Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2015, 7 (4):186-191
(http://scholarsresearchlibrary.com/archive.html)

Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Design and evaluation of levofloxacin floating tablet

Wajid Chaus* and Shriniwas Ingole

Dayanand College of Pharmacy, Latur, MS, India

ABSTRACT

The floating drug delivery systems are designed to retain in the stomach or gastric residence for prolonged and predictable period of time. It is helpful for enhance the bioavailability and reduces the fluctuations of the drug concentration also to achieve the controlled plasma level. In the present investigation, the floating dosage form contains levofloxacin as a main drug. The drug levofloxacin is first choice drug used for treatment of Helicobacter Pylori. These tablets or formulations contains drug, HPMC, Chitosan, Carbopol and some other additives were compressed by using wet granulation method. Tablets are evaluated for hardness, uniformity of weight, drug content friability, swelling index. All the readings are within standard limits and besides optimal floating lag time less than 30 sec. and total floating time less than 15 hrs. FTIR studies shows there is no interaction with the additives. In vitro release study was carried out by using 0.1N Hcl, at different time intervals like 2, 4, 6, 8, 10, 12 and 14hrs.

Key words: Floating tablets, Levofloxacin, *Helicobacter Pylori*. Chitosan, (HPMC-K4M), Carbopol

---

INTRODUCTION

Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation[1-2]. Drugs with short half-lives and drugs that easily absorbed from gastrointestinal tract (GIT) are eliminated quickly from the systemic circulation. For these types of drugs the development of oral sustained-controlled release formulations is an attempt to release the drug slowly into the gastrointestinal tract (GIT) and maintain an effective drug concentration in the systemic circulation for a long time. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinal tract (GIT)[3-4]But oral sustained drug delivery formulations show some limitations connected with the gastric emptying time; variable and too rapid gastrointestinal transit could result in incomplete drug release from the device into the absorption window leading to diminished efficacy of the administered dose.[5] Floating drug delivery system is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. This drug delivery system not only prolongs GI residence time but does so in an area of the GI tract that could maximize drug reaching its absorption site in solution and hence ready for absorption[5]

Floating Drug Delivery Systems are aimed to retain the drug in stomach and are useful for drugs that are poorly soluble or unstable in intestinal fluids. The main principle of floating drug delivery system is to make the dosage from less dense than gastric fluids. So, it can float on them. [6]

Levofloxacin is a synthetic fluroquinolone antibacterial agent that inhibits bacterial DNA replication. It is L-isomer of Ofloxacin. It has 6 hrs of half life period. The absorption of drug i.e. levofloxacin is dose dependent which increases with increase in dose. The drug levofloxacin is first choice drug used in treatment of *Helicobacter pylori* infections. Also the drug used to treat the various infections which are caused by the micro-organisms, such as bacillus anthracis, chalmadiya infections, epidydimitys, gonorrhea, etc.[7]

Helicobacter pylori is a prevalent human specific pathogen which is now believed to be the causative bacterium for chronic gastritis, peptic ulcer and adenocarcinoma. The tablets were prepared by using wet granulation method [8]

MATERIALS AND METHODS

Levofloxacin was obtained as gift sample from Mediwin Pharmaceutical limited Ahmedabad, HPMC K4M was obtained from SD fine chemical limited Mumbai ,Chitosan was obtained as gift sample from mahtani Chitosan Pvt ltd,veraval gujrat., carbopol, was obtained from maruti chemicals ahmedabad, sodium bicarbonate, citric acid, magnesium state, talc were obtained from commercial sources used for analytical grade.

Preparation of Levofloxacin Floating Tablets [8]:
Floating tablets of levofloxacin were prepared by using wet granulation method with different drugs and polymers such as levofloxacin, HPMC, Chitosan, Carbopol, sodium bicarbonate, magnesium sterate were mixed homogenously in mortar and pestle. Isopropyl alcohol was used as granulating fluid and then granules were prepared and passed through # 16 sieves. After that granules were dried at 60°C and again passed through #20/44 sieves. Sodium bicarbonate used as an gas generating agent, magnesium sterate used as lubricating agent and talc used as glidant just 4-5 min before compression. Table no. 1

Table no. 1 Formulations

Active ingredients (mg)	F1	F2	F3
Levofloxacin	250	250	250
HPMC K4M	80	70	60
Carbopol	20	20	20
Chitosan	50	50	50
Citric acid	25	30	35
Sodium bicarbonate	70	75	80
Magnesium sterate	3	3	3
Talc	2	2	2
Total	500	500	500

Table no. 2 Micromeritics properties of Levofloxacin granules formulated with different concentrations:

formulation code	Angle of repose	Bulk density	Tapped density	Compressibility Index	Haussners ratio
F1	22.33 ± 0.02	0.207±0.018	0.229 ± 0.003	11.140 ± 0.021	1.128 ± 0.012
F2	23.12 ± 0.04	0.221±0.015	0.298 ± 0.010	13.440 ± 0.018	1.150 ± 0.010
F3	24.52 ± 0.06	0.289±0.010	0.335 ± 0.016	13.410 ± 0.025	1.153 ± 0.016

Tablets Evaluation Tests
Evaluation of tablets:
1. **Hardness**[9]**:** The hardness of tablets was measured by Monsanto hardness tester. The lower plunger was placed in contact with the tablet and zero reading was taken. The plunger was then forced against spring by tuning the threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force. The hardness was measured in terms of kg/cm2. (Table no. 2)

2. **Drug content**[9]**:** 20 tablets were weighed and powdered the powder weight equivalent to 100 mg of levofloxacin was dissolved in100 ml of 0.1N HCL and filtered. 5 ml of this was diluted to 50 ml with water and drug content was estimated using UV-VISIBLE Spectrophotometer at 288 nm. (Table no. 2)

3. **Weight variation**[8]**:** Formulated tablets were tested for weight uniformity, 20 tablets were weighed collectively and individually. From the collective weight, average weight was calculated. The percent weight variation was calculated by using following formula-. (Table no. 2)

$$\% \text{ weight variation} = \frac{\text{Average weight- Individual weight}}{\text{Average weight}}$$

4 **Friability**[8]**:**The Roche friability test apparatus was used to determine the friability of the tablets. Twenty preweighed tablets were placed in the apparatus and operated for 100 revolutions and then the tablets were reweighed. The percentage friability was calculated according to the following formula- . (Table no. 2)

$$\text{Friability} = \frac{\text{Initial Weight - Final Weight}}{\text{Initial Weight}} \times 100$$

Table no. 3

Parameters	F1	F2	F3
Hardness (kg/cm2)	4.3 ± 0.039	4.2 ± 0.023	4.4 ± 0.018
Weight variation (mg)	449.79 ± 0.47	450.34 ± 0.39	451.08 ± 0.24
Friability (%)	0.34 ± 0.021	0.29 ± 0.014	0.40 ± 0.023
Drug content (%)	99.79 ± 0.19	98.91 ± 0.35	100.88 ± 0.18
Floating lag time (min)	16 sec	18 sec	26 sec
Total floating time (hrs)	>13	>16	>20

4. **Floating lag time: [15]** The time between introduction of dosage form and its buoyancy on the simulated fluid and the time during which the dosage form remained buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and the total duration of floating i.e. as long the dosage form remains buoyant is called as Total Floating Time (TFT). . (Table no. 2)

Formulations	Lag time (sec.)
F1	16
F2	18
F3	26

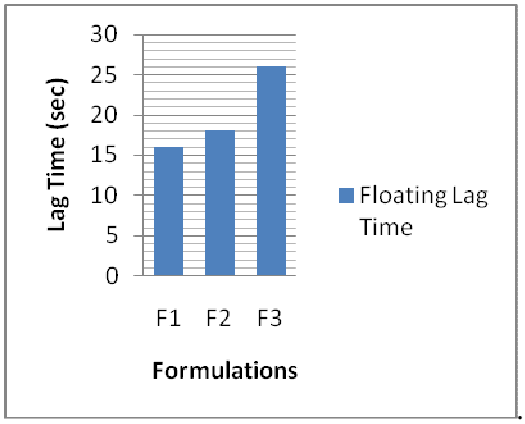

Figure no.1

a) Swelling Index [12]**:** formulated tablets were weighed individually (W0) and placed separately in Petri dish containing 50 ml of 0.1 N HCl. The Petri dishes were placed in an incubator maintained at 37±0.5oC. The tablets were removed from the petri dish, at predefined intervals of time and reweighed (Wt), and the % swelling index was calculated using the following formula:

% WU = (Wt-Wo/Wo) ×100

Where:
WU – Water uptake
Wt – Weight of tablet at time t
Wo – Weight of tablet before immersion.

Table no. 4

Sr. No.	Concentration (µg/ml)	Absorbance
1	2	0.113
2	4	0.201
3	6	0.314
4	8	0.429
5	10	0.503
6	12	0.634
7	14	0.778
8	16	0.831
9	18	0.921
10	20	1.023

Method for determining the calibration curve[13]:
10 mg of levofloxacin was dissolved in 100 ml of the solvent to obtain the working standard of 100 µg/ml. Aliqotes of 1 ml to 3.5 ml free from the stock solution representing 10 to 35 µg/ml of drug were transferred to 10 ml

volumetric flask and the volume was adjusted to 10 ml with the solvent. Absorbance of the above solution were taken at λ=288 nm against the blank solution prepared into the same manner without adding the drug.

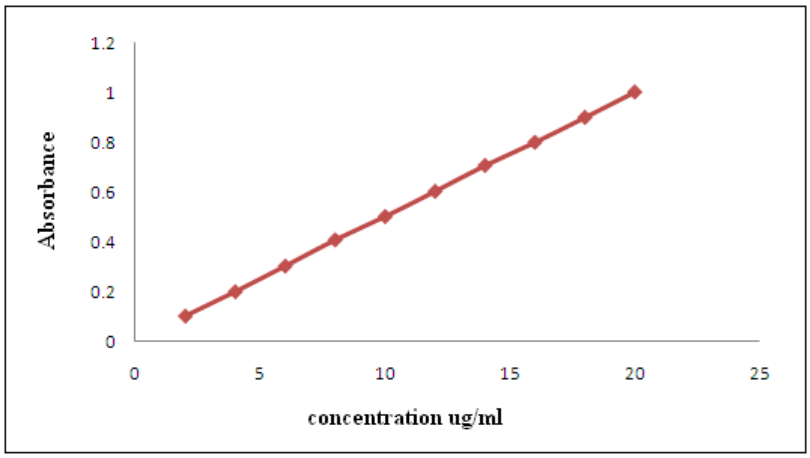

Figure no.2

INFRA RED (I.R.) Spectral analysis [10]:

FTIR spectral analysis was used to study the interactions between the drug, polymer and the excipients. The drug and excipients are compatible with one another. FTIR study shows that there is no interaction with the drug with the polymers used, all peaks are separated.

In *Vitro* dissolution test[11,17]**:**

The release of levofloxacin from the tablet was studied by using USP-type II paddle apparatus. Drug release profile was carried out in 900 ml of 0.1 N HCL maintained at 37+ 0.5°C temperatures at 100 rpm. 5ml of samples were withdrawn at regular time intervals. The samples was replaced by its equivalent volume of dissolution medium and was filtered through 0.45 µm wattman filter paper and analyzed at 2868nm by UV Spectrophotometer.

Table no. 04 Cumulative Percent drug release and Drug retained study for different time intervals

Time	F1		F2		F3	
	Cumulative % drug release	Cumulative % drug retained	Cumulative % drug release	Cumulative % drug retained	Cumulative % drug release	Cumulative % drug retained
0	0	100	0	100	0	100
2	9.31	90.69	21.08	80.68	22.02	81.20
4	20.20	79.80	33.23	68.37	33.93	68.98
6	32.16	67.84	44.56	57.41	66.89	36.10
8	44.42	56.58	72.46	27.79	90.95	11.88
10	65.45	34.52	90.12	12.16	-	-
12	71.60	28.40	-	-	-	-
14	89.31	11.30	-	-	-	-

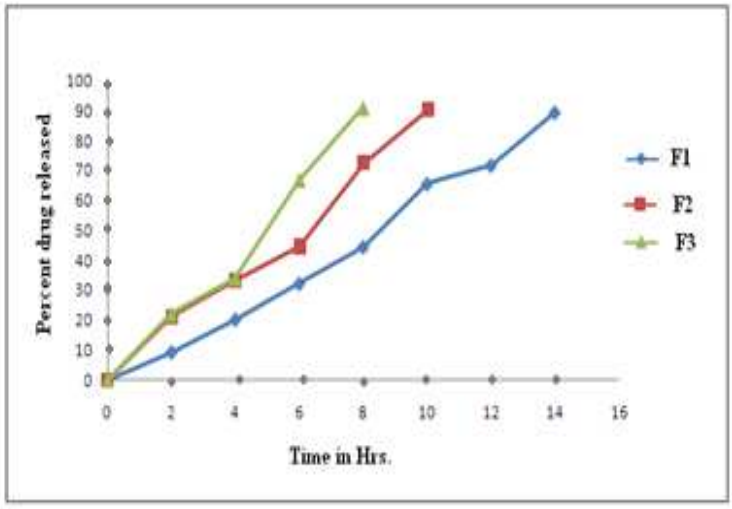

Figure no.3

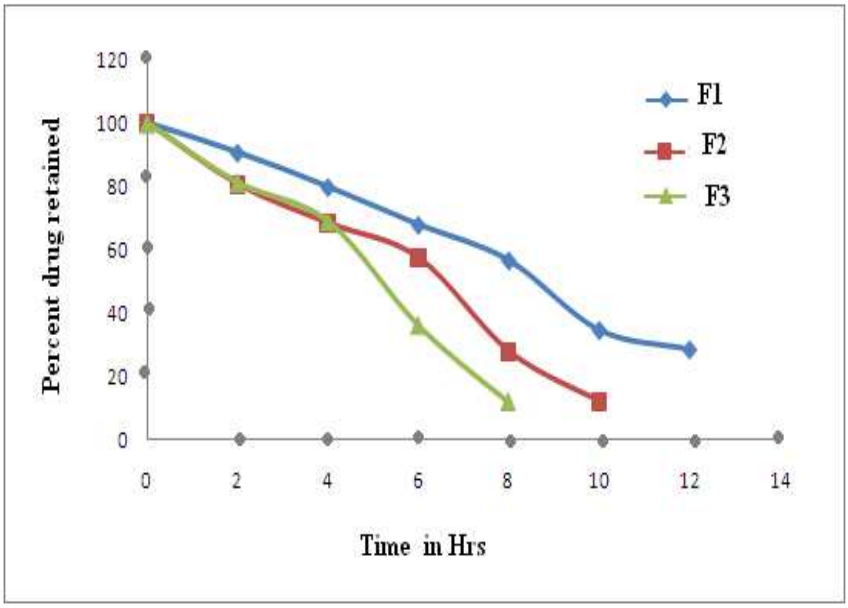

Figure no.4

Stability Study:

Stability studies were carried out on selected formulations (F1) at 4±2oc, 27±2oc and 45±2oc for 45 There was no significant changes in drug content, physical stability, hardness, friability and drug release for the formulations [14-16]

RESULT AND DISCUSSION

The present study was aimed to make the formulation remain in the stomach for longer period of time and to release the drug (Levofloxacin) in controlled rate. Chitosan was selected as a hydrophobic meltable material to impart sufficient integrity to the tablets. Sodium bicarbonate generates carbon dioxide gas in the presence of hydrochloric acid present in gastric dissolution medium.All the three prepared formulations shows sustained release of drug .formulation (F1) shows prolonged release rate than F2 and F3.

The hardness values were approximately 4.2 -4.4kg/cm2. All formulations showed floating lag time in between 16 to 26 minutes and duration of floating time was greater than 20 hours. Formulations (F2-F3) showed more than 90% of drug release in 10hrs of dissolution study. Formulations F1showed less than 89.31% of the drug release in 14hrs may be due to higher amount of bees wax was used. F1 also showed less than 80% of drug release in 12hrs may be due to higher amount of polymer. The IR spectrum showed that both drug and polymer were not interacted with each other and appeared as separate entities. The data for stability studies were carried out for the optimized Formulation F1at 4±2oc, 27±2oc and 45±2oc for 45 days and it revealed that no considerable differences in drug content and dissolution rate and buoyancy were observed.

CONCLUSION

Floating tablets of Levofloxacin prepared by HPMC, Carbapol and Chitosan could be used for treatment of gastric ulcers caused by *H.pylorii* infection by prolonging the gastric residence time and its controlled release in the gastric environment thus completely eradicating the *H.pylo* fromGIT.

REFERENCES

[1] Nayak K Amit, Maji Ruma and DasBiswarup: *Asian Journal of Pharmaceutical and Clinical Research*. **2010**; 3(1): 1-10.
[2] Nadigoti Jagadeesh and Shayeda, *International Journal of Pharmaceutical Sciences and Nanotechnology*. **2009;** 2(3): 595-604.
[3] A.Streubel , Siepmann J and Bodmeier R,*Expert Opin Drug Deliv*. **2006**; IJRPBS. 2011; 3(2): 217-33.
[4] A.V.Mayavanshi and S.S.Gajjar ,*Research J.Pharm. And Tech. Oct.-Dec.* **2008**; 1(4): 345-348.
[5] S.B.Bhise, N.H Aloorkar: *Indian Journal of Pharmaceutical Sciences*. **2008**; 70(2): 224- 227.

[6] Geetha A., J.Rajendra kumar, CH.Krishna mohan, V.Sateesh and P N Raju., *Int. J. Pharm. Research and Bio. Analysis*, **2012**.Vol-1,Issue 1, , 1-13
[7] Dayakar Reddy B, Sai Kishore V, Teja Krishna M, Prasada Rao K.V.S, , *journal of drug Delivery Research,ISSN-2319-1074*,**2013** vol-2, Issue 1
[8] Nirav Patel, Nagesh C. Jinal Patel, Chandrashekhar S., Jani Devdatt, *Asian J. Pharm. Tech.* **2012***;* Vol. 2: Issue 4, Pg 135-140
[9] Ravi Kumar, Swati Patil ,M. B. Patil, Sachin R. Patil1, Mahesh S. Paschapur *International Journal of ChemTech Research CODEN(USA): Oct-Dec* **2009** Vol.1, No.4, pp 815-825,
[10] Kavita K, Yadav SK, Tamizhamani T, *Int. J. of Pharm Tech Research,Apr-Jun* **2010**,2(2), p.N.-1513-1519.
[11] S.K. Sreekanth, S. palanichamy, T. Raja Sekharan, A. Thanga thirupathi, *int. J. of Pharm. and Bio. Sci.* **2010** 1(2), 763-767
[12] A.A.Deshpande , Shah NH, Rhodes CT, Malick W, *Pharm. Research*, **1997,**14(6), 815-819.
[13] Patel D.M, Patel N.M, Pandya NN, Jogani PD, *aaps. Pharm. Sci. Tech*, **2007**, 69(6), 763-767.
[14] Nirav Patel, Nagesh C,Jinal Patel,Chandrashekhar SJani Devdatt,. *Asian J. pharm. Tech. 2(4): Oct. - Dec*. **2012**; Page 135-140.
[15] Chandrasekhara Rao Baru, S. Vidyadhara, KV. Raghavendra Rao,K. Vanitha Prakash1and B.Umashankar, *IJPCBS* **2012**, 2(4), 472-481
[16] Saritha D, D. Sathish and Y. Madhusudan Rao, , *Journal of Applied Pharmaceutical Science* **2012:** 02 (03); 68-73.
[17] Daisy chella kumara S , S.Vengatesh, K. Elango , R. Devi Damayanthi ,N. Deattu, P.Christina, *Int. J. Drug Dev. &Res., October-December* **2012,** 4(4): 265-274