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Research Article

FORMULATION AND EVALUATION OF OFLOXACIN FLOATING TABLETS USING HPMC

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ABSTRACT

The present study outlines a systematic approach for designing and development of Ofloxacin floating tablets to enhance the bioavailability and therapeutic efficacy of the drug. Floating tablets of Ofloxacin have shown controlled release thereby proper duration of action at a particular site and are designed to prolong the gastric residence time after oral administration. Different formulations were formulated by wet granulation technique using HPMC K_4M, HPMC $K_{15}M$ and HPMC $K_{100}M$ (floating agent) as polymers along with sodium bicarbonate as gas generating agent. The formulations were evaluated for their physicochemical properties, buoyancy lag time, total floating time, swelling index and *in-vitro* drug release. It was found that the hardness of the tablets affects the Buoyancy characteristic of the dosage form. All six formulations possessed good floating properties with total floating time between 8 – 12 hrs. The *in-vitro* cumulative % drug release of the formulations F1A, F1B, F2A, F2B, F3A and F3B were 102.85%, 101.32%, 100.2%, 99.98%, 99.28% and 97.25%.

Keywords: Ofloxacin, Floating tablets, HPMC, Controlled release.

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 fed state.[1] Retention of drug delivery systems in the stomach prolongs the overall gastrointestinal transit time, thereby resulting in improved bioavailability. Scintigraphic 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.

Ofloxacin is an anti-bacterial agent that inhibits an enzyme called DNA gyrase which is an essential component of the mechanism that passes genetic information onto daughter cells when a cell divides. Ofloxacin is chemically 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 hemihydrates, off white to yellow crystal, insoluble in water, soluble in 0.1N hydro chloric acid. Ofloxacin exhibits pH dependent solubility. It is more soluble in acidic pH and slightly soluble in neutral or alkaline pH conditions.[4] Ofloxacin is incompletely absorbed from gastrointestinal tract, it has absorption window confined to upper part of gastrointestinal tract. It has a half life of 9 hours and its absolute bioavailability was reported to be about 45-50% of the administered dose, hence it was considered a suitable candidate for formulation as gastroretentive floating drug delivery system.

The present study aims in designing floating tablets of Ofloxacin using HPMC K_4M, HPMC $K_{15}M$ and HPMC $K_{100}M$ and evaluating the prepared tablets for physicochemical properties, buoyancy lag time, total floating time, swelling index and *in-vitro* drug release.

MATERIALS AND METHODS

Ofloxacin, Sodium bicarbonate and Lactose were procured from Micro Labs Ltd, Bangalore, Karnataka, India. HPMC (K_4M, $K_{15}M$ & $K_{100}M$), Hydrochloric acid and Aerosil were procured from S.D. Fine chemical Ltd, Bombay. PVP K 90 was purchased commercially from National Scientific Products, Mumbai. Talc and Magnesium stearate were procured from Loba Chemie, Mumbai. All the other chemicals used were of analytical reagent grade.

Preformulation studies

As per standard procedures, the preformulation studies including Compatibility study, Bulk density, Tapped density, Hausner's ratio and Angle of repose was performed for the crude drug, Ofloxacin.

Fabrication of floating tablets

Tablets were fabricated by using wet granulation technique. Ofloxacin (400 mg) was mixed with required amount of polymers and other excipients as shown in Table 1. All the excipients were passed through # 60 mesh (ASTM), mixed and granulated with 10% solution of PVP K 90 in isopropyl alcohol. The wet mass was passed through #16 mesh and dried at 45°C for 2 hrs. Dried granules were passed through #24 mesh and mixed with magnesium stearate and talc. Granules were compressed into tablets using 16 punch single station tablet compression machine (Cadmach).[5]

Determination of physicochemical parameters

Hardness test

Monsanto hardness tester was used for the determination of hardness of tablets.[6]

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.

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 37°±2°C and the time of

disintegration was recorded. The study was done at room temperature without disc being added.[7]

Determination of drug content

10 tablets were randomly selected from the batch, weighed and powdered. Powder equivalent to 250 mg of Ofloxacin was weighed and was diluted with a suitable volume of 0.1M sodium hydroxide to produce a solution containing 0.008% w/v of anhydrous Ofloxacin. The absorbance of the resulting solution was measured spectrophotometrically at the maximum wavelength of about 294 nm, using the solution as a blank which is prepared in the same manner omitting the substance being examined. Calculate the content of $C_{18}H_{20}FN_3O_4$ from the absorbance obtained by repeating the operation using Ofloxacin in place of the substance being examined and from the declared content of Ofloxacin.[8]

***In-vitro* dissolution study**

In-vitro release studies was carried out by using United States Pharmacopoeia (USP) 23 Dissolution Testing Apparatus II (Paddle method). The dissolution test was performed using 900 ml of 0.1N HCl (pH 1.2) at 37±0.5°C. 50 rpm was maintained, 5 ml of sample was withdrawn at predetermined time intervals for 24 hours and the same volume of the fresh medium was replaced. The absorbance of the withdrawn sample was measured spectrophotometrically at a wavelength of about 294 nm and cumulative percentage drug release was calculated using an equation obtained from a standard curve.[9]

Determination of floating parameter

a) *In-vitro* buoyancy test

The *in-vitro* buoyancy was determined by observing floating lag time, as per the method described by Rosa. The tablets were placed in a 100 ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was considered as the floating lag time.[10]

b) Swelling study

Swelling of hydrophilic polymer such as Hydroxy Propyl Methyl Cellulose greatly depends upon the contents of the stomach and the osmolarity of the medium. These eventually influences the release, slowing action and the residence time.

For each formulation, one tablet was weighed and placed in a beaker containing 200 ml of distilled water. After each hour the tablet was removed from beaker and weighed again upto 8 hours. The percentage weight gain by the tablet was calculated by using the formula.

Swelling index (S.I) = {(Wt-Wo)/Wo} x 100

Where, S.I. = swelling index

Wt = Weight of tablet at time t

Wo = Weight of tablet before immersion.

Table 1: Different floating tablets Formulations

S.No	Ingredients	Quantity for 1 tablets					
		F1A	F1B	F2A	F2B	F3A	F3B
Intra granular							
1	Oflaoxacin	400 mg	400 mg	400 mg	400 mg	400 mg	400 mg
2	Polymers	175 mg (HPMC K_4M)	210 mg (HPMC K_4M)	175 mg (HPMC $K_{15}M$)	210 mg (HPMC $K_{15}M$)	175 mg (HPMC $K_{100}M$)	210 mg (HPMC $K_{100}M$)
3	Lactose	44.5 mg	9.5 mg	44.5 mg	9.5 mg	44.5 mg	9.5 mg
4	Sodium bi carbonate	70.0 mg	70.0 mg	70.0 mg	70.0 mg	70.0 mg	70.0 mg
5	PVP K 90	3.5 mg	3.5 mg	3.5 mg	3.5 mg	3.5 mg	3.5 mg
6	Isopropyl alcohol	0.1 ml	0.1 ml	0.1 ml	0.1 ml	0.1 ml	0.1 ml
Extra granular							
7	Talc	2 mg	2 mg	2 mg	2 mg	2 mg	2 mg
8	Aerosol	2 mg	2 mg	2 mg	2 mg	2 mg	2 mg
9	Magnesium stearate	3 mg	3 mg	3 mg	3 mg	3 mg	3 mg

RESULTS AND DISCUSSION

In the Preformulation studies, compatibility studies were performed using FTIR spectrophotometer. The FTIR spectrum of pure drug and physical mixture of drug and polymer were studied. The peaks obtained in the spectra's of each formulation correlated with the peaks of pure drug spectrum. So it was concluded that no significant difference in peak pattern in IR spectrum of drug, polymer and the excipients exists.

The values obtained for the preformulation parameters for the formulations F1A & B, F2A & B, F3A & B are tabulated in Table 2.

The values for the angle of repose were found to be in the range of 27°.12′ to 30°.25′. This indicates good flow property of the powder blend. As the concentration of HPMC K_4M, HPMC $K_{15}M$, HPMC $K_{100}M$ increases, the angle of repose also increase while the flow rate decreases.

Compressibility index ranges between 16.33% and 21.69% indicating that the powder blend has the required flow property for wet granulation. Microscopic examinations of tablets from each formulation batches have showed cylindrical shape (oval) with no cracks.

Table 2: Preformulation studies of Ofloxacin crude drug

Batches	Bulk density (g/cm^2)	Tapped density (g/cm^2)	Compressibility index	Hausner's ratio	Angle of repose (θ)
F1A	0.458	0.589	16.33	1.23	27°.65′
F1B	0.469	0.698	17.12	1.49	28°.63′
F2A	0.502	0.756	18.96	1.23	27°.12′
F2B	0.456	0.603	18.02	1.16	29°.64′
F3A	0.523	0.631	21.69	1.58	29°.89′
F3B	0.536	0.689	20.36	1.25	30°.25′

Hydrodynamically balanced tablets of Ofloxacin (intra-gastric buoyant tablets) were prepared and evaluated to increase its local action and bioavailability. In the present study six formulations with variable concentration of polymer (HPMC) were prepared by wet granulation technique and evaluated for physicochemical properties, buoyancy lag time, total floating time, swelling index and *in-vitro* drug release. The results indicated that on immersion in 0.1N HCl solution at pH 1.2 at 37±0.5°C tablets float immediately and remain buoyant upto 8-12 hrs without disintegration. Floating property of the tablet is governed by both the swelling (hydration) of the polymer when it contacts with the gastric fluid, which in turn results in increase in the bulk volume and the presence of internal voids in the dry centre of the tablet (porosity). These two factors are essential for the tablet to acquire bulk density < 1, so that it remains buoyant on the gastric fluid. Hardness of the tablets was in the range of 3.5 to 5 kg/cm^2. This ensures good handling characteristics of all the batches. % weight loss in the friability test was less than 1% in all the cases, ensuring that the tablets were mechanically stable. All the floating tablets prepared contained the drug within 102±5% of the label claim. All the formulated tablets (F1A to F3B) passed the weight variation test as the % weight variation was within the Pharmacopoeial limits of ±5% of the average weight. The percentage of drug content was found to be 98.27% to 101.20% of Ofloxacin, which was within the acceptable limits. Table 3 shows the results of physicochemical characters of Ofloxacin tablets.

In the present study, the higher degree of swelling and slow drug release was found for tablets of F3B containing 30% HPMC K_{100}M. Thus, the concentration of polymer and ratio of lactose had major influence on swelling process, matrix integrity, as well as on floating capability. Hence from the above results it can be proved that linear relationship exists between swelling process and concentration ratio as shown in Table 4 and Fig. 1.

From the *in-vitro* drug profiles, it was found that drug release rate decreased as the concentration of polymers HPMC K_4M, HPMC K_{15}M and HPMC K_{100}M increases as shown in Table 5 and Fig 2.

Table 3: Physicochemical evaluation data parameters of Ofloxacin tablets formulations

Batches	Average weight of tablets (mg)	Hardness (Kg/cm^2)	Friability (%)	% Drug content	Buoyancy lag Time (sec)	Total floating time (hrs)
F1A	702	3.5	0.532	98.42	5.0	<12
F1B	698	3.5	0.658	99.50	4.5	<12
F2A	696	3.5	0.498	101.20	5.5	<12
F2B	704	4.0	0.456	98.27	5.0	<10
F3A	702	4.5	0.374	98.50	5.5	<10
F3B	700	5.0	0.412	98.98	6.0	<10

Table 4: Degree of swelling of Ofloxacin floating tablet formulations

Time (hrs)	F1A	F1B	F2A	F2B	F3A	F3B
1	78	90	86	95	90	102
2	82	98	103	116	121	138
3	90	119	116	129	144	152
4	112	125	131	156	165	176
5	129	141	156	178	185	192
6	138	156	181	250	221	236
7	156	172	198	248	256	265
8	172	191	232	268	272	294

Fig. 1: Photograph depicting degree of swelling in Ofloxacin floating tablet

Table 5: *In-vitro* dissolution profiles of Ofloxacin floating tablets

S.No.	Time in Hrs	Percentage cumulative drug release					
		F1A	F1B	F2A	F2B	F3A	F3B
1	0	0	0	0	0	0	0
2	0.5	10.69	9.42	12.52	12.01	15.29	14.77
3	1	22.15	17.31	23.02	22.91	25.20	23.93
4	2	32.08	30.04	32.68	32.18	33.60	31.06
5	4	45.82	44.30	43.96	43.69	43.28	42.51
6	6	62.37	61.86	69.15	68.95	59.82	57.53
7	10	83.75	81.97	80.81	80.00	77.14	76.12
8	12	93.40	89.86	86.20	84.30	82.02	77.64
9	24	102.85	101.32	100.20	99.98	99.28	97.25

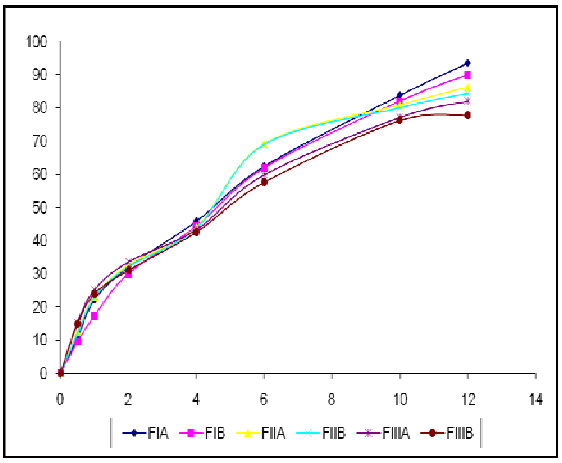

Fig. 2: Cumulative % drug release

X- axis - Time in hours; Y- axis- Percentage cumulative drug release

The percentage of drug release and total floating time was comparatively good in Formulation 1A and Formulation 1B compared with that of other formulations.

CONCLUSION

On the basis of the present study it was concluded that the floating tablets of Ofloxacin can increase the gastric residence time as well as bioavailability and thereby showing increased therapeutic efficacy.

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