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Formulation and Optimization Evaluation of Floating Tablet of Ofloxacin

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ABSTRACT

The objective of this present study is to formulate and evaluate the floating drug delivery system of Ofloxacin prepared by using synthetic polymers. Formulations were prepared by wet granulation technique and sodium bicarbonate, citric acid was incorporated as gas generating agent. Using different polymers of hydroxyl propyl methylcellulose (HPMC) such as, HPMC K100M, Carbopol 940, polyvinyl pyrrolidone (PVP) K30 and HPMC K100M for their gel-forming properties. The compressed Ofloxacin floating tablets were evaluated for physical parameters like Tablet Thickness, Hardness, % Friability, Weight variation, Content uniformity, In vitro buoyancy, Swelling index and In vitro dissolution study. Its bioavailability was reported about 45%-50%. As the concentration of the polymers in the formulations increased the drug release decreased. Hence it was considered suitable candidate for formulation as gastro-retentive floating drug delivery system Floating tablets has been accepted as a process to achieve controlled drug delivery by prolonging the residence time of the dosage form at the site of absorption, thereby improving and enhancing the bioavailability of drug.

Key words: Ofloxacin, Floating drug delivery system, Hydroxyl propyl methyl cellulose, Carbopol 940, PVP K30.

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INTRODUCTION

Gastro retentive dosage forms containing suitable drug candidates which would remain in the stomach and/or upper part of gastrointestinal tract for a prolonged period of time there by maximizing the drug release at desired site within the time before gastroretentive dosage forms left the stomach and upper part of the gastrointestinal tract, has provoked a great deal of increased interest in the formulation of such drugs as floating drug delivery system [1].

Floating systems or hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and 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. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal .Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres [2].

Ofloxacin is a flouroquinolone, broad spectrum antibiotic, rapidly well absorbed from the gastrointestinal tract. Half life of Ofloxacin is 9 hours and is used in the treatment of urinary, respiratory, gastrointestinal, skin and soft tissue infections [3].

MATERIALS AND METHODS

MATERIALS

Ofloxacin, Carbopol 940, HPMC K100M, PVP K30 was purchased from Balaji drug supplier surat, Gujarat, India. All other ingredients were used from my college's laboratory & those were the laboratory grade.

METHODS

Preparation Method of Ofloxacin Floating Tablets

Drug, polymer, sodium bicarbonate and citric acid were weighed and passed through sieve with mesh #40 and were mixed homogeneously in a poly-bag for about 5-10 min. and was taken in a mortar. 5% PVP K30 in isopropyl alcohol was used as granulating agent. The gas generating agent sodium bicarbonate and citric acid was using in ratio 3:1. The wet mass was passed through mesh #14 and dried in hot air oven at 50°C for 30 min. and dried granules were sieved through mesh #16. Finally well formed granules were lubricated with magnesium stearate and talc [3]. For formulations had been prepared by this method. The various formulation variables considered for optimization were shown in the table no.1

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Table No. 1 Formula for preparation of Ofloxacin floating tablet

INGREDIENT,S	F1	F2	F3	F4
Ofloxacin	200	200	200	200
HPMC K100M	170	…..	200	……
Corbopol 940	…..	170	……	200
PVP K30	2.5	2.5	2.5	2.5
Lactose	42.5	42.5	12.5	12.5
Sodium bicarbonate	60	60	60	60
Citric acid	20	20	20	20
Isopropyl alcohol	0.1	0.1	0.1	0.1
Magnesiumstearate	3	3	3	3
Talc	2	2	2	2

EVALUATION OF FLOATING TABLET

Thickness

Thickness of tablets was determined using Vernier caliper. Three tablets from each batch were used, and average values were calculated [4, 5].

Weight variation

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance, and the test was performed according to the official method [4, 5].

Hardness

The resistance of tablets to shipping or breakage, under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of tablet of each formulation was measured by Monsanto hardness tester. The hardness was measured in terms of kg/cm^2 [5].

Friability

Friability is the measure of tablet strength. Roche type friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min., the tablets were weighed and the percentage loss in tablet weight was determined [6].

$$\% \, loss = \frac{Intial\ wt.of\ tablets - Final\ wt.of\ tablets}{Intial\ wt.of\ tablets} \times 100$$

Determination of Swelling Index

The swelling index of tablets was determined in 0.1N HCl (pH 1.2) at room temperature. The swollen weight of the tablet was determined at predefined time intervals over a period of 24 h. The swelling index (SI), expressed as a percentage, and was calculated from the following equation. The percentage weight gain by the tablet was calculated by the formula. [7, 8]

$$Swelling\ \ index\ (\ S.I.\ ) = \{\frac{Wt - Wo}{Wo}\} \times 100$$

Where, S.I. = Swelling index
Wt = Weight of tablet at time t
Wo = Weight of tablet before immersion

***In vitro* buoyancy studies**

The randomly selected tablets from each formulation were kept in a 100ml beaker containing simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time (TFT) [7, 9].

Drug content uniformity*:*

10 tablets were weighed and triturated. The tablet triturate equivalent to 100 mg of the drug was weighed accurately, dissolved in pH 1.2 buffers and diluted to 100 ml with the same. Further dilutions were done suitably to get a concentration of 10mcg/ml with simulated gastric fluid pH 1.2. Absorbance was read at 294nm against the reagent blank, and the concentrations of Ofloxacin in mcg / ml was determined [10, 11].

***In-vitro* dissolution studies**

The *In-vitro* dissolution study was carried out in USP Dissolution Test Apparatus, Type 2 (paddle type). 900ml of simulated gastric fluid pH 1.2 was used as dissolution medium. The temperature of dissolution media was maintained at 37±0.5°C. The paddle rotation speed was kept at 50 rpm. One tablet at a time was weighed and taken for study. 5ml of the sample was withdrawn at every 1-hour interval for 12 hours and the same volume was replaced with pre warmed fresh dissolution media. The sample withdrawn was diluted to suitable volume with simulated gastric fluid and the absorbance was recorded at 294 nm using UV-VIS spectrophotometer [11, 12].

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RESULT AND DISCUSSION

Thickness

The thickness of floating tablets' were measured by Vernier caliper of formulation F1 to F4 and were range between 5.11 to 5.15 mm.

Table No. 2 Evaluation of floating tablets

Formulation	Thickness (mm)	Hardness Kg/cm^2	Weight variation mgs	Friability % loss	Drug content %
F1	5.11±0.04	5.0±0.13	504.24±0.73	0.53±0.31	94.10±0.22
F2	5.15±0.02	4.5±0.26	498.13±0.37	0.65±0.56	95.37±0.12
F3	5.14±0.03	5.5±0.34	500.16±0.29	0.49±0.42	92.18±0.15
F4	5.13±0.02	5.7±0.42	502.23±0.56	0.45±0.82	95.00±0.10

Weight variation

All the formulation tablet F1 to F4 passed the weight variation test as the percent weight variation was within the pharmacopeia limit of 5% of average weight.

Hardness

The hardness of the floating tablet was measured by the Monsanto tester of formulation F1 to F4 and was controlled between 4.5 to 5.7 kg/cm^2 .The standard hardness of the tablet is 4 kg/cm^2.

Friability

The friability of the floating tablet was measured by The Roche Friabilator of formulation F1 to F4 and were controlled between 0.45 to 0.65%. The standard friability of the tablet is below 0.8% according to IP and 1% according to USP.

Drug content uniformility

The percent drug content of formulation F! to F4 was found to be 92.18 to 95.37% of Ofloxacin in which was within the acceptable limit, the standard drug content uniformity 100±10%

In vitro buoyancy studies

On immersion of tablets of different formulations from F1 to F4 in 0.1N HCl solution at 37±5°C, the tablets floated, and remained buoyant without disintegration, the results of the buoyancy lag time (BLT) and total floating time (TFT) were shown in Table. Buoyancy lag time (BLT) and total floating time (TFT) of different formulation were noted. With reference

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to buoyancy studies results it can be concluded that as the amount of HPMC polymers increase, the formulation showed good buoyancy lag time (BLT) and total floating time (TFT). The formulation of F1 to F4 buoyancy lag time (sec.) between 125 to 142 sec. and total floating time (hr) 10 to 12 hr. or more.

Table No. 3 Evaluation of floating tablets

Formulation	Buoyancy lag time(sec.)	Total floating time (hr.)	Swelling index after 6 hr(%)
F1	135	> 12	55.69±0.25
F2	142	>11	60.58±0.32
F3	137	>10	48.12±0.11
F4	125	>12	54.25±0.18

Swelling index study

The Swelling Index for different formulations was shown in table. formulation F2 shows max swelling index comparing to other formulation after 6 hrs. while formulation F3 shows less swelling index as concentration of Carbopol 940 increases may be due to high viscosity and hydrophilic nature**.**

***In vitro* dissolution study**

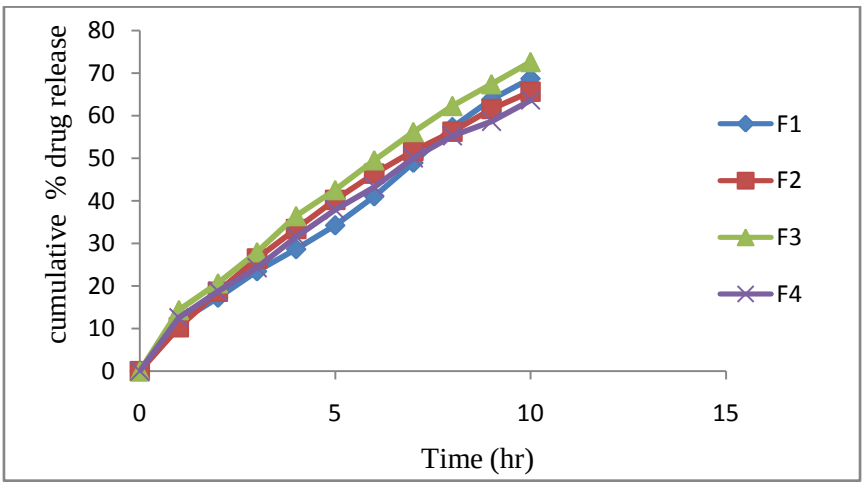

Figure No.1 % cumulative drug release of Ofloxacin floating tablet

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Table no. 4 *In vitro* dissolution floating tablet of Ofloxacin

Time (hr)	F1	F2	F3	F4
1	11.5±0.50	10.27±0.58	14.35±0.063	12.56±0.12
2	17.23±0.36	18.63±0.65	20.65±0.64	18.77±0.62
3	23.45±0.60	26.45±0.74	27.96±0.21	24.3±0.25
4	28.65±0.23	33.36±0.14	36.45±0.22	31.56±0.34
5	34.25±0.56	40.23±0.85	42.56±0.62	37.89±0.57
6	41.06±0.38	46.38±0.12	49.58±0.52	43.25±0.45
7	48.96±0.88	51.74±0.42	56.21±0.11	50.08±0.23
8	57.34±0.28	56.23±0.16	62.33±0.64	55.29±0.11
9	63.84±0.65	61.58±0.25	67.45±0.31	58.67±0.87
10	68.75±0.75	65.63±92	72.66±0.425	63.65±0.21

In vitro drug release studies exhibited a decrease drug release with an increase in polymer concentration which may be due to increase in viscosity of the gel as well as the gel layer with longer diffusion path. Formulations containing high viscosity grade HPMC showed slower drug release compared to formulations containing low viscosity polymers. There was no considerable effect of gas generating agents on the release of the drug.
Drug release profile of batches of Ofloxacin floating tablet F1-F4 was found 68.75%, 65.63, 72.66, 63.65 respectively. F2 formulation of Ofloxacin floating tablet shows highest release of drug among the all batches.

CONCLUSION

The objective of the study was to formulate and evaluate Ofloxacin floating tablets. The tablets were formulated using wet granulation method using varying quantities of the excipients. The formulated tablets were tested for the parameters such as weight variation, hardness, thickness, friability and drug content and were found to be within the limits. The floating lag time and the floating duration of the tablets are the most important parameters. Hence, diffusion controlled Ofloxacin gastro retentive tablets were formulated and evaluated and formulation F2 was concluded as the best formulation for the manufacture of Ofloxacin gastro retentive tablets which can assure 100% bioavailability.

Floating drug delivery tablets of Ofloxacin were developed to enhance gastric residence time and there by eradication of Helicobacter pylori infection. The optimized formula F2 showed better sustained drug release and which also had good floating properties.

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