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Formulation and invitro evaluation of lafutidine effervescent tablets

Yogendra Kumar Gupta*, R. Mohan Babu

Sushrut Institute of Pharmacy, Taddanapally village, Pulkal madal, Medak, Sangareddy

***Corresponding Author: Yogendra K G**

Email Id: gupta_yogi79@rediffmail.com

ABSTRACT

The Floating Sustained released tablets using effervescent agent containing Lafutidine SR tablets were successfully prepared by wet granulation method. The physiochemical evaluation results for the granules of all trials pass the official limits in angle of repose, compressibility index. The prepared granules were also maintained the physiochemical properties of tablets such as thickness, hardness, weight variation, friability. The optimized formulation contains the average thickness of 3.11±0.02, average hardness of 7.94±0.05, average weight of 300±0.05, friability of 0.45. The optimized formulation F7 which releases the Lafutidine in sustained manner in 1st hour it releases 9.3% but the remaining drug release was sustained up to 12 hours.

Key words: Lafutidine, angle of repose, compressibility index.

INTRODUCTION

Gastroretentive drug delivery system

Oral route has been the commonly adopted and the most convenient route for the drug administration. It has been received more attention in the pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery design for other route. Although tremendous advances have been seen in oral controlled drug delivery system in the last two decades, this system has been of limited success in the case of drugs with a poor absorption window throughout the GIT (Gastro Intestinal Tract). In the development of oral controlled drug delivery system, one of the main challenges is to modify the GI transit time. Gastric emptying of pharmaceuticals is highly variable and is dependent on the dosage form and the fasted state of the stomach. Normal gastric residence times usually range between 5min to 2h. In the fasted state the electrical activity in the stomach –the interdigestive myoelectric cycle or migrating myoelectric complex (MMC) governs the activity and, hence, the transit of dosage forms. It is characterized by four phases: Phase I–Period of no contraction (40-60min), phase II–Period of intermittent contractions (20-40min), phase III–Period of regular contractions at the maximal frequency that travel distally also known as housekeeper wave.(10-20min) and phase IV–Period of transition between phase III and phase I (0-5min)[1].

However, this approach is bedilled with several physiological difficulties such as inability to restrain and locate the controlled drug delivery system within the desired region of the gastrointestinal tract (GIT) due to variable gastric emptying and motility. Furthermore, the relatively brief gastric emptying time (GET) in humans which normally averages 2-3h through the major absorption zone, i.e., stomach and upper part of the intestine can result in incomplete drug release from the drug delivery system leading to

reduced efficacy of the administered dose[2]. This has led to the development of oral gastroretentive dosage forms. Gastroretention is essential for drugs that are absorbed from the stomach, drugs that are poorly soluble or degraded by the higher pH of intestine, and drugs with an absorption which can be modified by changes in gastric emptying time.

Gastroretentive dosage forms are also useful for local as well as sustained drug delivery for certain conditions, like H. pylori infection which is the cause of peptic ulcers. This dosage form improves bioavailability, therapeutic efficacy and may even also allow a possible reduction in the dose because of steady therapeutic levels of drug, for example Furosemide and Ofloxacin. The reduction in fluctuations in therapeutic levels minimizes the risk of resistance especially in case of -lactam antibiotics (Penicillins and Cephalosporins)[3]. Gastroretensive 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[4].

Suitable drug candidates for gastroretention

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. Drugs delivered in this manner have a lower level of side effects and provide their therapeutic effects without the need for repeated dosages or with a low dosage frequency. Sustained release in the stomach is also useful for therapeutic agents that the stomach does not readily absorb, since sustained release prolongs the contact time of the agent in the stomach or in the upper part of the small intestine, where absorption occurs and contact time is limited. Under normal or average conditions, for example, material passes through the small intestine in as little as 1-3h[5].

In general, appropriate candidates for CRGRDF are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT:

1. Narrow absorption window in GIT, e.g., Riboflavin and Levodopa
2. Primarily absorbed from stomach and upper part of GIT, e.g., calcium supplements, Chlordiazepoxide and Cinnarazine.
3. Drugs that act locally in the stomach, e.g., antacids and Misoprostol.
4. Drugs that degrade in the colon, e.g., RHCL and Metronidazole.
5. Drugs that disturb normal colonic bacteria, e.g., Amoxicillin trihydrate

The need for gastroretentive dosage forms (GRDFs) has led to extensive efforts in both academia and industry towards the development of such drug delivery systems.

These efforts resulted in GRDFs that were designed, in large part, based on the following approaches.

1. Low density form of the DF that causes buoyancy in gastric fluid[6].
2. High density DF that is retained in the bottom of the stomach[7].
3. Bioadhesion to stomach mucosa[8].
4. Slowed motility of the gastrointestinal tract by concomitant administration of drugs or pharmaceutical excipients[9].
5. Expansion by swelling or unfolding to a large size which limits emptying of the DF through the pyloric sphincter[10].

AIM AND OBJECTIVE OF PRESENT STUDY

The aim of the present study was to fabricate and evaluate effervescent floating tablets of Lafutidine, using different natural polymers like Guar gum and Xanthum gum which is suitable for delivering the drug for sufficient long time and reduce frequency of dose.

Objectives

- To perform the drug – excipient compatibility studies as per ICH guidelines
- To optimize the concentration of Polymer for effervescent floating sustained release tablets of Lafutidine.
- To evaluate the formulation parameters like weight variation, hardness, friability, assay.
- To evaluate the In-vitro studies for the sustained tablets.

- To conduct the accelerated stability studies for the prepared tablets as per ICH guidelines

METHODOLOGY

Formulation development

The pharmaceutical development studies have to be carried out with the purpose of selecting right dosage form and a stable formulation. These studies give detailed description of all the steps involved in the process of formulation development. Such details are intended towards identifying critical parameters involved in the process, which have to be controlled in order to give reliable and reproducible quality product.

Formulation of effervescent floating tablets

This sustained release tablets was prepared by wet granulation method.

Sieving

The active ingredient was passed through the sieve#40 followed by the other ingredients were passed the same sieve.

Dry mixing

Lafutidine, Micro Crystalline Cellulose, natural polymers and sodium bicarbonate were taken in a poly bag and mixed for 5minutes to ensure uniform mixing of the ingredients with the drug.

Preparation of binder solutionPVP-K_{30} IPA Weigh PVP K-30 accurately and it is mixed with IPA to form a solution is used as binder solution and kept separately.

Then the granulation, drying and sieving were followed by lubrication for final compression. Magnesium stearate and talc were weighed and they were passed through sieve#20.Then mixed with dried granules of Lafutidine in a polybag for 5minutes to get a uniform blend. Then the lubricated granules of Lafutidine were weighed accurately and fed into the die of single punch machinery and compressed. For this 9mm round punch was used for compression.

Formulation of effervescent floating tablets

Development of sustained release tablets of Lafutidine was carried out. Sustained release tablets were prepared using formulae given below. Sustained release tablets were prepared on 16 station tablet compression machine by wet granulation. The tablets of different formulations were punched with 9mm round punch on compression machine.

Composition of effervescent floating tablets

Table No 1: Formulation table for effervescent floating sustained release tablets

Formulation	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
Lafutidine	50	50	50	50	50	50	50	50
Xanthum gum	40	80	120	160	-	-	-	-
Guar gum	-	-	-	-	40	80	120	160
MCC	160	120	80	40	160	120	80	40
PVP K-30	20	20	20	20	20	20	20	20
NaHCO3	30	30	30	30	30	30	30	30
IPA	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Magnesium stearate	2	2	2	2	2	2	2	2
Talc	8	8	8	8	8	8	8	8
Total weight	300	300	300	300	300	300	300	300

PVP- Polyvinyl pyrrolidone, IPA- Isopropyl alcohol. All the ingredients are in ‘mg

RESULTS AND DISCUSSION

Compatability studies

The spectrum obtained after the analysis is shown in Figure No: The spectrum of the standard and the samples were then superimposed to find out any possible interactions between the drug and the polymers. All the characteristic peaks of Lafutidine mentioned in Table No: were also found in the spectrum formulations. The results suggest that the drug is intact in the formulations and there is no interaction found between the drug and the excipients.

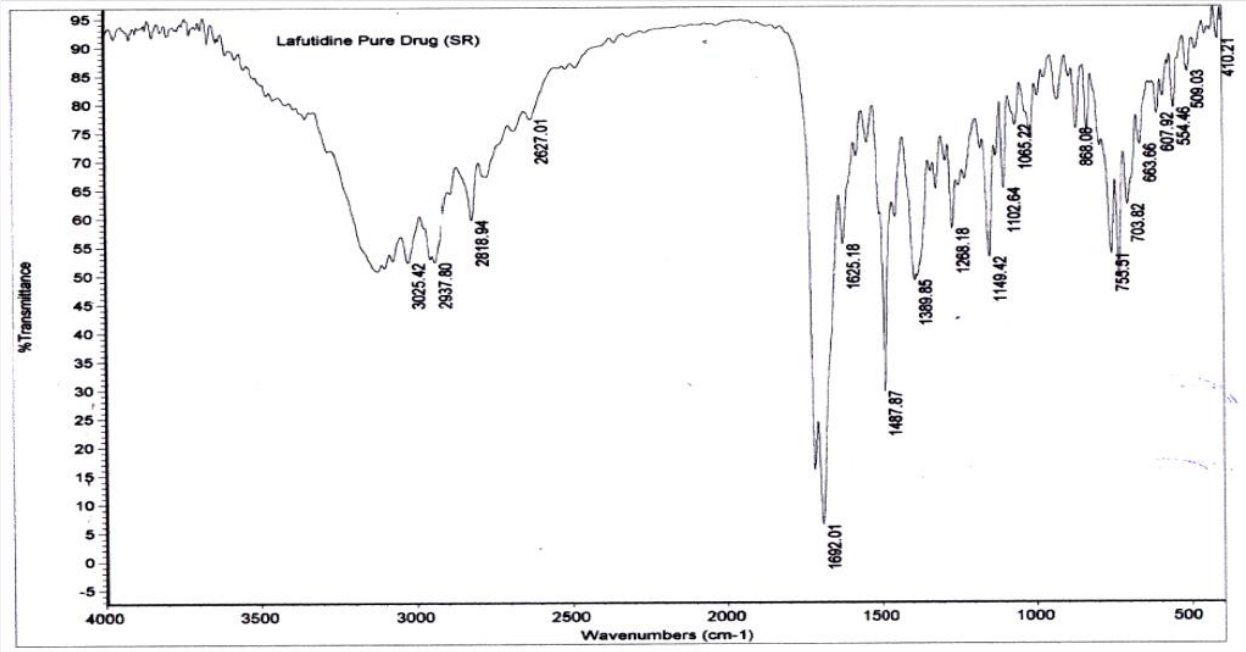

Fig No 1: FTIR graph of Pure Lafutidine drug

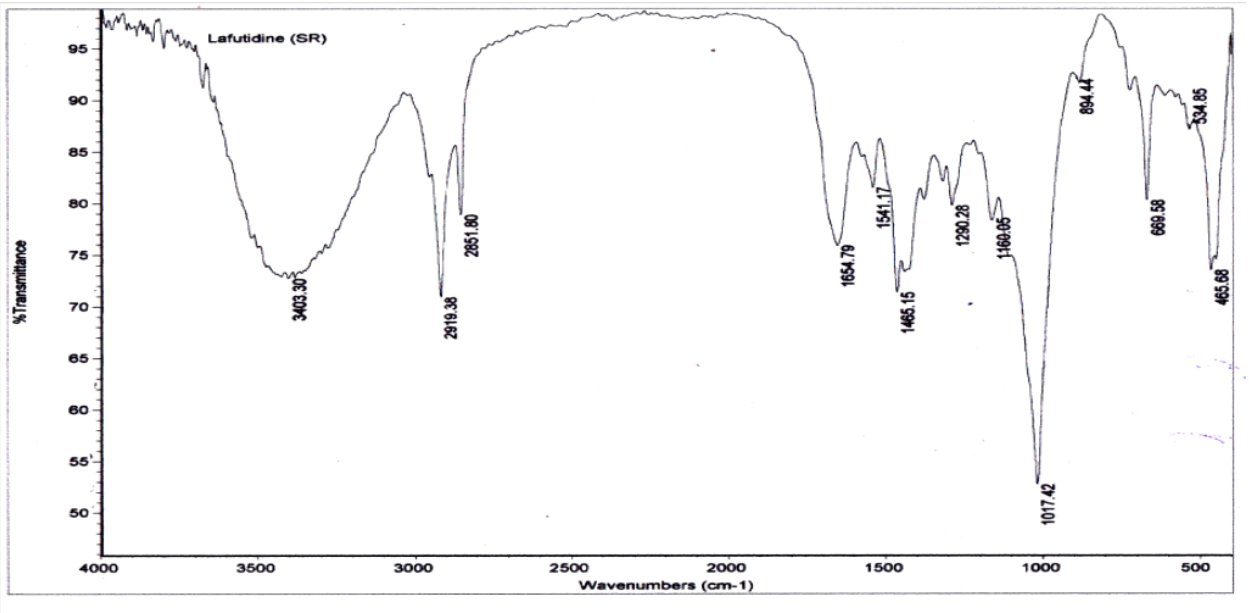

Fig No 2: FTIR graph of Lafutidine optimized formulation

Pre compression parameters

Table No 2: Pre compression parameters for SR tablets

Formulations	Angle of Repose (θ)	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	%Compressibility	Hausner's ratio	RESULT

F1	28.38±0.06	0.614±0.01	0.754±0.04	18.56±0.05	1.22±0.03	Excellent
F2	27.36±0.04	0.661±0.01	0.812±0.03	18.59±0.06	1.22±0.02	Excellent
F3	25.55±0.03	0.648±0.02	0.793±0.02	18.27±0.03	1.23±0.03	Excellent
F4	29.11±0.06	0.612±0.01	0.766±0.03	20.12±0.03	1.25±0.02	Excellent
F5	27.72±0.07	0.668±0.01	0.828±0.02	19.34±0.03	1.23±0.02	Excellent
F6	28.14±0.07	0.663±0.03	0.820±0.03	19.19±0.05	1.23±0.02	Excellent
F7	28.39±0.06	0.676±0.02	0.847±0.03	20.19±0.02	1.25±0.04	Excellent
F8	26.31±0.02	0.659±0.02	0.831±0.02	20.67±0.01	1.26±0.04	Excellent

F.Code	Hardness (kg/cm^2) †	Thickness (mm) ‡	Weight (mg) ‡	Friability (%)
F1	7.25±0.02	3.40±0.03	300±0.01	0.58±0.05
F2	7.53±0.02	3.32±0.03	300±0.03	0.50±0.05
F3	7.46±0.01	3.40±002	300±0.03	0.52±0.05
F4	7.31±0.03	3.40±0.01	300±0.02	0.33±0.05
F5	7.59±0.03	3.41±0.01	300±0.03	0.31±0.03
F6	7.87±0.02	3.41±0.01	300±0.03	0.32±0.05
F7	7.94±0.05	3.11±0.02	300±0.05	0.45±0.04
F8	7.81±0.06	3.11±0.03	300±0.04	0.49±0.01

Table No 3: Post compression parameters

Formulation Code	Drug content (%)	Floating lag time(sec)	Swelling index (%)	Floating duration(hrs)
F1	98.42	25	121.2	>12
F2	99.40	24	139.5	>12
F3	98.34	15	142.5	>12
F4	98.45	45	144.85	>12
F5	99.34	54	129	>12
F6	99.29	2min	142	>12
F7	97.38	1min 24sec	145	>12
F8	99.43	3mins	156	>12

Invitro dissolution studies for floating sr tablets - dissolution study

Buffer Stage

Medium : 1.2pH 0.1N HCl
Type of apparatus : USP - II (paddle type)
RPM : 50
Volume : 900ml
Time : 12hrs

a) In-Vitro Drug Release Studies for SR tablets

Table No 4: Cumulative percentage drug release from sustained release tablets

Time	F1	F2	F3	F4	F5	F6	F7	F8
1	12	11.5	10.2	7.5	11.3	12.5	9.3	9.5
2	20	16	13	12.3	15.2	20	15	13.9
3	34	28	27	25	36.4	35	34	33
4	45	37	35	34	45.2	46	42	45.8
5	61	55	52	42	42.4	59	57	60
6	70	71	67	53	50.2	68	70	74.5
8	82	80.5	74	65	65.3	77	79.6	79.3
10	--	--	80	78	83.2	90	83.4	80.8
12	--	--	--	84.7	--	--	94.7	89.7

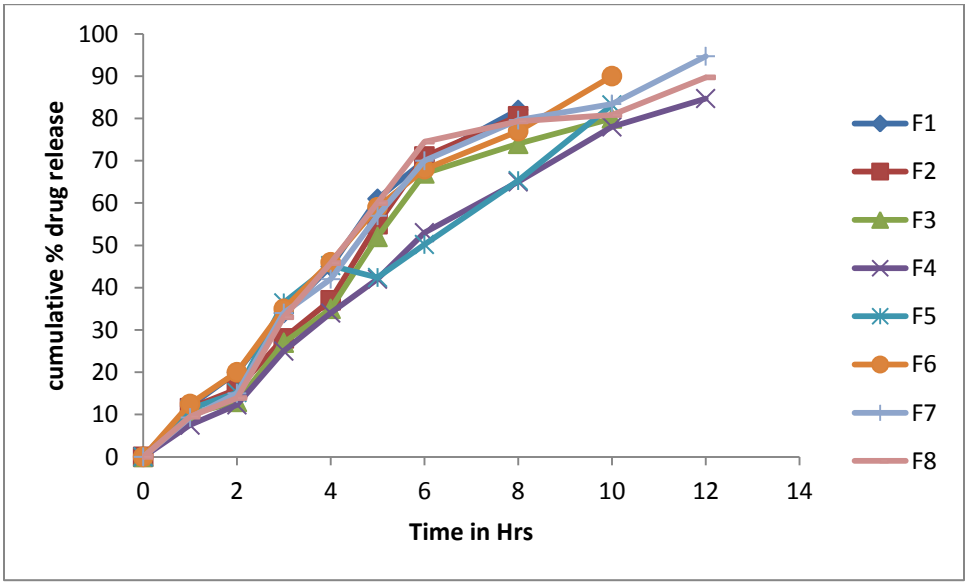

Fig No 3: Dissolution graph for sustained release formulations

Kinetic release models

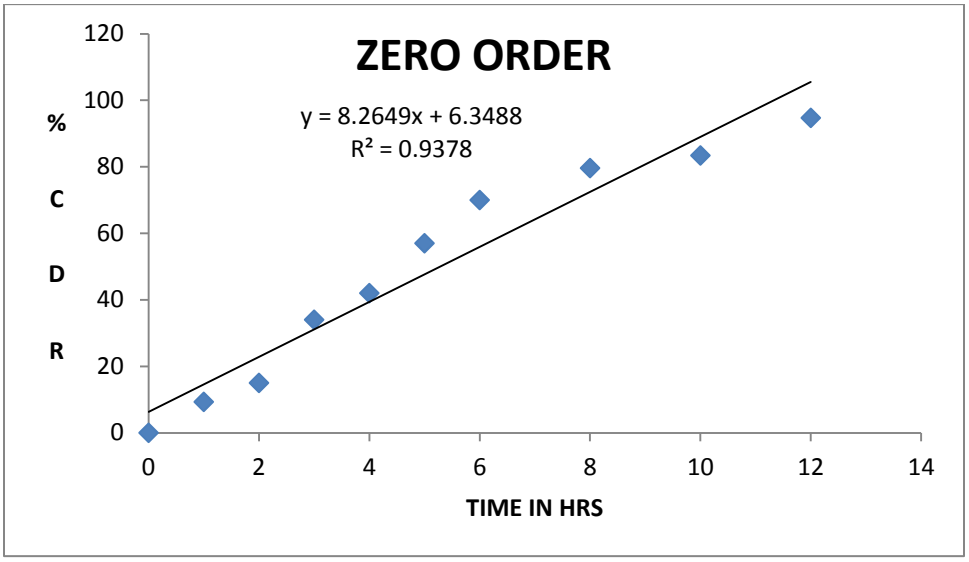

Fig No 4: Zero order release graph for F7 sustained release formulation

Fig No 5: First order release graph for F7 sustained release formulation

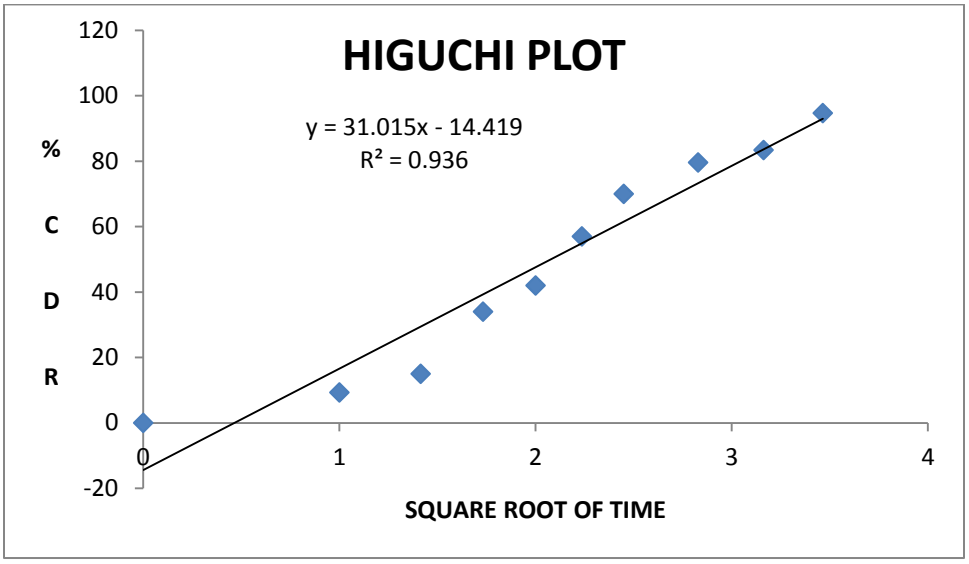

Fig No 6: Higuchi model graph for F7 sustained release formulation

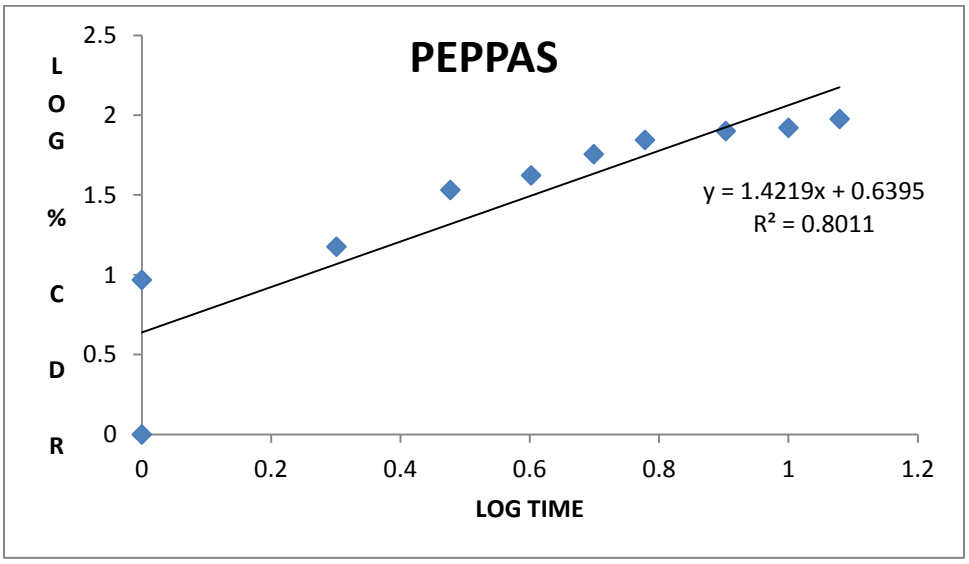

Fig No 7: Peppas model for F7 sustained release formulation

Table No 5: Release kinetics for F7 formulation for sustained release tablets

	ZERO % CDR Vs T	FIRST Log % Remain Vs T	HIGUCHI %CDR Vs √T	PEPPAS Log C Vs Log T
Slope	8.264938805	-0.100994807	31.0147686	1.421895774
Intercept	6.348812095	2.098533714	-14.41850882	0.639539655
Correlation	0.968384256	-0.978301696	0.967474051	0.895062581
R 2	0.937768067	0.957074209	0.936006039	0.801137024

DISCUSSION

The physiochemical evaluation results for the granules of all trials pass the official limits in angle of repose, compressibility index. The prepared granules were also maintained the physiochemical properties of tablets such as thickness, hardness, weight variation, friability. The optimized formulation contains the average thickness of 3.11±0.02, average hardness of 7.94±0.05, average weight of 300±0.05, friability of 0.45. The optimized formulation F7 which releases the Lafutidine in sustained manner in 1st hour it releases 9.3% but the remaining drug release was sustained up to 12 hours.

CONCLUSION

The Floating Sustained released tablets using effervescent agent containing Lafutidine SR tablets were successfully prepared by wet granulation method. The physiochemical evaluation results for the granules of all trials pass the official limits in angle of repose, compressibility index. The prepared granules were also maintained the physiochemical properties of tablets such as thickness, hardness, weight variation, friability. The optimized formulation contains the average thickness of 3.11±0.02, average hardness of 7.94±0.05, average weight of 300±0.05, friability of 0.45. The optimized formulation F7 which releases the Lafutidine in sustained manner in 1st hour it releases 9.3% but the remaining drug release was sustained up to 12 hours.

REFERENCES

[1]. Shah SH, Patel JK, Patel NV. Stomach specific floating drug delivery system: a review. Int J PharmTech Res 2009; 1(3):623-633.
[2]. Rouge N, Buri P, Doelker E. Drug absorption sites in the gastrointestinal tract and dosage forms for site specific delivery. Int J Pharm 1996; 136:117-139.
[3]. Singh BM, Kim KH. Floating drug delivery systems: an approach to controlled drug delivery via gastric retention. J Control Rel 2000; 63:235–259.
[4]. Mayavanshi AV, Gajjar SS. Floating drug delivery systems to increase gastric retention of drugs: A Review Research J Pharm Tech 2008; 1(4):165-178.
[5]. Khan FN, Dehghan HG. Gastroretentive Drug Delivery Systems: A Patent Perspective. Int J Health Res 2009; 2(1):23.
[6]. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled-releasesystem for gastric retention. Pharm Res 1997; 14:815-819.
[7]. Davis SS, Stockwell AF, Taylor MJ. The effect of density on the gastric emptying of single and multiple unit dosage forms. Pharm Res 1986; 3:208-213.
[8]. Lehr CM. Bioadhesion technologies for the delivery of peptide and protein drugs to the gastrointestinal tract. Crit Rev Ther Drug Carrier Syst 1994; 11:119-160.
[9]. Groning R, Heun G. Oral dosage forms with controlled gastrointestinal transit. Drug Dev and Ind Pharm 1984; 10:527-539.
[10]. Klausner EA, Lavy E, Friedman M, Hoffman A. Expandable gastroretentive dosage forms. J Control Release 2003; 90:143-162.
[11]. Hilton AK, Deasy PB. In vitro and in vivo evaluation of an oral sustained release floating dosage form of amoxicillin trihydrate. Int J Pham.1992; 86:79-88.
[12]. Seth PR, Tossounian J. The hydrodynamically balanced system, a novel drug delivery system for oral use. Drug Dev and Ind Pharm 1984; 10:313-339.
[13]. Harrigan RM. Drug delivery device for preventing contact of undissolved drug with the stomach lining, US Patent 1977 4, 055, 178, October 25,
[14]. Whitehead L, Fell JT, Collett JH. Development of a gastroretentive dosage form. Eur J Pharm Sci 1996; 4 (Suppl.): S182.

[15]. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. Hollow microspheres for use as a floating controlled drug delivery system in the stomach. J Pharm Sci 1992; 81:135-140.

[16]. Rubinstein A, Friend DR. Specific delivery to the gastrointestinal tract, In Domb AJ (Ed.) Polymeric site specific pharmacotherapy, Wiley, Chichester, 1994; 282-283.