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FORMULATION AND EVALUATION OF OFLOXACIN FLOATING TABLETS

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ABSTRACT

Ofloxacin acts intracellularly by inhibiting DNA gyrase. DNA gyrase is an essential bacterial enzyme that is a critical catalyst in the replication, transcription, deactivation, and repair of bacterial DNA. In this study Floating tablets of Ofloxacin was formulated with HPMC to retain the tablet dosage form in the stomach and to release the drug in a controlled manner for increasing the oral bioavailability of the Ofloxacin. In the present work direct compression method were used to prepare floating matrix tablets of Ofloxacin. The tablets were found to be floating immediately upon contact with the release medium showing no lag times in floating behaviour because of the low density material. Extended floating times are achieved due to the air entrapped within the drug particles.

KEYWORDS

Ofloxacin, HPMC, Floating Tablets, DNA Gyrase and bioavailability.

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INTRODUCTION[1,2]

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation, etc. From immediate release to site specific delivery, oral dosage forms have really progressed. However, it is a well-accepted fact that it is difficult to predict the real *in vivo* time of release with solid, oral controlled release dosage forms. Thus, drug absorption in the gastrointestinal (GI) tract may be very short and highly variable in certain circumstances.

Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying, leading to incomplete drug release, non-uniform absorption profiles and shorter residence time of the dosage form in the stomach. This leads to incomplete absorption of drugs having absorption window especially in the upper part of the small intestine, as once the drug passes down the absorption site, the remaining quantity goes unabsorbed. The most important parameters affecting gastric emptying and, hence the gastric retention time of oral dosage forms include, Density, size, shape of the device and concomitant ingestion of food and its nature, caloric content, and frequency of intake and simultaneous administration of drugs with impact on gastrointestinal transit time, eg: drugs acting as anticholinergic agents (eg: atropine, propantheline), opiates (eg: codeine) and prokinetic agents (eg: metoclopramide, cisapride). To overcome these limitations, various approaches have been proposed to increase gastric residence of drug delivery systems in the upper part of the GIT. Dosage forms that can be retained in the stomach are called gastro retentive drug delivery systems (GRDDS). GRDDS can improve the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a prolonged period of time before it reaches its absorption site, thus ensuring its optimal bioavailability.

MATERIALS AND METHOD[3,4]

MATERIALS

Ofloxacin, Hydroxy propyl methyl cellulose (K4M and E15), Carbapol 940, Propylcellulose, Chitosan, Magnesium state and Talc.

METHOD

The Ofloxacin floating tablets were prepared by using the HPMC K_4M, HPMC $K_{15}M$ and Carbopol 940 as polymers in different ratios based on the give formula by direct compression method. All the ingredients mixed thoroughly and passed through sieve no.20 (Table No.1).

EVALUATION PARAMETERS

Pre-Compression Studies[5,6]

Precompression parameters like Bulk density, Tapped density, True density, Angle of Repose, Compressibility index and Hausner's Ratio are performed and the results were tabulated in the Table No.2.

Bulk Density

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve#20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. It is expressed in g/ml and is given by

$$D_b = M/Vb$$

Where,

M is the mass of powder

Vb is the bulk volume of the powder.

Tapped Density

It is the ratio of the total mass powder to the tapped volume of the powder. It was determined by placing a graduated cylinder, containing a known mass of drug-excipients blend. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10cm at 2 second intervals. The tapping was continued until no further change in volume was noted.

$$D_t = M/Vt$$

Where,

M is the mass of powder

Vt is the tapped volume of the powder.

Angle of Repose

It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. The angle of repose was determined by the funnel method suggested by Newman. Angle of repose is determined by the following formula.

$$\text{Tan } \theta = h/r$$

Therefore $\theta = \text{Tan}^{-1} h/r$

Where,

θ = Angle of repose

h = height of the cone

r = Radius of the cone base.

Compressibility Index

The compressibility index has been proposed as an indirect measure of bulk density, size, shape, surface area, moisture content and cohesiveness of materials because all of these can influence the observed compressibility index.

Carr's compressibility index (%) = $[(D_t-D_b)$ X100]/ D_t

Where,

D_t is the tapped density

D_b is the bulk density

Hauser's Ratio

Hausner's ratio is an indirect index of the ease of powder flow. It is calculated by the following formula.

Hausner's ratio = D_t/D_b

Where, Dt is the tapped density,

Db is the bulk density.

POST COMPRESSION STUDIES

Evaluation of Ofloxacin Floating Tablets

Weight Variation, Thickness, Hardness Test, Friability Test, Assay and *In-Vitro* Release Study.

The floating tablets are evaluated by the tests and the results are tabulated in the Table No.3.

Tablet Thickness Test

Randomly 10 tablets were taken from each formulation trial batch and their thickness was measured using a Venire calipers.

Weight Variation Test

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. The total weight of 20 tablets from each formulation was determined and the average was calculated. The individual weights of the tablets were also determined accurately and the weight variation was calculated.

Measurement of Tablet Hardness

The hardness of tablet is an indication of its strength. The force is measured in kg and the hardness of about 3-5 kg/cm2 is considered to be satisfactory for uncoated tablets. Hardness of 10 tablets from each formulation was determined by Monsanto hardness tester.

Friability Test

It is measured of mechanical strength of tablets. Roche Friabilator is used to determine the friability by following procedure. Twenty tablets were weighed and placed in Roche Friabilator where the tablets were exposed to rolling and repeated shocks resulting from free falls within the apparatus. After 100 revolutions, tablets are removed, dedusted and weighed again. The friability was determined as the percentage loss in weight of the tablets.

% Friability = (loss in weight / Initial weight) X 100

***In vitro* Dissolution Studies**

Apparatus (Basket)	: USP Apparatus 1
Medium	: Simulated gastric fluid
Volume	: 900 ml
RPM	: 50 RPM
Temperature	: 37°C ± 0.5°C
Sampling Interval	: $1^{st,}$ 2^{nd}, 4^{th}, 6^{th}, 8^{th}, 10^{th} and 12^{th} hour.

Determination of Floating Parameter

a) *In vitro* Buoyancy Test

b) Swelling Study.

RESULTS AND DISCUSSIONS

Evaluation of Micromeritic Properties of Prepared Tablet Mixture

The physical properties like bulk density, Tap density, Carr's Compressibility Index and Hausner's ratio are given in the following Table No.2.

DISCUSSION

In the present study, an attempt has been made to formulate and evaluate floating tablets of Ofloxacin by wet granulation method; employing swellable polymers like hydroxy propyl methyl cellulose (HPMC K_{100} LV, HPMC 50SH60), Carbopol 940p, HPC and Chitosan are taken along with other Excipients nine formulations are prepared. The formulation is subjected to both pre and post formulation studies.

Hardness and Friability

The hardness of the tablet formulations was found to be in the range of 4.5 to 5.5 kg/cm^2. The friability

values were found to be in the range of 0.341 to 0.541 %.

Uniformity of Weight

All the prepared tablets of Ofloxacin hydrochloride were evaluated for weight variation. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed IP limits of ±5%.

Uniformity of Drug Content

The low values of standard deviation indicate uniform drug content within the tablets. The percent drug content of all the tablets was found to be in the range of 99.43 to 100.43 percent (which was within the acceptable limits of ±5%.

***In vitro* Dissolution Study**

In vitro dissolution studies were performed in buffers 0.1N HCL on the above promising formulation.

Buoyancy lag Time

It was observed 25 to 62 seconds.

Total Floating Time (hrs)

It was observed upto 16hours.

Table No.1: Formula for Development of Ofloxacin Floating Tablets

S.No	Name of Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Ofloxacin	300	300	300	300	300	300	300	300	300
2	HPMC K4M	100	80	60	-	-	-	60	-	60
3	HPMC 50 SH 60	-	-	-	100	80	60	-	60	60
4	Carbopol 940p	30	30	30	30	30	30	100	80	60
5	Lactose	62	82	102	62	82	102	32	52	12
6	Mg. Stearate	5	5	5	5	5	5	5	5	5
7	Talc	3	3	3	3	3	3	3	3	3
Total Tablet Weight		500	500	500	500	500	500	500	500	500

Table No.2: Pre-Compression Parameters of Ofloxacin

S.No	Formulation Code	Angle of Repose (θ)	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Carr's index (%)	Hausner's Ratio (H_R)
1	OFT1	25.73±0.12	0.472±0.01	0.509±0.02	7.27±0.12	1.079±0.12
2	OFT2	26.83±0.45	0.374±0.02	0.398±0.06	6.03±0.53	1.064±0.07
3	OFT3	24.69±0.53	0.398±0.07	0.425±0.05	6.26±0.41	1.066±0.05
4	OFT4	25.14±0.76	0.404±0.02	0.432±0.06	6.48±0.12	1.069±0.02
5	OFT5	27.7±1.51	0.472±0.03	0.509±0.05	7.27±0.51	1.079±0.07
6	OFT6	25.94±0.21	0.447±0.06	0.481±0.02	7.07±0.53	1.075±0.12
7	OFT7	26.42±0.35	0.432±0.06	0.463±0.05	6.71±0.41	1.072±0.05
8	OFT8	24.82±0.41	0.447±0.03	0.472±0.05	5.29±0.51	1.056±0.05
9	OFT9	25.43±0.67	0.417±0.02	0.455±0.06	9.17±0.12	1.089±0.02
10	OFT10	24.64±0.36	0.421±0.03	0.463±0.05	9.07±0.55	1.09±0.05
11	OFT11	25.70±0.67	0.418±0.04	0.460±0.02	9.13±0.12	1.10±0.07
12	OFT12	24.87±0.46	0.425±0.05	0.466±0.05	8.79±0.58	1.09±0.12
13	OFT13	26.34±0.36	0.431±0.01	0.472±0.06	8.68±0.41	1.09±0.05
15	OFT14	27.51±0.37	0.438±0.02	0.487±0.02	10.06±0.12	1.11±0.02
16	OFT15	27.14±0.59	0.440±0.04	0.480±0.05	8.33±0.53	1.09±0.05

Table No.3: Physical Parameters of Ofloxacin Floating Tablets

S.No	Formulation code	Average weight of tablets (mg)	Hardness (Kg/cm2)	Friability (%)	Diameter of the tablet (mm)	Buoyancy lag Time (sec)	Total floating Time (hrs)
1	OFT1	504	4.5	0.541	11	30	<10
2	OFT2	501	4.3	0.231	11	38	<12
3	OFT3	503	4.5	0.54	11	49	<10
4	OFT4	498	5.1	0.341	11	45	<12
5	OFT5	501	5.5	0.369	11	30	<10
6	OFT6	503	4.5	0.541	11	25	<10
7	OFT7	504	4.6	0.543	11	31	<10
8	OFT8	501	4.7	0.440	11	36	<12
9	OFT9	502	5.1	0.387	11	35	<10
10	OFT10	498	5.5	0.489	11	44	<14
11	OFT11	497	5.1	0.512	11	38	<16
12	OFT12	503	5.3	0.435	11	39	<14
13	OFT13	499	5.4	0.511	11	62	<12
14	OFT14	501	4.9	0.412	11	44	<15
15	OFT15	496	4.8	0.589	11	40	<16

Table No.4: *Invitro* dissolution of Ofloxacin floating Tablets (OFT1 to OFT3) employing HPMC K4M

S.No	Sampling time (hr)	Cumulative % Drug Release (mean ± SD) (n=3)		
		OFT1	OFT2	OFT3
1	0	0.000	0.000	0.000
2	1	48.58±0.53	96.55±0.23	61.64±0.66
3	2	80.63±0.34	96.55±0.23	70.83±0.23
4	4	85.83±0.76	96.55±0.23	73.99±0.25
5	6	86.24±0.48	96.55±0.23	95.22±0.55
6	8	86.24±0.76	96.55±0.23	95.43±0.23
7	10	86.63±0.76	96.55±0.23	95.53±0.23
8	12	86.63±0.76	96.55±0.23	95.53±0.23

Table No.5: *Invitro* dissolution of Ofloxacin floating Tablets (OFT4 to OFT6) employing HPMC E15

S.No	Sampling time (hr)	Cumulative % Drug Release (mean ± SD) (n=3)		
		OFT4	OFT5	OFT6
1	0	0.000	0.000	0.000
2	1	16.43±0.53	22.67±0.23	22.25±0.66
3	2	26.53±0.34	36.13±0.23	30.92±0.23
4	4	33.07±0.76	45.82±0.23	40.52±0.25
5	6	49.80±0.48	67.36±0.23	63.07±0.55
6	8	64.20±0.76	78.31±0.23	75.93±0.23
7	10	82.87±0.76	83.79±0.23	85.83±0.23
8	12	86.63±0.76	92.66±0.23	95.4±0.23

Table No.6: *Invitro* dissolution of Ofloxacin floating Tablets (OFT7 to OFT9) employing HPMC K4 M and HPMC E15

S.No	Sampling time (hr)	Cumulative % Drug Release (mean ± SD) (n=4)		
		OFT7	OFT8	OFT9
1	0	0.000	0.000	0.000
2	1	23.57±0.53	20.71±0.23	21.3±0.66
3	2	34.9±0.34	33.79±0.23	32.4±0.23
4	4	42.15±0.76	45.82±0.23	40.12±0.25
5	6	63.79±0.48	60.73±0.23	63.02±0.55
6	8	78.59±0.76	73.48±0.23	75.1±0.23
7	10	80.32±0.76	76.04±0.23	86.4±0.23
8	12	83.69±0.76	77.87±0.23	95.01±0.23

Table No.7: *Invitro* dissolution of Ofloxacin floating Tablets (OFT10 to OFT12) employing HPC

S.No	Sampling time (hr)	Cumulative % Drug Release (mean ± SD) (n=4)		
		OFT10	OFT11	OFT12
1	0	0.000	0.000	0.000
2	1	3.5±0.53	20.06±0.23	4.7±0.66
3	2	7.8±0.34	32.41±0.23	8.3±0.23
4	4	10.8±0.76	40.32±0.23	14.1±0.25
5	6	18.2±0.48	63.02±0.23	20.1±0.55
6	8	27.2±0.76	66.06±0.23	35.6±0.23
7	10	34.2±0.76	76.67±0.23	42.4±0.23
8	12	57.5±0.76	91.23±0.23	62.1±0.23

Table No.8: *Invitro* dissolution of Ofloxacin floating Tablets (OFT13 to OFT15) employing Chitosan

S.No	Sampling time(hr)	Cumulative % Drug Release (mean ± SD) (n=4)		
		OFT13	OFT14	OFT15
1	0	0.000	0.000	0.000
2	1	4.7±0.53	21.3±0.23	22.25±0.66
3	2	8.3±0.34	35.3±0.23	31.04±0.23
4	4	14.1±0.76	42.2±0.23	40.73±0.25
5	6	20.1±0.48	53.5±0.23	55.41±0.55
6	8	35.6±0.76	63.2±0.23	67.57±0.23
7	10	42.4±0.76	74.4±0.23	84.36±0.23
8	12	62.1±0.76	88.4±0.23	96.07±0.23

Table No.9: *Invitro* dissolution of Ofloxacin floating Tablets OFT12 employing HPC

S.No	Sampling time (hr)	Cumulative % drug release
1	1	23.2±0.73
2	2	35.03±0.31
3	4	42.37±0.67
4	6	52.03±0.19
5	8	63.97±0.76
6	10	79.24±0.85
7	12	99.1±0.46

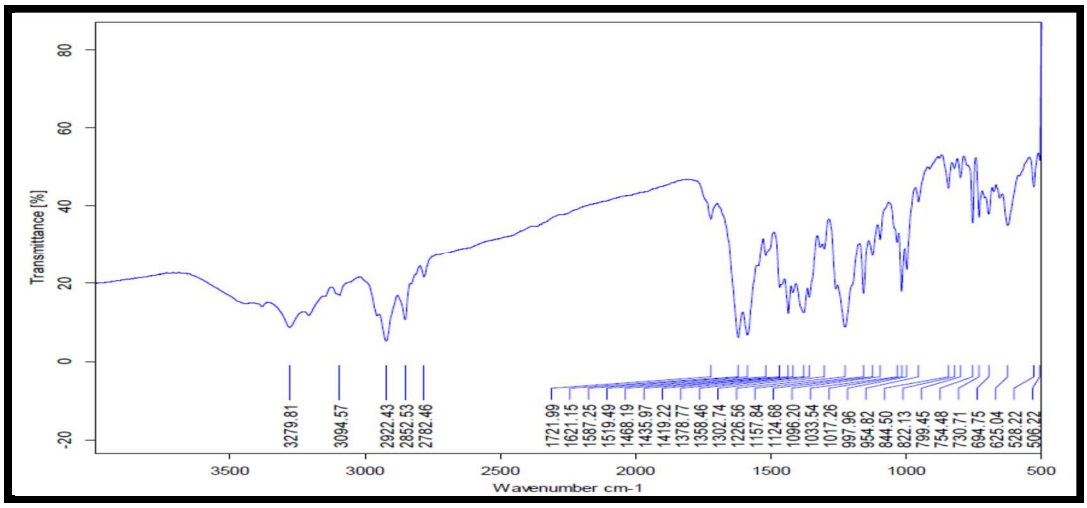

Figure No.1: FT-IR Spectrum of Ofloxacin Pure Drug

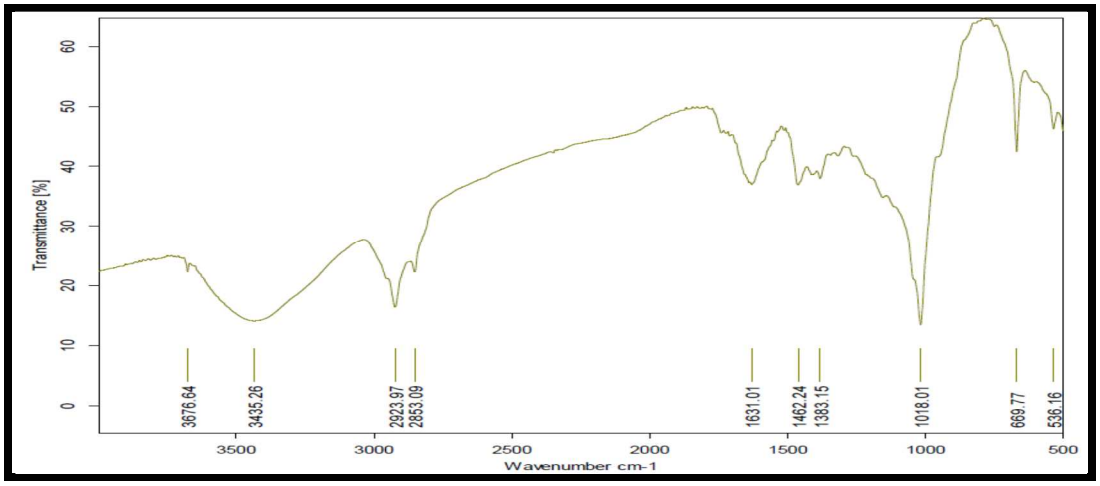

Figure No.2: FT-IR Spectrum of Ofloxacin Drug and Mixture of Excipients

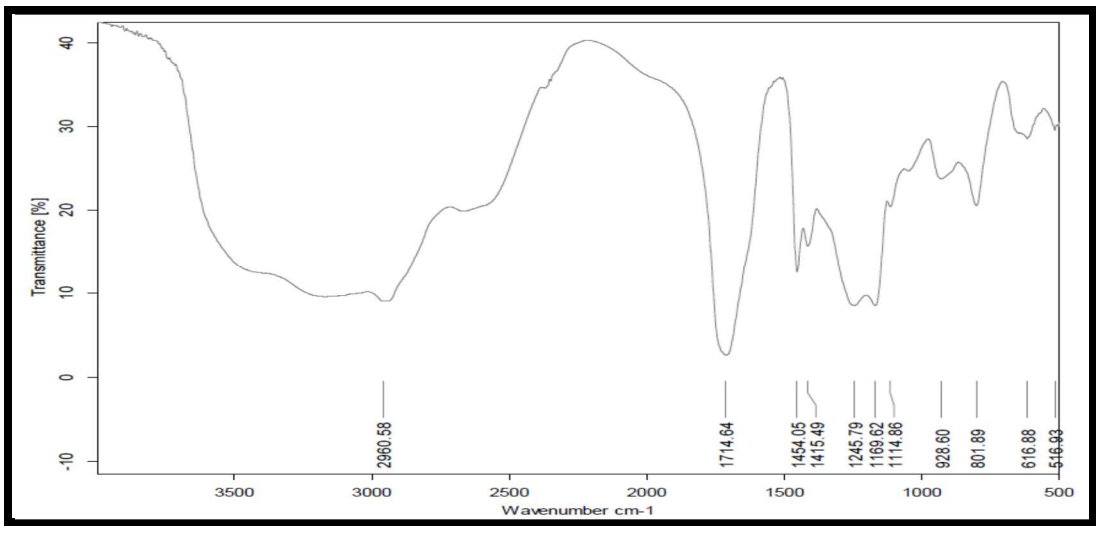

Figure No.3: FT-IR Spectrum of Ofloxacin Formulated Tablet

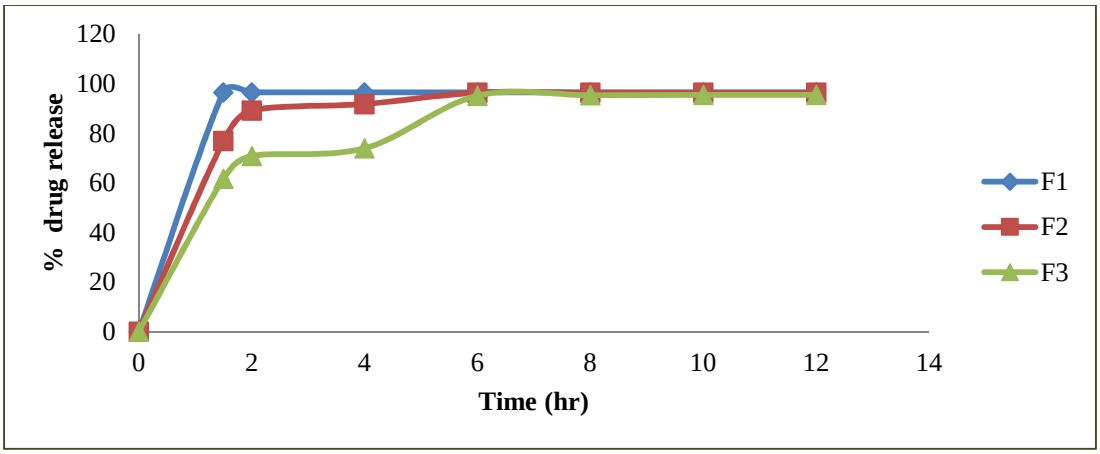

Figure No.4: *Invitro* dissolution of Ofloxacin floating Tablets (OFT1 to OFT3) employing HPMC K4M

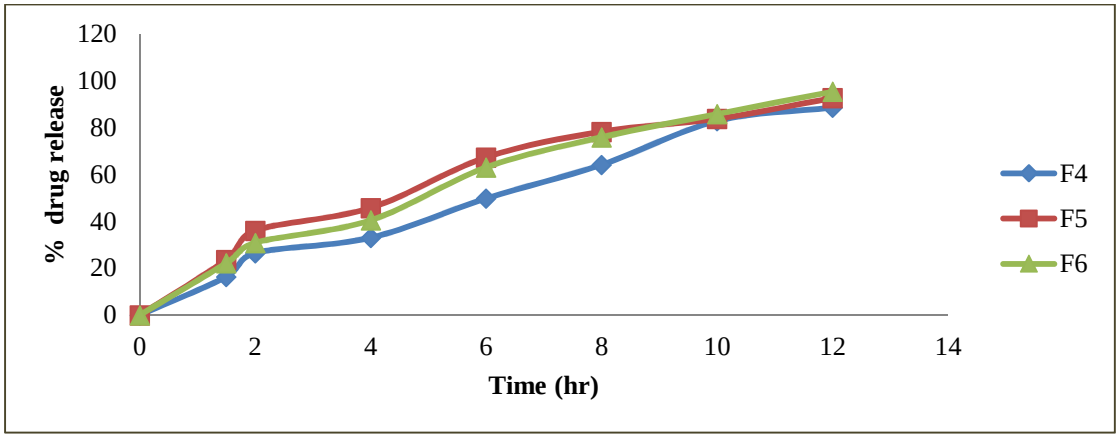

Figure No.5: *Invitro* dissolution of Ofloxacin floating Tablets (OFT4 to OFT6) employing HPMC E15

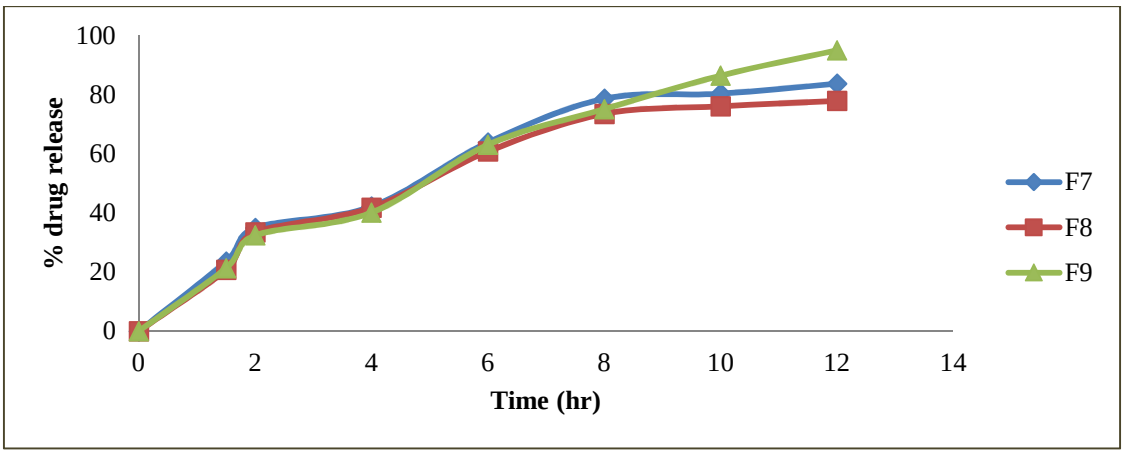

Figure No.6: *Invitro* dissolution of Ofloxacin floating Tablets (OFT7 to OFT9) employing HPMC K4 M and HPMC E15

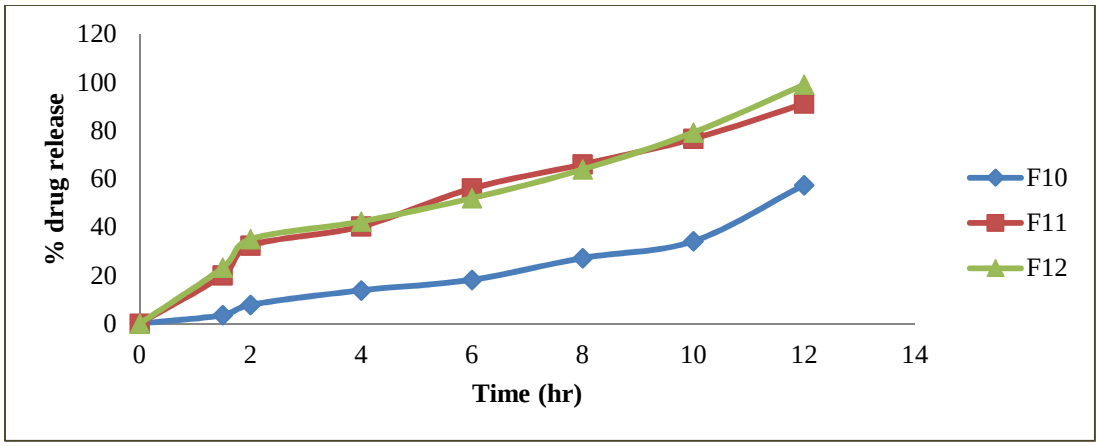

Figure No.7: *Invitro* dissolution of Ofloxacin floating Tablets

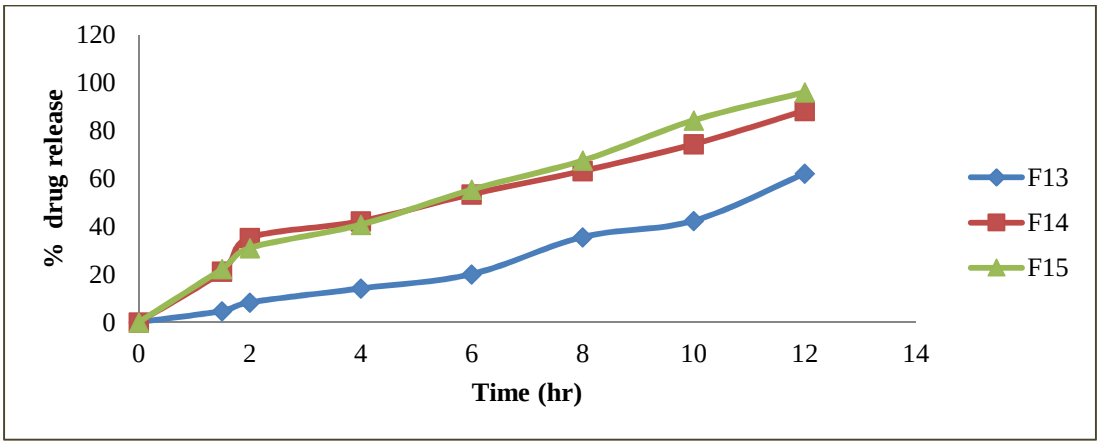

Figure No.8: *Invitro* dissolution of Ofloxacin floating Tablets (OFT13 to OFT15) employing Chitosan

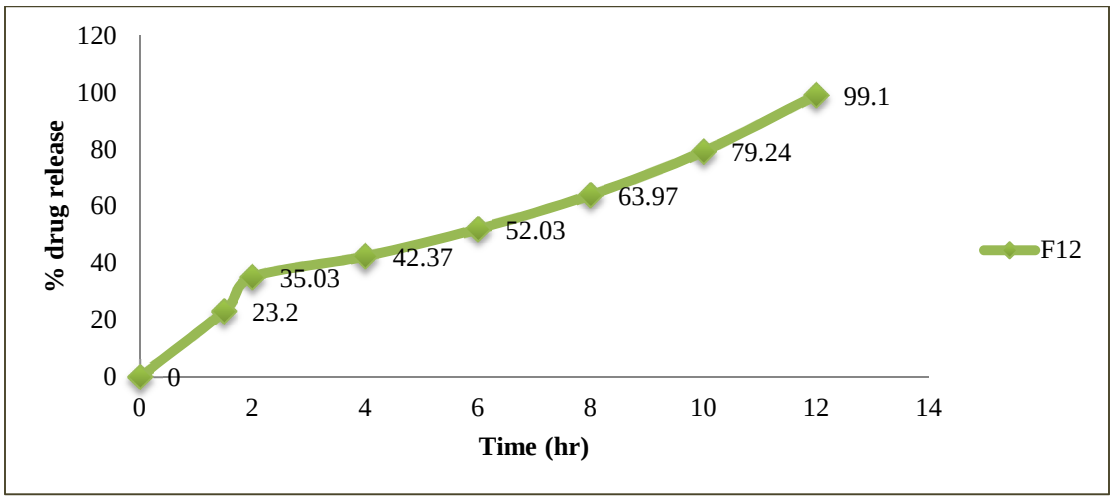

Figure No.9: *Invitro* dissolution of Ofloxacin floating Tablet (OFT 12) employing HPC

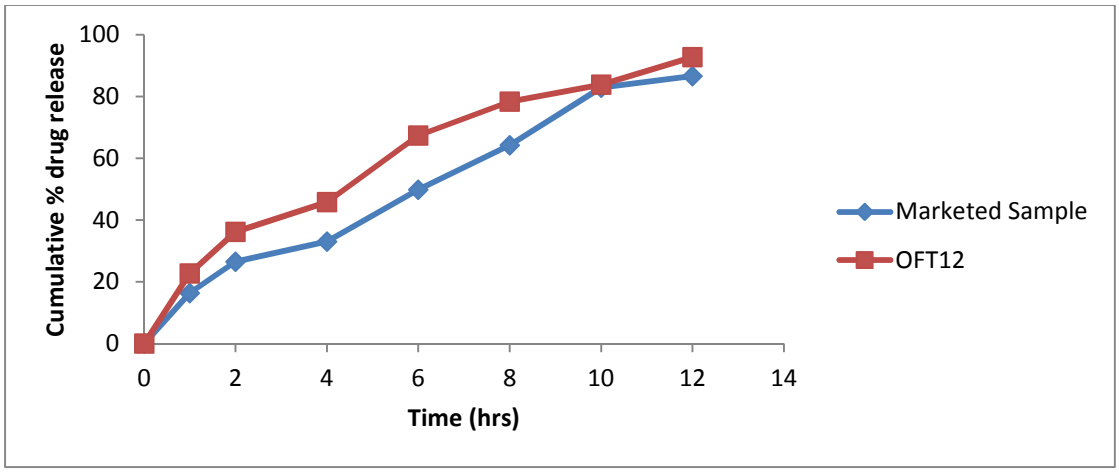

Figure No.10: Comparison of *Invitro* Dissolution of Optimized Formulation with Marketed Tablet

CONCLUSION

In the present work, floating tablets of Ofloxacin were prepared by direct compression method. All the tablets were subjected to weight variation, drug content uniformity, and hardness, and friability, water absorption ratio, wetting time, dissolution, drug excipients interaction and short-term stability studies. Tablets prepared by direct compression method were found to be good without any chipping, capping and sticking. The hardness of the prepared tablets was found to be in the range of 4.5 to 5.5 kg/ cm^2. The friability values were found to be in the range of 0.341 to 0.541 %. Formulation nine showed good results than rest of the five formulations in pre and post compression studies. The low values of standard deviation for average weight and drug content of the prepared tablets indicate weight and drug content uniformity within the batches prepared. Formulations nine displayed drug release considered in 0.1N HCL and Formulation five shows better drug release in dissolution profile. Short-term stability studies of promising formulations indicated that there are no significant changes in drug content. IR-spectroscopic studies indicated that there is no drug - excipients interactions. In the present investigation gastric retentive system of Ofloxacin were prepared with HPMC K_{100}LV, HPMC 50 SH 60, HPC and Chitosan polymers. Ofloxacin has site-specific absorption in the upper part of the stomach and hence these systems are useful in the improving the absorption of the drug. An attempt was made to deliver Ofloxacin via floating drug delivery system could be formulated as an approach to increase gastric residence time and there by improve its bioavailability. It was found that increase in the HPC concentration will increases floating lag time and increases floating duration. Tablets of batch F_{15} and F_{12} have considerable *in vitro* drug release, and also showing good floating lag time. But F_{12} drug release was found to be 99.1%; hence it is considered as best formula due to chitosan in the F_{15} formulation was natural polymer it may grow the microorganisms during storage. From the above experimental results it can be concluded that, formula F_{12} is best formulation.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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