Formulation and Evaluation of Ofloxacin Loaded Floating Microballons

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ABSTRACT

The present study involves preparation and evaluation of floating microballoons of Ofloxacin for improving the bioavailability by prolongation of gastric residence time in GIT. Ofloxacin, a sparingly water-soluble drug, was selected and microballoons were prepared by emulsion solvent diffusion method using Eudragit RS-100, CAP as a polymer, in ethyl alcohol and dichloromethane organic solvent system. The formation of a sphere and hollow within the sphere was confirmed through SEM studies. The percentage of drug entrapment and recovery was found to be 75- 80%. The micromeritic properties indicated better flowability and packability of the spheres. The Buoyancy test showed good floatability of Ofloxacin microballoons in the simulated gastric fluid for more than 24 h. In vitro dissolution profile showed prolonged release of drug from the formulations. Thus, microballoons of Ofloxacin with acrylic polymers prepared by emulsion solvent diffusion method show to be an ideal novel floating dosage form that is adaptable to any intragastric condition for controlled drug delivery and enhanced bioavailability.

Keyword- *Floating Microballons, ofloxacin**,** controlled drug delivery*

INTRODUCTION-

The importance of controlled drug delivery systems that release drug over an extended period of time has long been recognized in the pharmaceutical field. Application of such controlled release technology to oral drug delivery system however has been limited because the actual time for effective drug delivery is restricted by gastrointestinal transit time. Gastric retention devices are designed to prolong the gastric residence time of oral controlled release dosage forms. They thus result in increased contact time for drugs that act locally,Increased absorption of drugs that have absorption windows in upper part of gastrointestinal tract (GIT), and better absorption for drugs less soluble in the intestinal fluid Several approaches have been developed to achieve extended gastric residence time of the oral drug delivery systems such as bio adhesive system, swelling and expanding systems, floating systems and delayed gastric emptying devices. Amongst these methods, floating drug delivery system is preferred one that offers a simple and practical approach to achieve Gastroretention.

Floating dosage forms have a bulk density lower than that of gastric fluids and therefore remain buoyant on the stomach contents to prolong the gastric retention time

Ofloxacin is widely used fluoroquinolone and has been reported as one among the five most frequently prescribed antibiotics in Nepal [8]. It is a broad spectrum antibiotic effective against wide range of Gram-negative and Gram-positive microorganisms. Biological half-life of this drug is from 5 to 6 h due to which frequent administration is required. To avoid the drawbacks of frequent administrations such as plasma level fluctuations and patient non-compliance it is desirable to have a controlled release dosage form of ofloxacin. It has been reported that bioavailability of ofloxacin is strongly dependent on the local physiology of GIT. It is readily soluble in the acidic environment of the stomach and thus is preferentially absorbed from the upper part of GIT.In the alkaline environment of intestine, precipitation of the drug occurs decreasing its absorption. This study was conducted with an aim to develop floating gastroprotective microballoons formulation incorporating 400 mg ofloxacin with polymer and other except in to the release of the drug in stomach and upper part of GIT in a controlled manner. Since ofloxacin has site-specific absorption from these regions, gastroretention of the dosage form will improve its oral bioavailability.

MATERIAL AND METHOD-

MATERIAL: The gift sample of Ofloxacin was obtained from Yarrow Chem Products, Mumbai. CAP and polyvinyl alcohol, Eudragit S100 and Eudragit RS100 and other reagents and solvents used were of analytical grade provided by Kailash Institute of Pharmacy & Management GIDA, Gorakhpur.

METHOD:
Microballoons were prepared by the emulsion solvent diffusion method reported by Awasthi et al [13]. Briefly, Ofloxacin and Eudragit S100 or in a ratio of 1:2.5 and CAP were dissolved in a mixture of dichloromethane, ethanol and isopropyl alcohol (7:6:2) at room temperature (15 ml). This solution was introduced to an aqueous solution of polyvinyl alcohol (0.5 or 1% % w/v, 200 ml) at 40^{o}C, forming oil in water type emulsion. The resultant solution was stirred, employing a mechanical stirrer at 300 rpm. Finally dispersed droplets were solidified in the aqueous phase via diffusion of the solvent. Dichloromethane, evaporated from the solidified droplets was removed by drying in hot air oven at 40^{o}C overnight, leaving hollow structure inside the microballoons. After agitating the system for 1 h at 300 rpm, the resulting polymeric particulate systems were filtered and dried overnight at 40^{o}C in hot air oven to produce hollow microballoons.

CHARACTERIZATIOIN OF THE OPTIMIZED MICROBALLOON- [15-20].

1. Morphology-
The surface morphology of microballoons selected on the basis of optical microscopy was visualized by scanning electron microscopy. The samples for SEM were prepared by lightly sprinkling the microballoons powder on a double adhesive tape which s tuck to an aluminum stub. The stubs were then coated with gold to a thickness of about 300oA using a sputter coater. These samples were than randomly scanned and photomicrographs were taken which are shown in Fig.

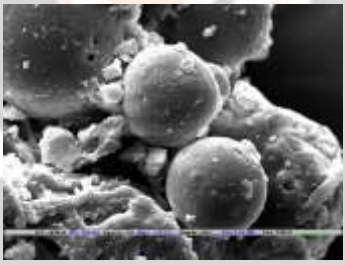

Figure 1: SEM of floating microballoons (2.39 K X)

2.Particle size-
The size of microballoons of each formulation was determined using a microscope fitted with an ocular micrometer, and stage micrometer and average particle size was determined The outcomes of particle size exhibited that on increasing the polymer ration , it increases the particle size of microballoons.

3. Percent yield of microballoons
The prepared microballoons were collected and weighed. The weight of microballoons was divided by the total weight of all the non-volatile components used for the preparation of the microballoons.
% yield = weight of microballoons collected / wt. of all non-volatile components used for the preparation x 100
4. Percentage drug loading efficiency: The prepared microballoons were digested in minimum quantity of ethanol (95%), and then diluted with acetate buffer (pH 4.6) up to 10 ml. The digested homogenate was centrifuged at 3000 rpm for 3 minutes and the supernatant after suitable dilution was assayed for ofloxacin spectrophotometrically.
The percentage drug entrapment is calculated from the equation given below.
% Drug entrapped = Amount of drug in the microballoons (actual content)/ Amount of drug used in formulation (theoretical content) x 100

5. Determination of physical parameters: Prepared microballoons were evaluated for their physical properties like density, porosity and angle of repose.

6. In vitro floating behavior (In-vitro (%) buoyancy)-

Microballoons (100 mg) were dispersed in USP dissolution apparatus containing simulated gastric fluid (SGF 900 ml) containing Tween 20 (0.02% w/v). It was agitated by paddle at 100 rpm for 12 h. After predetermined time interval, the layer of floating particles is separated from settled particle. Both fractions of particles were dried in vacuum desiccators. Both the fractions of microballoons were weighed and buoyancy was determined by using the formula.

Percent buoyancy (%) = Qf / (Qf + Qs) × 100

Where Wf and WS are the weights of the floating and sinking microballoons, respectively.
Percent buoyancy-The buoyancy percentage for all batches almost above 50% which was study for 12 h.

7.In-vitro drug release study-
The drug release study was carried out in USP paddle type dissolution apparatus (elctrolab). Microballoons containing drug equivalent to 100 mg were gently spread over the surface of 900 ml of dissolution media (SGF, pH 1.2 and Ph6.8). The speed of rotation was maintained at 100 rpm and the temperature of dissolution medium was thermostatically controlled at37±0.5. ^{0}C The samples were withdrawn at suitable time interval from the dissolution apparatus. The initial volume of fluid was maintained by adding fresh dissolution fluid after each withdrawal. The samples withdrawn were assayed spectrophotometrically using UV–visible spectrophotometer (Shimadzu 1800, Japan). In-vitro drug release studies was done by simulated gastric fluid pH 1.2 and Ph6.8 for 24h. The in-vitro release profile was biphasic with an initial burst release (11.08±0.92%) upto 1.0 h which may be attributed to surface associated drug, followed by a slower release phase as the entrapped drug slowly diffused into the release medium. Percentage of the drug released up to 24 h was 81.04±0.62. There was sustained release of drug at a constant rate.

Table no1 –Formulation of microballoons of ofloxacin floating drug delivery system

Ingredients (mg)	OCF1	OCF2	OCF3	OCF4	OCF5	OCF6
Ofloxacin	1	1	1	1	1	1
Eudragit RS 100	2	2	2	2.5	2.5	2.5
CAP	1	2	2.5	1	2	2.5
Ethanol	7	7	7	7	7	7
Isopropyl alcohol	6	6	6	6	6	6
Dichloromethane	2	2	2	2	2	2
Polyvinyl alcohol	0.5	0.5	0.5	1	1	1

Table-2. Particle size-

S. NO	OCF1	OCF2	OCF3	OCF4	OCF5
Particle size (μm)a	75.63 ± 1.05	84.10 ± 3.10	101 ± 2.85	85.96± 2.12	98.32 ± 1.50

Each value indicates the mean ± SD (n = 3).

Table 3: Effect of polymer: polymer ratio (CAP: Eudragit RS 100)

S. NO	**FORMULATION CODE**	**EUDREGIT RS100: CAP**	**%YIELD**
1	OCF1	2:1	90.1
2	OCF2	2.2	88.2
3	OCF3	2.25	89.2
4	OCF4	2:1	86.3
5	OCF5	2:2	87.2
6	OCF5	2:2.5	83.4

Table 3: Density and porosity of different formulations

S.NO	FORMULATION CODE	DENSITY	% POROSITY	ANGLE OF REPOSE (0)
1	OCF1	0.718	46.7	27.4
2	OCF2	0.801	54.8	30.3
3	OCF3	0.786	55.3	31.8
4	OCF4	0.724	49.8	29.7
5	OCF5	0.712	47.7	28.4
6	OCF6	0.741	47.7	27.4

Table 4: invitro release profile different formulations (pH 1.2)

S. No.	/Time Formulation code	% Cumulative drug release profile (hour)							
		1	2	3	4	5	6	7	24
1	OCF1	7.2	14.0	20.3	26.6	32.2	37.2	41.3	89.6
2	OCF2	6.1	8.2	9.8	10.3	11.1	11.6	12.2	21.3
3	OCF3	11.6	25.9	37.8	46.2	54.3	61.3	64.4	93.2
4	OCF4	7.6	16.9	25.7	36.8	43.9	51.4	54.8	91.3
5	OCF5	8.0	20.2	32.9	41.3	48.7	56.2	60.1	92.3
6	OCF6	7.4	15.8	23.2	30.1	37.3	42.6	46.4	90.3
7	OCF7	6.8	13.6	18.4	23.1	29.0	32.1	36.2	76.9
8	OCF8	6.6	11.8	14.9	20.1	22.8	26.0	29.7	56.2

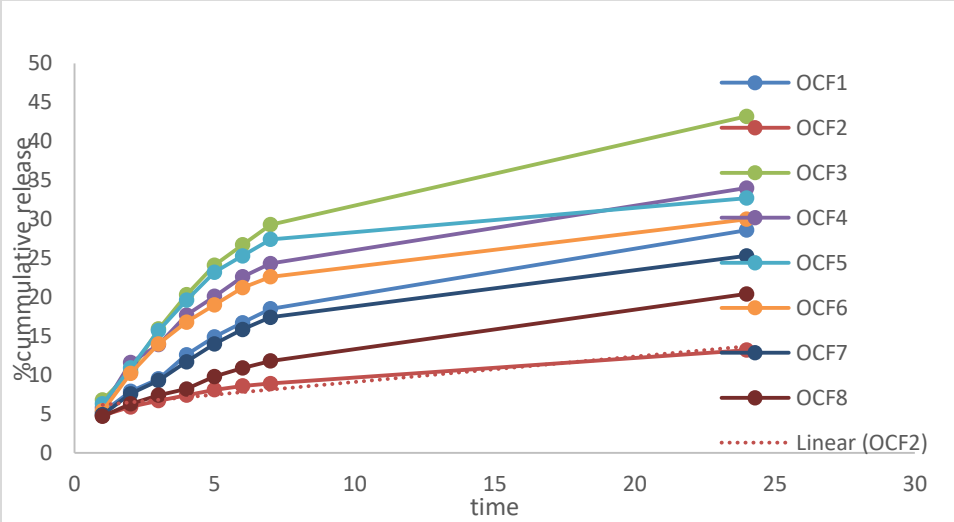

Fig. 2. In vitro drug release profile of Ofloxacin from optimized microballoons in SGF (pH 1.2)

Table 5: invitro release profile different formulations (pH 6.8)

S. No.	/Time Formulation code	% Cumulative drug release profile (hour)							
		1	**2**	**3**	**4**	**5**	**6**	**7**	**24**
1	OCF1	5.2	7.9	9.5	12.6	14.9	16.7	18.5	28.6
2	OCF2	4.8	5.9	6.7	7.4	8.1	8.6	8.9	13.2
3	OCF3	6.8	10.4	15.9	20.3	24.1	26.7	29.3	43.2
4	OCF4	5.8	11.6	13.9	17.7	20.1	22.6	24.3	34
5	OCF5	6.3	10.9	15.7	19.6	23.2	25.3	27.4	36.9
6	OCF6	5.4	10.2	14	16.8	19	21.2	22.6	32.7
7	OCF7	4.9	7.6	9.3	11.7	14	15.8	17.4	25.3
8	OCF8	4.7	6.3	7.4	8.2	9.8	10.9	11.8	20.4

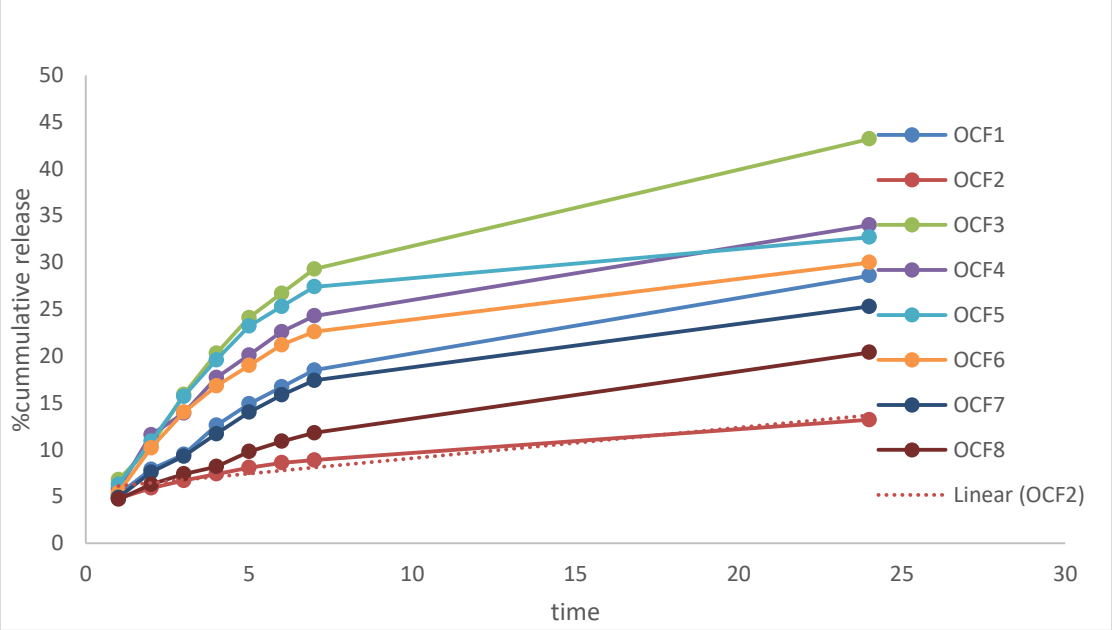

Fig. 3In vitro drug release profile of Ofloxacin from optimized microballoons in SGF (pH 6.8)

Conclusion

In-vitro data obtained for microballoons of ofloxacin showed excellent buoyancy. Microballoons of ofloxacin floated in SGF for a prolonged period of time and sustained drug release from the beads over a period of 24 h. The in-vitro floating efficiency of beads was satisfactory; beads were retained in rat stomach for extended period. Thus, the microballoons may prove to be promising candidate for obtaining stomach specific drug delivery.It was observed that the release of drug from formulation (OCF1 to OCF8) had been nearly complete and since the in vitro floating test suggested a fair rate of buoyancy, it can be concluded that the designed preparations would release the drug in the upper GI tract. The release in mixed phosphate buffer (pH 6.8) was due to the porous nature of Eudragit RS 100 and increase in the pores of floating microballoons due to swelling of Eudragit L 100, but the release was less as compared to the release in SGF which may be due to less solubility of the drug at pH 6.8. The drug release in acetate buffer (pH 4.6) was more or less similar to solution mediums; drug release in these mediums was maximum due to diffusion through the pores.

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