Research Article

Available Online at: www.ijpir.com

International Journal of Pharmacy and Industrial Research

ISSN	Print	2231 – 3648
	Online	2231 – 3656

Formulation and evaluation of gastro retentive floating tablets of Loratadine

Nansri Saha[1], Pawan Kumar[2], Satyabrata Bhanja[3], Soumik Ghosh[1], Sarita Tiwari[4]

[1]Research Scholar, Department of Pharmaceutical Sciences, Singhania University, Pacheri Bari, Jhunjhunu, Rajasthan 333515, India.

[2]School of Life Sciences, Singhania University, Pacheribari, Jhunjhunu, Rajasthan 333515, India.

[3]Malla Reddy College of Pharmacy, Maisammaguda, Dhulapally, Secunderabad, Telangana 500014, India.

[4]School Of Applied Sciences, Singhania University, Pacheri Bari , Jhunjhunu, Rajasthan 333515, India.

ABSTRACT

Loratadine a long-acting tri-cyclic antihistamine with selective peripheral histamine H1-receptor antagonistic activity, is used for the symptomatic relief of allergic conditions like runny nose, itchy or watery eyes, sneezing and nasal or throat itching and chronic urticaria. It is stable in acidic pH, has a narrow therapeutic absorption window in the GI tract and found to be absorbed at proximal part of small intestine. Thus it is decided to prolong the gastric residence time in terms of making floating gastro retentive drug delivery system to increase drug absorption and hence bioavailability. In this study Loratadine floating tablets were prepared by using two different techniques like Effervescent floating tablets and Non Effervescent floating tablets using Ethyl cellulose, Karaya gum and HPMC K4 M as polymers and gas generating agents like sodium bicarbonate and citric acid and polypropylene foam powder as a selling agent in non effervescent floating tablets. The tablets prepared by direct compression technique were evaluated in terms of their pre-compression parameters and post compression characteristics such as physical characteristics, total buoyancy, buoyancy lag time, swelling index and *in vitro* release. The best formulation showed no significant change in physical appearance, drug content, total buoyancy time, buoyancy lag time or *in vitro* release after storage at 40˚C /75% RH for three months. The *in vitro* release studies confirmed that the formulation (F15) containing 90 mg of karaya gum showed sustained drug release (100.02 ±0.18%) for 12 h and remained buoyant for more than 12 h.

Keywords: Loratadine, HPMC K4 M, Formulation

Author for Correspondence:
Nansri Saha
Research Scholar, Department of Pharmaceutical Sciences,
Singhania University, PacheriBari, Jhunjhunu,
Rajasthan 333515, India.

INTRODUCTION

The oral route represents the predominant and most preferable route for drug delivery unlike the majority of parenteral dosage forms it allows ease of administration by the patient and highly convenient way for substances to be introduced in to the human body. Oral drug delivery systems are divided in to immediate release and modified release systems [1]. Modified release systems have been developed to improve the pharmacokinetic profiles of active pharmaceutical ingredients and patient compliance as well as reducing side effects. Oral modified release delivery systems commonly include delayed release, extended release programmed release and site specific or timed release. Oral extended release dosage forms offer the opportunity to provide constant or nearly constant drug plasma levels over an extended period of time following administration. Extended release drug delivery systems offer several advantages compared to conventional drug delivery system including avoiding drug level fluctuations by maintenance of optimum therapeutic plasma and tissue concentrations over prolonged time periods, avoiding sub therapeutic as well as toxic concentrations, thus minimizing the risk of failure of the medical treatment and undesirable side effects, reducing the administered dose and reduced frequency of administered dose while achieving comparable results, Targeting or timing of the drug action. Hence it is highly desirable to develop sustained drug delivery system releasing the drug at predetermined rates to achieve optimal plasma drug levels and/or at the site of action [2, 3]

Majority of drugs are preferentially absorbed in the upper part of the small intestine. So, Gastro retentive drug delivery systems are preferred. The retention of oral dosage forms in the upper GIT causes prolonged contact time of drug with GI mucosa leading to higher bioavailability and hence therapeutic efficacy, reduced time intervals for drug administration, potentially reduced dose size and thus improved patient compliance [4-6].

FDDS are preferred as they are economic and has improved patient compliance and they are advantageous for drugs absorbed from the stomach[7-8] eg: ferrous salts and for drugs meant for local action in the stomach eg: antacids, drugs with narrow absorption window in the small intestine region eg: L-Dopa. When there is a vigorous intestinal movement and a short transit time as might occur in certain type of diarrhoea, poor absorption is expected. Under such circumstances also it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response. [9, 10]

The present work is an attempt to develop FDDS in the form of tablets taking Loratadine as the model drug. Loratadine is a long acting tricyclic second generation antihistamine. It is an antagonist at peripheral histamine (H1) receptors. DesLoratadine (decarboethoxy Loratadine) is the active metabolite of Loratadine and produces the same pharmacological effect as the parent compound. An oral dose of Loratadine or desLoratadine typically begins to inhibit the wheal and flare reaction after intradermal histamine injection within 1-3 hours reaches a peak effect within 8-12 and lasts for approximately 24hours. Some of the common adverse effects are sleepliness, headache, nausea, stomach ache or rash. But the adverse effects were generally not so bad that people would stop taking the drugs. The main safety concern with antihistamines is possible adverse effects on the heart this did not happen in these trials. But Loratadine has short absorption window, preferentially absorbs at proximal part of small intestine [11].

In this regard, Loratadine gastroretentive floating tablets were prepared by using effervescent and Non Effervescent floating technique using polymers such as Ethyl cellulose, Karaya gum and HPMC K4 M as polymers and gas generating agents like sodium bicarbonate and citric acid and polypropylene foam powder as a selling agent in non effervescent floating tablets. The tablets prepared by direct compression technique concentrations using direct compression technology to enhance gastric retention and to increase its bioavailability and duration of action.

MATERIALS AND METHODS

Materials

Loratadine was procured from Cadila pharmaceuticals Ltd., Ethyl cellulose, Karaya gum

and HPMC K4 M were purchased from S.D. Fine Chemicals (Mumbai, INDIA), sodium bicarbonate and other excipients were procured from spectrum pharma research solutions, Hyderabad.

Preparation of floating tablets By direct compression method [12]

All ingredients were collected and weighed accurately. Drug with polymers were sifted and passed through sieve #60 and then the remaining excipients were rinsed over after pre blending all ingredients in mortar for 15minutes. The entire mixture was blended for 5minutes. Then magnesium stearate was added and blended again for 5-6 minutes, lubricated powder was compressed under 8mm punch of tablet punching machine, (Cadmach model DC16 16-Station Tablet Press). The composition of different formulations is shown in the above tables**.**

EVALUATION OF FORMULATIONS

Pre compression parameters

It includes Angle of repose, Bulk density, Tapped density, Cars index, Hausner's ratio.

Pre compression parameters

It includes Weight variation, Hardness, Friability, Thickness and diameter, Drug content, *In-vitro* buoyancy studies, Swelling index and *In-vitro* dissolution studies.

RESULTS AND DISCUSSION

Gastro retentive floating tablets were formulated by Loratadine by Effervescent technique (i.e., from F1-F9) and by Non effervescent technique (i.e., F10-F18).The formulated tablets have shown the results as given below:

UV Spectra of Loratadine at 10µg/ml concentration. Wavelength of maximum absorption in 0.1N HCL solution was found to be 276 nm, with uv range of loratadine was found to be 5-30mcg/ml with a regression value of 0.999.

Compatibility studies by FT-IR

From the compatibility studies it was concluded that the functional groups that were presented in the pure drug were present in the optimized formulation with very minute changes, from this we can concluded that the drug and excipients have no interactions.

In vitro floating buoyancy studies

All the formulated tablets were evaluated for the buoyancy studies for the determination of Floating Lag Time and Total Floating Time. The formulations having higher polymer concentrations exhibits total floating time for more than 12hours than the other formulations.

Swelling Studies

From the swelling studies of the floating tablets it was identified that the tablets formulated by Non effervescent technique have higher swelling index than the effervescent floating tablets, among them karaya gum having 90mg have higher swelling index.

Table 1: Composition of Loratadine floating tablets by Effervescent floating technique

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Loratadine	10	10	10	10	10	10	10	10	10
Ethyl cellulose	30	60	90	-	-	-	-	--	-
Karaya gum	-	-	-	30	60	90	-	-	-
HPMC K 4M	-	-	-	-	-	-	30	60	90
PVP K30	20	20	20	20	20	20	20	20	20
MCC	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
NAHCO3	50	50	50	50	50	50	50	50	50
Citric acid	5	5	5	5	5	5	5	5	5
MG -stearate	3	3	3	3	3	3	3	3	3
Talc	4	4	4	4	4	4	4	4	4
Total wt (mg)	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Table 2: Composition of Loratadine floating tablets by Non - Effervescent floating technique

Ingredients	F10	F11	F12	F13	F14	F15	F16	F17	F18
Loratadine	10	10	10	10	10	10	10	10	10
Ethyl cellulose	30	60	90	-	-	-	-	--	-
Karaya gum	-	-	-	30	60	90	-	-	-
HPMC K 4M	-	-	-	-	-	-	30	60	90
PVP K30	20	20	20	20	20	20	20	20	20
Polypropylene foam powder	50	50	50	50	50	50	50	50	50
MCC	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
MG -stearate	3	3	3	3	3	3	3	3	3
Talc	4	4	4	4	4	4	4	4	4
Total wt (mg)	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Table 3: Precompression parameters & Post compression parameters

Parameters	Range	Parameters	Range
Angle of repose (θ) ±SD	21.54±0.31-29.85±0.52	**Average wt in (mg)±SD**	198.4± 0.84-201.2± 0.32
Bulk density (gm/cm)±SD	0.310±0.28-0.327±0.16	**Hardness (Kg/cm2)±SD**	4.35± 0.20-5.24± 0.20
Tapped density (gm/cm) ±SD	0.360±0.010-0.382±0.011	**Diameter in (mm)±SD**	7.82± 0. 772-8.12± 0.54
Hausner's ratio (HR)±SD	1.12±0.010-1.18±0.018	**Thickness in (mm)±SD**	2.36± 0.04-3.42± 0.07
Carr index (C.I) ±SD	10.49±0.511-16.23±0.732	**Friability(%)±SD**	0.33± 0.07-0.79± 0.32
		Drug content uniformity (%)±SD	86.29±0.26-99.67±0.61

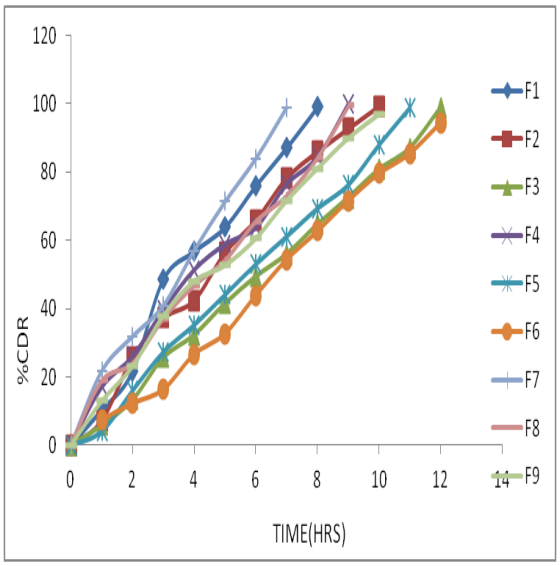

Fig 1:% CDR of F1-F9

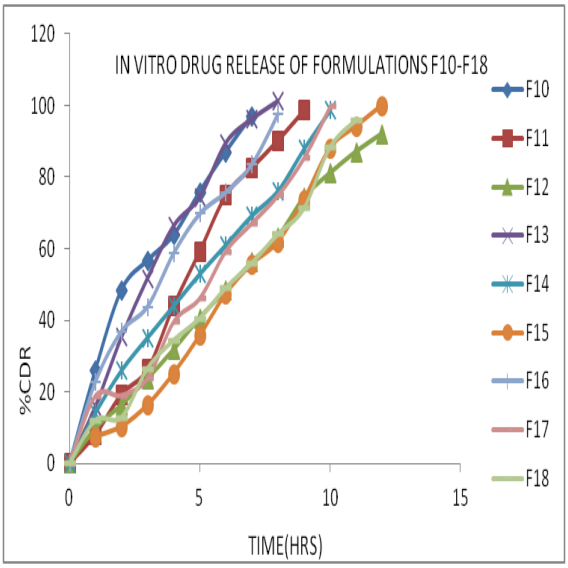

Fig 2: % CDR of F10-F18

IN-VITRO DRUG RELEASE STUDIES

In-vitro drug release data of Loratadine floating tablets by effervescent technique

From the drug release studies of the gastro retentive floating tablets of loratadine formulated by effervescent technique the maximum amount of drug release was found in F6 formulation containing karaya gum(90mg) as a rate retarding polymer as it has higher efficiency for retarding the drug release in the dissolution medium.

So the drug release kinetics were studied for the F6 formulation, and it follows zero order drug release and the drug release mechanism was found to be super case II transport mechanism.

In-vitro drug release data of Loratadine floating tablets by Non-Effervescent technique

From the drug release studies of the gastro retentive floating tablets of loratadine formulated by Non effervescent technique the maximum amount of drug release was found in F15 formulation containing karaya gum(90mg) as a rate retarding polymer as it has higher efficiency for the drug release in the dissolution medium. As we are formulating the gastroretentive floating tablets our main aim was to release the maximum drug in the gastric medium, so by comparing the dissolution profiles of F1-F18 the maximum drug release was found in the F15 formulation than the F6 formulation containing karaya gum in higher concentration formulated by using Effervescent floating technique.

So the drug release kinetics were studied for the F15 formulation, and it follows zero order drug release and the drug release mechanism was found to be super case II transport mechanism.

Based on the in vitro drug release studies the drug release from gastro retentive floating tablets of loratadine the tablets formulated by using Non Effervescent technique F15 formulation shows 100%drug release at the end of 12hours when compared with the Effervescent formulations.

Stability studies

From the stability studies it was indicated that there was no change of drug release from the floating tablets of loratadine after performing the stability studies.

CONCLUSION

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.

So for increasing the gastric retention time of the some poorly acidic absorption drugs were selected for increasing the gastric retention time for increasing the bioavailability of the drug.

From the results obtained it was concluded that the in vitro drug release profiles of the formulations F1-F18 the maximum drug release was found in the F15 formulation containing karaya gum(90mg) as a rate retarding polymer formulated by using Non effervescent floating technique.

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