Research Article **ISSN:2321-2624**

International Journal of Medicine and Pharmaceutical Research
www.pharmaresearchlibrary.com/ijmpr

Formulation and *In Vitro* Evaluation of Oral Floating Tablets of Levofloxacin Hydrophilic Matrix

[1]Mohan kumar Atluri*[1], K. Saravan kumar[1], Jagadesh kumar Yadav kalluri[1], P. Sravan kumar[2], Yagagowri[1], P. Sravanthi[3]

Department pharmaceutics, Sree Vidyanikethan College Pharmacy, A. Rangampet, Tirupati, A.P, India-517102.
[2]Department pharmaceutics, Krishna Teja College of Pharmacy, Tirupati, A.P, India-517102.
[3]Department pharmaceutics, JNTUA OTRI, Anantapure, A.P, India
Received: 15 June2014, Accepted: 19 July 2014, Published Online: 10 August 2014

Abstract

The present study was aimed at preparing a Floating drug delivery system for the model drug levofloxacin, and evaluating the various processing parameters including the buoyancy studies and *in vitro* drug release studies. Four formulations containing varying proportions of polymers like HPMC K4M and Ethyl cellulose and fixed amount of gas generating agent such as Sodium bicarbonate and hydrophobic meltable material like bees wax were prepared. The tablets were prepared by melt granulation technique and the prepared tablets remained buoyant for more than 7hrs in the release medium. The proportions of the polymers showed significant difference in the release of the drug. All the formulations exhibited diffusion dominant drug release and were found to be stable.

Keywords: Floating tablets, Buoyancy, Sustained release, levofloxacin

Contents

***Corresponding author**
Mohan kumar Atluri
Department pharmaceutics,
Sree Vidyanikethan College Pharmacy,
A. Rangampet, Tirupati, A.P, India-517102.
Manuscript ID: IJMPR2168

PAPER-QR CODE

1. Introduction

During the last decade, many studies have been performed concerning the sustained release dosage forms of drugs, which have been aimed at the prolongation of gastric emptying time (GET). The GET has been reported to range from 2 to 6 hrs. in humans in the fedstate[1]. Retention of drug delivery systems in the stomach prolongs the overall gastrointestinal transit time, thereby resulting in improved bioavailability. Scintigraphy studies determining gastric emptying rates revealed that orally administered controlled release dosage forms are subjected to basically two complications, that is short gastric residence time and unpredictable gastric emptying rate[2]. Depending on the

mechanism of buoyancy, two distinctly different methods viz., effervescent and non-effervescent systems have been used in the development of floating drug delivery systems (FDDS) [3]. Effervescent drug delivery systems utilizes matrices prepared with swellable polymers such as methocel or polysaccharides and effervescent components like sodium bicarbonate and citric or tartaric acid. FDDS offers important advantages like they are less prone to gastric emptying resulting in reduced intra and inter subject variability in plasma drug levels, effective for delivery of drugs with narrow absorption windows, reduced dosing and increased patient compliance, reduced Cmax and prolonged drug levels above the minimum effective concentration and improved safety profile for drugs with side effects associated with high Cmax.

Levofloxacin is a synthetic antibacterial agent. The levofloxacin is chemically(-)-(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid hemihydrate. Mode of action of Levofloxacin inhibits DNA-gyrase in susceptible organisms there by inhibits relaxation of super coiled DNA and promotes breakage of DNA strands. The peak plasma concentrations are usually attained within one hour. The absolute bioavailability of Levofloxacin is approximately 99%, metabolism (Hepatic, Minimal) in humans, excreted as unchanged drug in the urine. Half- life of Levofloxacin ranges from 6 to 8hours. The total body clearance and renal clearance range from approximately 144 to 226 ML/min and 96 to 142 ML/min respectively. The present study aims in designing floating tablets of levofloxacin using HPMCK4M as the hydrophilic matrix and sodium bicarbonate as the gas generating agent, evaluating the prepared tablets for physicochemical properties, buoyancy lag time, total floating time, swelling index and *in-vitro* drug release.

2. Materials and Method

Materials

Levofloxacin was obtained as a gift sample from A TO Z Pharmaceuticals, Chennai, India. HPMC K4 and Microcrystalline cellulose were purchased from Mohan chemicals, Tirupathi. Ethyl cellulose and Beeswax, Magnesium stearate and Talc were purchased from SD Chemie Pvt.Ltd, Mumbai.

Methods

1. Preparation of Floating tablets by Meltgranulation technique

The Required quantity of bees wax was weighed and melted in a large china dish over a water bath. The drug was added to the molten wax and mixed well. Previously weighed quantities of HPMC K4M, Ethyl cellulose and sodium bi carbonate were added to the drug-wax mixture and mixed well. After mixing the china dish was removed from water bath and cooled. The coherent mass was then scrapped from the china dish and was passed through sieve no.60. Granules were lubricated with talc and magnesium stearate was added. The lubricated granules were then passed through sieve no.100. The granules were then compressed using a single punch tablet machine (Sree Vidyanikathan College of Pharmacy, Tirupathi).

Table 1: Different floating tablets Formulations

Fomulation Code	Levofloxacin (mg)	HPMCK4M (mg)	Sodium Bicarbonate (mg)	Bees Wax (mg)	Ethyl Cellulose (mg)	Talc (mg)	Magnesium Stearate (mg)
F1	250	162.5	25	37.5	25	10	5
F2	250	137.5	25	37.5	50	10	5
F3	250	125	25	37.5	62.5	10	5
F4	250	100	25	37.5	87.5	10	5

2. Evaluation of granules

Preformulation studies: The Preformulation studies including Compatibility study, Bulk density, Tapped density, Hausner's ratioand Angle of repose was performed for the levofloxacin granules.

Angle of repose: Flow property of the granules was evaluated bydetermining the angle of repose and the compressibility index. Static angle of repose was measured according to fixed funnel method and free standing cone method of Banker and Anderson[4]. The angle of repose was calculated using the equation, Tan _ = h/r ….(1) where is the angle of repose.

Bulk density

Loose bulk density (LBD) and Tapped bulk density (TBD) were determined for the prepared granules.

LBD and TBD was calculated using the formula,

LBD = Wt of Powder / Vol. of Powder ……..(2)

TBD = Wt of Powder / Tapped Vol. of Powder….(3)

Compressibility Index

Carr's Compressibility Index[5] for the prepared granuleswas determined by the equation,

Carr's Index (%) = TBD – LBD/TBD x 100 … …(4)

Hausner's ratio

Hausner's ratio can be determined by the following equation,

Hausner's ratio = TBD / LBD

Table 2: Granule Properties of all formulations

S.No	Parameter	F1	F2	F3	F4
1	Hardness(Kg/cm2)	4.2	4	4	4
2	Friability(%)	0.17	0.61	0.38	0.2
3	Uniformity of Weight(mg)	515	515	515	516
4	Drug content(%)	98.1	97	99.2	99.3
5	Thickness (mm)	4.4	4.5	4.2	4.4
6	Buoyancy Lag Time(minutes)	7	6	5	4
7	Duration of Buoyancy(Hours)	>16	>16	>16	>16

Where, TBD -Tapped bulk densities & LBD- Loose bulk densities

3. Evaluation of Tablets

Friability: Twenty tablets were accurately weighed and placed in the friabilator (Roche's Friabilator) and operated for 100 revolutions. The tablets were dedusted and reweighed. The tablets that loose less than 1% weight were considered to be compliant [6].

Weight variation: 10 tablets were selected randomly from the lot and weighed individually to check for weight variation.

Disintegration test: Tablets were taken and one tablet was introduced in each tube of (VEEGO-microprocessor based) disintegration apparatus and placed in 1litre beaker containing water at 370±20C and the time of disintegration was recorded. The study was done at room temperature without disc being added [7].

Drug content estimation

Five tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 40mg of drug was transferred to 100ml standard flask. The powder was dissolved in 5mlof Methanol and made up to volume with 0.1N HCl. The sample was mixed thoroughly and filtered through whatmanfilter paper. The filtered solution was diluted suitably and analysed for drug content by UV spectrophotometer at amax of about 245nm [8].

***In Vitro* Buoyancy studies:** *In Vitro* buoyancy studies was performed for all the four formulations as per the method described by Rosa *et al*15.The randomly selected tablets from each formulation werekept in a 100ml beaker containing simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise tothe surface and float was taken as floating lag time. The overall floating time was calculated during the dissolution studies [9].

***In Vitro* Dissolution studies:** The *in vitro* dissolution studies were carried out in 0.1N HCl using USP XXII Dissolution test apparatus employing paddle stirrer. One tablet was placed inside the dissolution medium and the paddle was rotated at 75rpm. 5ml samples were withdrawn at specific time intervals and the same volume was replaced to maintain sink conditions. The samples were analysed for drug content spectrophotometrically at 245nm.

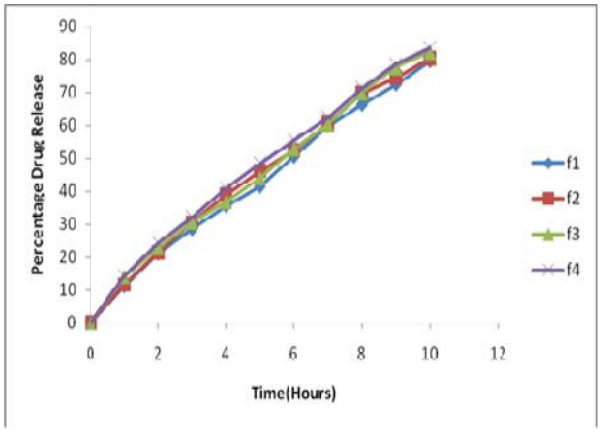

Figure 1: In-Vitro Dissolution profile of Levofloxacin formulations 1 To 4 in 0.1 N HCl

Table 3: In-Vitro Dissolution profile of Levofloxacin formulations 1 To 4 in 0.1 N HCl

S.No	Time of Sampling (hour)	Percentage Drug Release				
		F1	**F2**	**F3**	**F4**	**Marketed product**
1	0	0	0	0	0	98.99
2	1	11.2	11.6	14.1	14.2	-
3	2	21.1	21.5	22.8	24.4	-
4	3	28.6	30.5	30.6	32.12	-
5	4	35.6	39	36.8	40.8	-
6	5	41.5	46.2	44	48.4	-
7	6	50.6	52.5	52.8	55.6	-
8	7	59.8	60.6	60.3	62.4	-
9	8	66.4	69.9	69.8	71.2	-
10	9	72.5	74.5	77.5	78.5	-
11	10	79.6	80.4	82.2	83.5	-

4. Results and Discussion

The role of polymer was to control the release as well as to make the formulation buoyant. Bees wax was selected as a hydrophobic meltable material to impart sufficient integrity to the tablets. Sodium bicarbonate generates carbon-di-oxide gas in the presence of hydrochloric acid present in dissolution medium. Ethyl cellulose was used as a floating enhancer. The tablets were prepared by melt granulation method. The granules of different formulations were evaluated for angle of repose, bulk density, tapped density, compressibility index, Hausner'sratio and drug content.(table10). The results show that the angle of repose(31-35), compressibility index values ranges from 11-16 and Bulk density, Tapped density values favour the good flow property of the granules.

The tablets of all the formulation were subjected to many in-process parameters such as hardness, friability, thickness, content uniformity and weight variation. The hardness values of approximately 4-4.2 kg/cm2. The weight loss was less than 1% in the friability test (0.37-0.5) was considered as acceptable value for conventional tablet. This indicates the tablet could withstand the mechanical shock while doing handling. Good uniformity in drug content was found among different formulations of the tablet and the percentage drug content was more than 95%. All the formulations showed the thickness in the range of 4.2- 4.6mm.All formulations showed buoyancy lag time in between 5 to 11 minutes and duration of buoyancy was greater than 16hours.

Levofloxacin release from tablets was slow and extended over longer periods of time. The results of dissolution studies of all formulations (F1-F4) were shown in the table16. Formulations F2, F3, F4 showed more than 80% of drug release in 10hrs of dissolution study. Formulations F1 showed 79.6 % of the drug release in 10hrs.So formulation-1 is considered as better formulation compared to other formulations (F2,F3,F4).

5. Conclusion

The effervescent based floating drug delivery was a promising approach to achieve invitro buoyancy. The addition of gel forming polymer (HPMC K4M) and gas generating agent sodium bicarbonate were essential to achieve the invitro buoyancy. The drug release from the tablets was sufficiently sustained due to the presence of polymer and Bees wax. Levofloxacin floating tablet drug delivery system showed improved in vitro bioavailability and extended drug release which may favour the reduced dose frequency and patient compliance. Further clinical evaluation may prove the efficacy of this formulation.

6. References

1. Chavanpatil M, Jain S, Chaudari S, Shear R, Vavia P.Development of sustained release gastroretentive drugdelivery system for Ofloxacin: *Invitro*and *invivo*evaluation. IntJ Pharm, **2005**, 304: 178-184.
2. Swamy PV, Bhosale UV, Hiremath SN, Shirsand SB, Raju SA.Formulation and Optimization of Gastric Floating DrugDelivery System of Atenolol Using 3^2 Full Factorial Design.Indian Drugs, **2008**, 45: 293-300.
3. Hilton AK, Deasy PB. *Invitro*and *invivo*evaluation of an oralsustained-release floating dosage form of amoxicillin trihydrate.Int J Pharm, **1992**, 86: 79-88.
4. Banker GS, Anderson NR. Tablets. In: Lachman L, Lieberman HA, Kanig JL, Editors. The Theory andPractice of Industrial Pharmacy, 3rd Edn., Mumbai:Varghese Publishing House, **1984**, 283.
5. Carr R L., Evaluating flow properties of solids, Chem.Engg., **1965**, 18: 163-168.

6. Sreenivas SA, Gadad AP. Formulations & Evaluation ofOndansetron HCl directly compressed mouth disintegratingtablets. Indian drugs, **2006**, 43(1): 3538.
7. Ziyaur R, Mushir A, Khar RK. Design and Evaluation of bilayerfloating tablets of captopril.Acta pharm **2006**, 56: 4957.
8. Rockville MK. USP. 27th revision, USP convention INC, **2004**.
9. Rosa M, Zia H, Rhodes T. Dosing and testing *invitro*of abioadhesive and floating drug delivery system for oralapplication. Int J Pharm, **1994**, 105: 65-7.
10. Gohel MC, Mehta PR, Dave PK, Bariya NH. More relevantdissolution method for evaluation of PDDS. Dissolution technol, **2005**, 11: 225.