2	1.520 ± 0.14
F3	1.910 ± 0.12
F4	1.620 ± 0.80
F5	1.315 ± 0.56
F6	1.091 ± 0.20
F7	1.245 ± 0.23
F8	1.520 ± 0.14
F9	1.310 ± 0.12
F10	1.220 ± 0.80

CONCLUSION

The gastroretantive floating drug delivery is a promising approach to achieve in vitro buoyancy by using Euryale ferox seeds polymerslike HPMC K4 and xanthum gum $HPMCK_4$ (F1 TOF5) was prepared and xanthum gum (F6 TO F10) formulations was developed F1 to F5 formulations shows best results with the comparison of xanthum gum formulations because of we are increasing the concentration of HPMC K4 an EFSP. EFSP increasing the conc. We get floating lag time 0 mines and control release of drug up to 12 hrs.Optimized formulation was F5when characterized with FTIR studies shows no interaction between the drug and polymer so the conclusion was HPMC K4 polymer EFSP is the best combination for the development of gastro retentive floating tablets of lafutidine. Finally we concluded Euryale ferox seed powder acting as efficient floating agent so it gives best results for the development of non effervescent floatingtablets.

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