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FORMULATION AND EVALUATION OF FLOATING BEADS OF OFLOXACIN USING ELECTRON MICROSCOPY

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Keywords:

Antibiotic, Absorption window, Gastric residence time, Polymer mixture, Stomach

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ABSTRACT: Floating Drug delivery systems are designed to prolong the gastric residence time after oral administration. Ofloxacin is an antibacterial fluoroquinolone, widely prescribed in gastric and duodenal ulcers. It exhibits pH dependent solubility, more soluble in acidic pH and slightly soluble in neutral or alkaline pH. Precipitation of the drug occurs in the intestine, which adversely affects the absorption in the lower sections of the intestine. So there is a need for systems that reside in the stomach over a relatively long period and release the active compound in a sustained manner. The aim of the present study was to develop a delivery system wherein the retention of Ofloxacin could be achieved for increasing local action in the gastric region against *Helicobacter pylori*, with the development of rice bran oil entrapped zinc pectinate beads containing Ofloxacin. Various formulations of floating beads of Ofloxacin were developed using polymers like Low Methoxy Pectin alone and in combination with rate controlling polymers such as Gellan Gum, Karaya Gum and Xanthan Gum. The beads were prepared by emulsion gelation method. Rice bran oil was used to impart buoyancy to the beads due to its low density. The beads were spherical in nature and beads formulated with a mixture of Low Methoxy Pectin and Gellan Gum showed the highest drug content and drug entrapment. The buoyancy studies on the beads proved that a minimum of 25% w/w of rice bran oil was required to impart satisfactory buoyancy to the beads.

INTRODUCTION: Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying, leading to non uniform absorption profiles, incomplete drug release and shorter residence time of the dosage form in the stomach.

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This leads to incomplete absorption of drugs having an absorption window in the upper part of the small intestine, as once the drug passes down the absorption site, the remaining quantity goes unabsorbed. All the above requirements can be met and effective delivery of the drugs to the absorption window, for local action and for the treatment of gastric disorders such as gastro-esophageal reflux, can be achieved by floating drug delivery systems (FDDS). Floating drug delivery system (FDDS) or hydro-dynamically balanced systems (HBS) have a bulk density, lower than gastric fluids and thus remains buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of

time. While the systems are floating on the gastric contents, the drug is released slowly at a desired rate from the system. This results in an increase in the Gastric residence time (GRT) and a better control of fluctuations in plasma drug concentrations in some cases. Ofloxacin is a broad-spectrum antibiotic that is active against both Gram positive and Gram-negative bacteria. Formulation of FDDS of H2 antagonists can be applied for effective treatment of gastric and duodenal ulcers and for the eradication of the Helicobacter pylori from the stomach.

MATERIALS AND METHODS:

Materials: Ofloxacin was a gift sample from Apex formulations Pvt. Ltd, Ahmedabad, Gujarat, India whereas Gellan gum was a gift sample from Sigma Aldrich chemicals, Hyderabad, India and Xanthan gum was purchased from Sigma Aldrich, USA. Karaya gum was obtained from Morning Star Enterprises, Mumbai, Maharashtra, India and Rice bran oil from Sri Anjanaya Agrotech Pvt. Ltd, Harihar, Karnataka, India. All other chemicals and reagents used were of analytical grade.

Methods:

Development of Calibration Curve: Ofloxacin equivalent to 100 mg was dissolved in 100 ml of 0.1 N hydrochloric acid buffer (pH 1.2) to get a stock solution A. 10 ml was pipetted out and the volume was made upto 100 ml with 0.1 N hydrochloric acid buffer to get a stock solution B. From the stock solution B, aliquots were diluted to10ml with 0.1 N hydrochloric acid buffer to get 1 to 8µg/ml solutions and measured at 294.5nm. (Spectrophotometer UV-1601, Shimadzu, Japan) [1].

Drug Polymer Compatibility Studies:

Differential Scanning Calorimetry (DSC): Physical mixture of Ofloxacin and other polymers were subjected to compatibility studies using Differential Scanning Calorimetry (DSC-60, Shimadzu, Japan). The heating rate was kept at 10 °C/ min up to 350 °C. Nitrogen gas was used forpurging at 30 ml/min.[2]

Fourier Transform Infrared Spectroscopy (FTIR): Spectra of drug and polymers were taken and analyzed for any major interaction using IR spectrophotometer (Shimadzu, model 840, Japan). These were done qualitatively in order to assess the pattern of peaks and for comparison purposes [2].

Preparation of Floating Zinc Pectinate Beads: Ofloxacin, LMP, GG, XG and KG were passed through sieve no 80 separately. Ofloxacin (20% w/w of dry polymer weight) was dissolved in distilled water. LMP (3% w/v) alone and polymer mixtures (3% w/v) containing LMP and GG, LMP and XG, and LMP and KG in three different ratios were dissolved in above dispersion and one formulation was prepared with only polymer mixtures (3% w/v) containing GG, XG, KG and LMP.

TABLE 1: FORMULATION VARIABLES OF VARIOUS OFLOXACIN BEAD FORMULATIONS

Formulation code	LMP:GG (3% W/V)	LMP:XG (3% W/V)	LMP:KG (3% W/V)	LMP:GG:XG:KG (3% W/V)	RICE BRAN OIL(3%W/V)
F	10:0	10:0	10:0	-	15
	10:0	10:0	10:0	-	20
	10:0	10:0	10:0	-	25
F1	9:1	-	-	-	25
F2	8:2	-	-	-	25
F3	7:3	-	-	-	25
F4	-	9:1	-	-	25
F5	-	8:2	-	-	25
F6	-	7:3	-	-	25
F7	-	-	9:1	-	25
F8	-	-	8:2	-	25
F9	-	-	-	8:0.66:0.66:0.66	25

To the above mixture rice bran oil (25% w/w) was added and stirred to form a homogeneous emulsion. The drug-loaded emulsion was extruded through a 23 G syringe needle into zinc chloride solution (5% w/v) maintained under gentle agitation. The beads were allowed to remain in the same solution for 30 min to improve their mechanical strength. The formed beads were separated, washed with water and allowed to dry at room temperature overnight.

Table 1 lists the formulation variables for different formulations of Ofloxacin loaded floating beads. Blank beads without Ofloxacin were also prepared using the same technique [3, 4].

Evaluation of Physicochemical Parameters of Floating Beads of Zinc Pectinate:

Determination of Bead Diameter: The diameter of a sample of gel beads (25 beads) of each formulation was determined using a dial thickness meter.

Drug Content: An accurately weighed sample of beads (100mg) was crushed in a mortar and added to100ml of 0.1N hydrochloric acid buffer (pH 1.2) and kept overnight under stirring to elute complete drug from the polymer matrix. It was filtered and analyzed at of 294.5nm (UV spectrophotometer, 1601, Shimadzu, Japan) against blank bead mixture, which was treated similarly. The drug content of each formulation was recorded as mg/100mg of gel beads [5].

Drug Entrapment Efficiency: The percentage drug entrapment efficiency (% EE) of each bead formulation was calculated using the following equation: [5]

$$EE\ (\%) = \frac{\text{Actual Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

Determination of Swelling Index: The swelling behavior of the zinc pectinate beads was studied in 0.1 N HCl (pH 1.2) buffer. Approximately 100mg of beads were taken in a dissolution basket and weighed (W_1); the baskets along with the beads were immersed in 0.1N HCl buffer. The weight (W_2) of the basket along with the beads was determined for 8 h: every 30 minutes for the first 2 h, and then every h after that. The swelling index (SI) of each formulation was calculated using the following equation:

$$\%\ SI = \frac{W2 - W1}{W1} \times 100$$

Buoyancy Studies: The time between the introduction of the FDDS into the medium and its buoyancy to the upper one third of the dissolution vessel (floating lag time) and the time for which the formulation constantly floated on the surface of the medium (floating duration) were measured simultaneously as a part of dissolution studies by visual observation [6].

***In vitro* Drug Release Studies:** *In vitro* release characteristics of ofloxacin floating gel beads (n = 3) were evaluated employing USP XIV dissolution testing apparatus 2 (paddle method) using 500ml of 0.1 N HCl buffer as dissolution medium maintained at 37 ± 0.5 °C. The contents were stirred at 50 rpm. A 5ml aliquot of the solution was withdrawn at predetermined time intervals for 8 h and fresh 5ml dissolution media was replaced to maintain sink condition. The sample aliquots were analyzed at a wavelength of 294.5 nm[7].

Stability Studies: Stability studies were carried out according to ICH guidelines by storing the formulation F1 at 40 ± 2 °C and relative humidity 75 ± 5% for a period of two months in a programmable environmental test chamber (CHM-10S, Remi Instruments Ltd., Mumbai, India). The samples were withdrawn at 30 and 60 days and analyzed for the drug content, floating behavior and *in vitro* drug release [8].

Scanning Electron Microscopy (SEM): Morphological examination of the surface and external structure of the dried beads of formulation F1, F4 and F7 (Both drug loaded and blank beads) was performed using a scanning electron microscope (SEM) (model JEOL, JSM-840A). The samples were gold coated prior to the scanning [9].

RESULTS AND DISCUSSION:

Development of Calibration Curve: Concentration and absorbance obtained for standard plot of Ofloxacin in 0.1 N hydrochloric acid buffer (pH 1.2) are shown in **Fig. 1.**

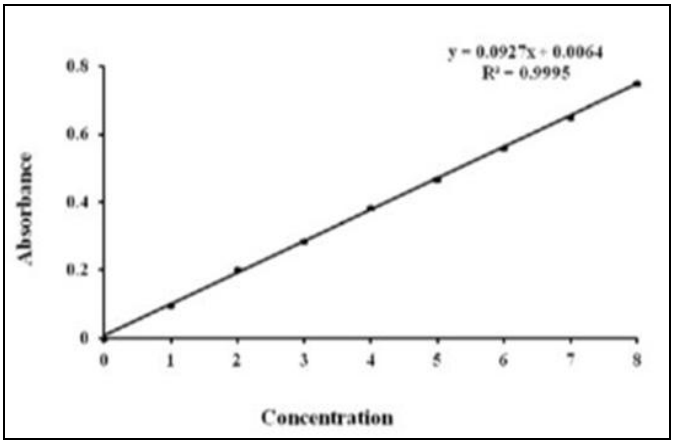

FIG. 1: CALIBRATION CURVE OF OFLOXACIN

Drug Polymer Compatibility Studies:

Differential Scanning Calorimetry (DSC): The DSC themograms of physical mixture of Ofloxacin and the polymers showed that characteristic peaks of polymers and Ofloxacin peaks were still present in the physical mixture but slightly shifted from their original positions as shown in **Fig. 2.** The findings indicate that the drug and polymers are compatible with each other.

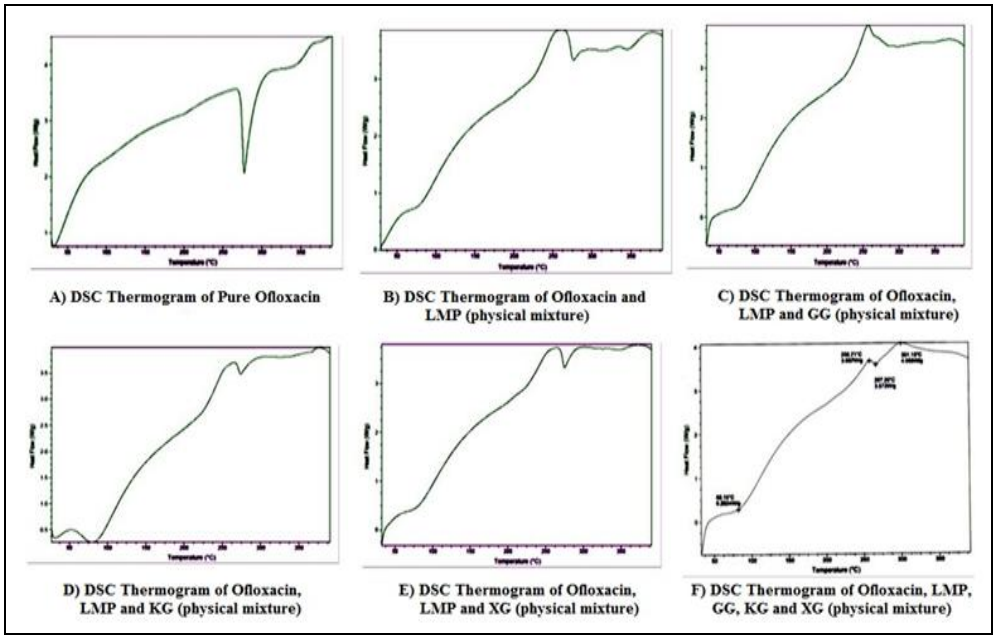

FIG. 2: DSC THERMOGRAM OF PURE OFLOXACIN, OFLOXACIN AND LMP, OFLOXACIN, LMP AND GG, OFLOXACIN, LMP AND KG, OFLOXACIN, LMP AND XG, OFLOXACIN, LMP, GG, KG AND XG

Fourier Transform Infrared Radiation (FTIR): All the above bands associated with the pure drug are present in the FTIR spectra of drug in combination with gellan gum, karaya gum and xanthan gum as seen in **Fig. 3**. This shows that there is no chemical interaction taking place between drug and excipients.

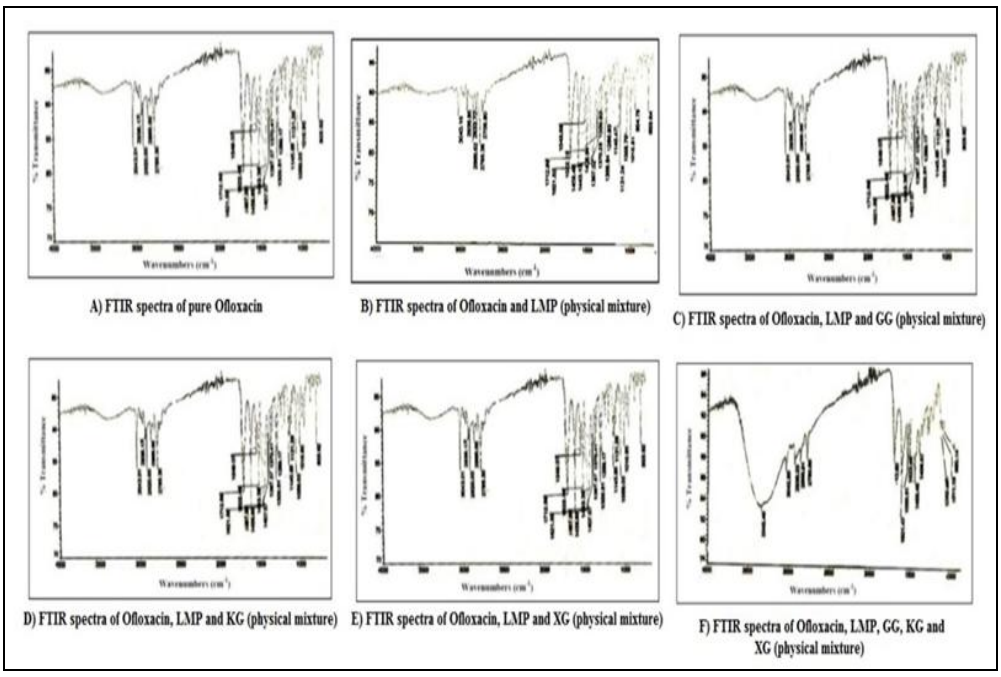

FIG. 3: FTIR SPECTRA OF PURE OFLOXACIN, OFLOXACIN AND LMP, OFLOXACIN, LMP AND GG, OFLOXACIN, LMP AND KG, OFLOXACIN, LMP AND XG, OFLOXACIN, LMP, GG, KG AND XG

Evaluation of Physicochemical Parameters of Floating Beads of Zinc Pectinate:

Determination of Bead Diameter: The prepared beads were almost spherical and translucent. The mean surface diameter of 10 formulations was between 1.691 ± 0.022 (mean ± SD) and 2.099 ± 0.041 (mean ± SD).

Drug Content, Drug Entrapment Efficiency and Swelling Index: The percent drug content, entrapment efficiency and swelling index for various Ofloxacin floating bead formulations is shown in **Table 2.**

TABLE 2: CHARACTERIZATION OF FLOATING ZINC PECTINATE BEADS

Formulation Code	Mean diameter ± SD (mm)	Drug content (mg)	% EE	% Swelling Index
F blank	1.691±0.022	-	-	-
F	1.693±0.015	2.437±0.037	57.49	0.74
F1	1.751±0.023	1.236±0.017	78.81	2.42
F2	1.841±0.022	1.620±0.054	69.16	1.79
F3	1.898±0.018	1.551±0.114	72.13	2.21
F4	2.193±0.017	1.681±0.023	76.20	1.01
F5	1.836±0.018	1.621±0.063	60.61	3.75
F6	2.057±0.069	1.362±0.035	74.28	1.22
F7	2.009±0.027	1.713±0.111	65.40	2.10
F8	2.099±0.041	1.417±0.027	62.98	1.74
F9	2.008±0.063	1.434±0.240	58.95	0.72

Buoyancy Studies: The floating ability of prepared beads was evaluated along with dissolution studies. The beads without oil sank immediately in 0.1 N HCl (pH 1.2), while beads containing sufficient amount of rice bran oil (25%) demonstrated instantaneous and excellent floating properties **(Table 3).**

TABLE 3: BUOYANCY CHARACTERISTICS OF FLOATING BEADS

Formulation Code	Amount of oil (%w/w)	FLT (min)	Floating Duration (h)
F Blank	-	NF	NF
F	10	NF	NF
F	15	NF	NF
F	25	0	24
F1	25	0	24
F2	25	0	24
F3	25	0	24
F4	25	0	24
F5	25	0	24
F6	25	0	24
F7	25	0	24
F8	25	0	24
F9	25	0	24

***In vitro* Drug Release Studies:** *In vitro* drug release study of Ofloxacin floating beads was carried in 0.1N HCl (pH 1.2), for a period of 8 h. In the 0.1N HCl, the beads exhibited a biphasic release profile as an initial rapid drug release phase (burst effect) followed by a sustained, gradually increasing drug release phase after 1 h extending up to 8 h. Formulation F contained only LMP could not sustain the Ofloxacin release up to 8 h. It released complete drug at the end of 4 h **(Table 4)**.

TABLE 4: *IN VITRO* RELEASE CHARACTERISTICS OF FORMULATION F

Serial Number	Time (h)	SQRT	Log time	Cum. % drug release	Log % drug remaining	Log % drug release
1	0	0	-	0	2	-
2	0.5	0.7071	-0.3010	65.92±1.71	1.5325	1.8190
3	1	1	0	74.47±2.20	1.4071	1.8721
4	1.5	1.2247	0.1760	82.01±0.77	1.2550	1.9139
5	2	1.4142	0.3010	86.26±1.04	1.1481	1.9358
6	3	1.732	0.4771	93.56±0.99	0.8089	1.9711
7	4	2	0.6020	99.14±0.86	-0.0655	1.9962

TABLE 5: *IN VITRO* RELEASE CHARACTERISTICS OF FORMULATIONS

Time (h)	Cumulative % drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	47.46±1.59	36.98±2.00	44.59±3.05	45.89±0.94	30.74±	47.71±1.28	40.16±0.96	32.6±1.91	32.6±1.91
1	51.68±1.52	45.55±2.73	52.33±2.29	57.21±2.17	43.50±2.96	58.12±1.04	44.84±0.91	38.78±0.99	40.09±0.15
1.5	58.01±1.56	52.62±1.23	57.47±0.57	59.51±3.02	46.37±2.60	61.28±1.52	49.91±2.28	44.76±0.76	45.13±0.79
2	60.36±2.25	57.15±3.35	59.89±1.46	63.16±1.98	48.34±1.05	63.94±3.49	52.77±2.56	47.47±0.37	47.47±0.37
3	68.36±1.88	61.1±3.42	61.59±1.04	66.49±2.06	51.01±3.13	66.39±0.98	55.92±0.62	51.15±1.03	51.15±1.03
4	71.6±1.84	65.65±3.51	63.81±2.59	68.27±3.01	53.14±2.69	68.37±1.84	58.67±0.68	55.13±0.59	55.13±0.59
5	77.65±0.27	69.07±1.47	66.83±2.58	71.97±1.81	54.86±0.60	71.71±1.29	60.89±1.07	57.92±0.62	57.92±0.62
6	78.48±0.84	70.28±0.91	69.71±0.32	75.58±1.14	56.66±2.42	73.50±0.98	63.78±0.96	60.44±1.51	58.87±0.51
7	83.05±3.47	73.09±1.082	72.52±1.08	78.78±0.37	58.96±1.19	75±0.24	66.59±0.27	63.47±3.21	60.66±0.57
8	87.51±1.14	74.33±0.04	74.76±1.90	80.74±4.11	59.85±2.15	76.41±2.89	68.52±0.96	66.00±1.16	62.40±1.87

Formulations containing GG; F1, F2 and F3 released 87.51%, 74.33 and 74.76% of drug, formulations containing XG; F4 and F5 released 80.74% and 59.85% of the drug, formulations containing KG; F6, F7 and F8 released 76.41%, 68.52% and 66.00% of the drug and the formulations containing GG, XG and KG; F9 released 62.40% of the drug at the end of 8 h respectively. Hence on the basis of *in vitro* dissolution studies formulation F1 was chosen as the best formulation giving 87.51% of drug release till 8 h **(Table 5).**

Analysis of Release Pattern: To analyze the drug release from the beads, the in vitro dissolution data was fitted to [10, 11]:

a) Zero order (Cumulative percentage drug released *vs* Time).

b) First order (Log cumulative percentage drug remaining *vs* Time).

c) Higuchi release model (Cumulative percentage drug released *vs* Square root of time).

d) Korsemeyer and peppas model (Log percentage drug released *vs* Log time) as shown in **Table 6**.

TABLE 6: KINETICS OF RELEASE PATTERN

S. no.	Formulation code	R^2 for zero order equation	R^2 for first order equation	R^2 for higuchi equation	n value for peppas equation	R^2 for peppas equation
1	F	0.606	0.944	0.870	0.198	0.998
2	F1	0.683	0.922	0.887	0.225	0.986
3	F2	0.657	0.980	0.880	0.246	0.983
4	F3	0.567	0.762	0.793	0.170	0.979
5	F4	0.583	0.823	0.815	0.185	0.976
6	F5	0.567	0.695	0.810	0.206	0.915
7	F6	0.503	0.715	0.753	0.154	0.967
8	F7	0.604	0.779	0.832	0.189	0.995
9	F8	0.692	0.840	0.899	0.247	0.995
10	F9	0.634	0.774	0.863	0.226	0.988

Stability Studies: In view of potential utility of the formulation, stability studies were carried out on formulation F1 for two months according to ICH guidelines. At the end of each month, the formulations were subjected to drug assay, floating behavior and *in vitro* release studies. The results are shown in **Table 7**.

TABLE 7: STABILITY STUDY OF FORMULATION F1

Time	Drug content ± SD (mg)	Floating behavior		Drug release at the end of 8h
		FLT (min)	Floating duration (h)	
Zero month	1.236±0.017	0	24	87.51±1.14
First month	1.222±0.021	0	24	80.21±1.21
Second month	1.182±0.056	0	24	75.32±1.32

Scanning Electron Microscopy: The scanning electron microscopy of blank and drug loaded beads (both external and internal) are shown in **Fig. 4, 5, 6** and **7**.

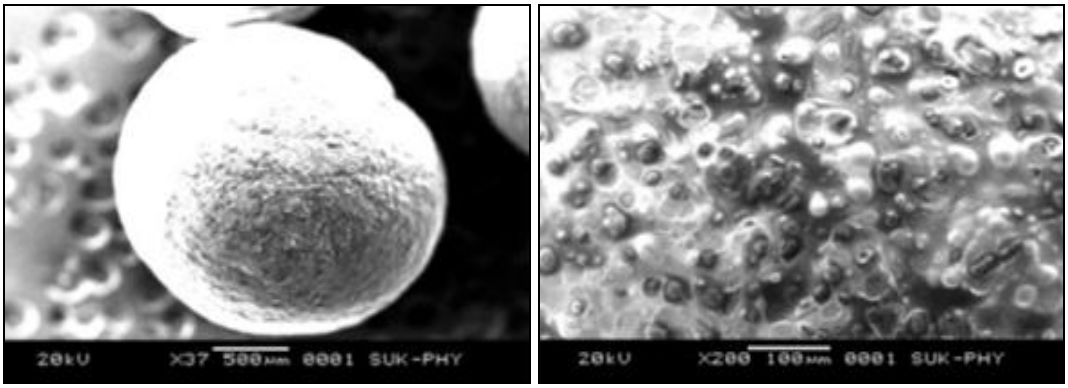

FIG. 4: SCANNING ELECTRON MICROSCOPY OF (A) EXTERNAL AND (B) SURFACE MORPHOLOGY OF DRUG LOADED FLOATING BEADS (F0)

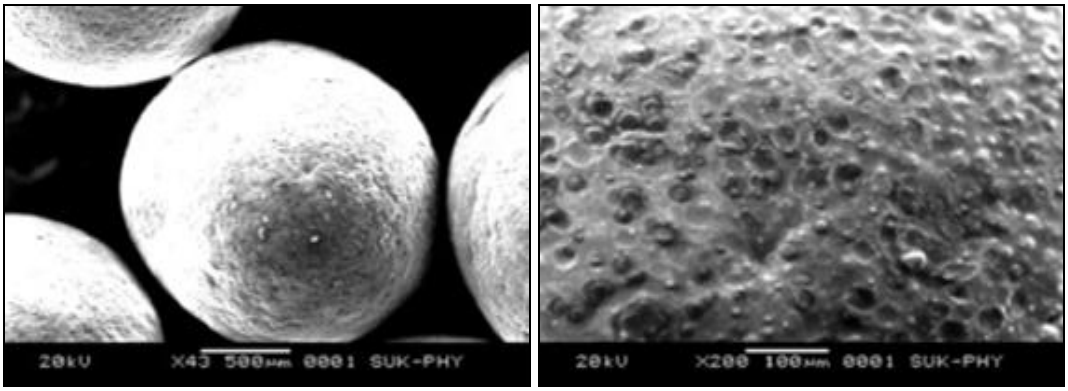

FIG. 5: SCANNING ELECTRON MICROSCOPY OF (A) EXTERNAL AND (B) SURFACE MORPHOLOGY OF DRUG LOADED FLOATING BEADS PREPARED USING GELLAN GUM (F1)

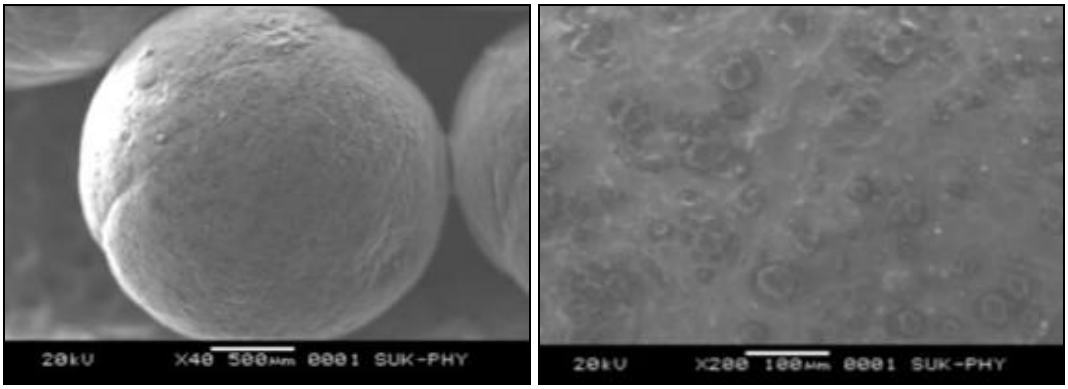

FIG. 6: SCANNING ELECTRON MICROSCOPY OF (A) EXTERNAL AND (B) SURFACE MORPHOLOGY OF DRUG LOADED FLOATING BEADS PREPARED USING XANTHAN GUM (F4)

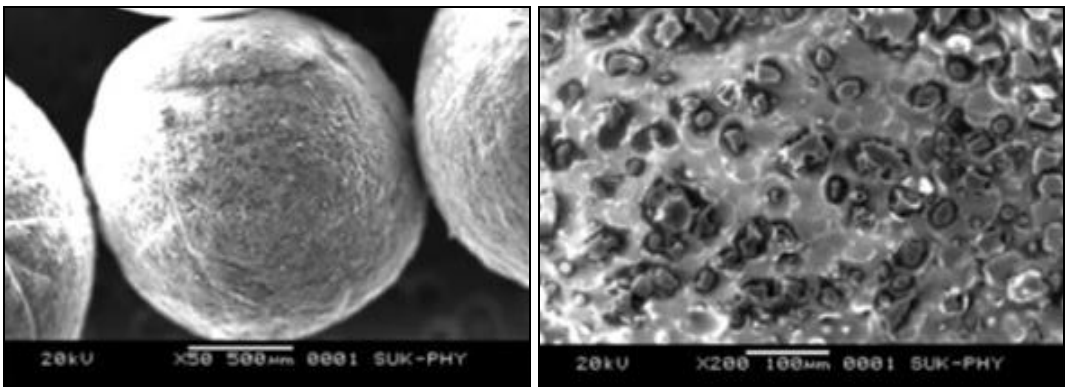

FIG. 7: SCANNING ELECTRON MICROSCOPY OF (A) EXTERNAL AND (B) SURFACE MORPHOLOGY OF DRUG LOADED FLOATING BEADS PREPARED USING KARAYA GUM (F7)

DISCUSSION:

Drug Polymer Compatibility Studies:

Differential Scanning Calorimetry (DSC): The DSC thermograph of pure Ofloxacin showed one endothermic peak at 274.5 °C. The DSC thermograms of physical mixture of Ofloxacin and the polymers showed no characteristic peaks of the polymers, and Ofloxacin peaks were still present but slightly shifted from their original positions which could be due to an ionic interaction and this characteristic features of drug melting suggested no problem of incompatibility.

Fourier Transform Infrared Radiation (FTIR): FTIR spectra showed that there is no chemical interaction taking place between drug and polymers.

Preparation of Floating Zinc Pectinate Beads: Pectin with low degree of esterification (DE) can form gel by ionotropic gelation with Zn^{2+} ions. When an emulsion of rice bran oil containing pectin was dropped into zinc chloride solutions, spherical gel beads were then formed instantaneously in which intermolecular cross-links were formed between the metallic zinc ions and negatively charged carboxyl groups of the pectin molecules **(Fig. 8)**.

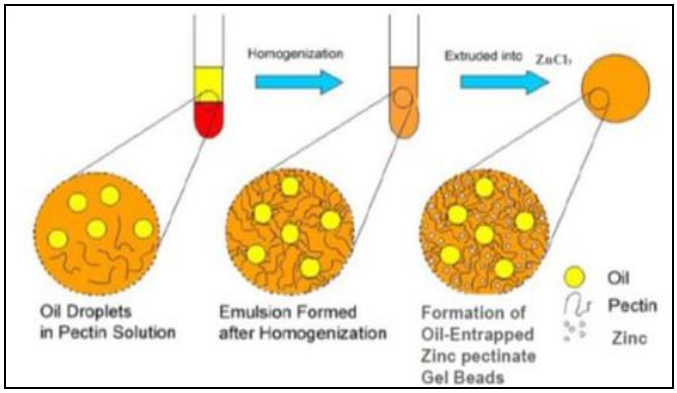

FIG. 8: PROPOSED MODEL OF EMULSION-GELATION PROCESS BY WHICH THE OIL ENTRAPPED ZINC PECTINATE GEL BEADS ARE FORMED

It was found that homogenization of emulsion is a must as without homogenization; the oil separated from the pectin solution despite being mixed by stirrer. Pectin helped to emulsify the mixture of water and oil phase during the homogenization process. However the emulsifying property was limited when the oil concentration was increased to more than 30% w/w. At and above this concentration the oil started eluting from the beads. The oil-entrapped beads were spherical, translucent and slightly yellowish. It was found that a minimum of 25% w/w rice bran oil was necessary to impart satisfactory buoyancy to the beads [12-14].

Evaluation of Physicochemical Parameters of Floating Beads of Zinc Pectinate:

Determination of Bead Diameter: The formed beads were spherical. The mean particle diameter of the blank oil entrapped zinc pectinate beads containing no drug were found to be 1.691 ± 0.022 (mean ± SD), but the added materials were responsible for the change in the size of the zinc pectinate beads [15].

Drug Content: The drug content was found to be between 2.437 ± 0.037 and 1.434 ± 0.240

Drug Entrapment Efficiency: The percentage drug entrapment efficiency (% EE) of the beads was obtained in the range of 57.49% to 78.81%. Formulation F1 showed the highest drug entrapment and formulation F showed the lowest entrapment of drug. The low drug entrapment efficiency of the F formulation may be attributed to the highly porous nature of the zinc pectinate matrix, due to which the drug may diffuse back into the cross linking solution from the bead matrix during cross linking period. The drug entrapment also increases with addition of the copolymers into the bead formulation. Here zinc chloride was used as cross linking agent, as, calcium chloride reacted with Ofloxacin and tends to solubilize the drug in the cross linking medium itself [16].

Determination of Swelling Index: The swelling behavior study of the beads was performed in 0.1 N HCl. No change in the swelling ratio of the beads in 0.1 N HCl was observed. The beads were also not swollen much or eroded during the dissolution studies in 0.1 N HCl. Thus, from these results, it could be assumed that the drug release was not under the control of the swelling behavior but rather was controlled by the dissolution of the Ofloxacin in the dissolution medium and diffusion of the Ofloxacin through polymer matrix [17].

Buoyancy Studies: The floating ability of prepared beads was evaluated along with dissolution studies. The beads without oil sank immediately in 0.1 N

HCl (pH 1.2), while beads containing sufficient amount of rice bran oil (F to F9) demonstrated instantaneous and excellent floating ability. It was found that a minimum of 25% w/w of rice bran oil was necessary to impart buoyancy to the gel beads. Thus, floating ability was found to be directly related to the amount of oil entrapped in the polymer matrix. The beads remained afloat throughout the study period (8 h) and the beads continued to float till 24 h (**Table 3**). It was found that varying the polymer and copolymer concentrations in the bead formulations did not affect the floating lag time or the floating duration of the beads in the dissolution media.

***In vitro* Drug Release Studies:** According to the *in vitro* drug release profile of all the bead formulations (F to F9) by conventional method, the gel beads in the 0.1 N HCl (pH 1.2), exhibited a biphasic release profile as an initial rapid drug release phase was followed by a slower and sustained, gradually increasing drug release phase after 1 h.

The results show that incorporation of rate controlling polymers such as GG, KG and XG to the bead formulations can sustain the drug release from the oil entrapped zinc pectinate beads. Incorporation of these copolymers into the zinc pectinate matrix increases the viscosity of the polymers matrix and correspondingly decreases the drug release. Results also show that as the concentration of the copolymers increases in the formulation, the viscosity of the polymer matrix is enhanced and more sustaining drug release is observed.

Kinetics of Drug Release: The *in vitro* release data of all the batches were fitted to zero order, first order, Higuchi and Korsemeyer and Peppas equations. It was observed that for the formulation F, F1 and F2 the r^2 was higher when fitted to first order equation ($r^2 = 0.944$), which indicates that a first order release from the formulation F, whereas all the other formulations, F3 to F9 followed Higuchi model. The n values of the Korsemeyer-peppas model for all the formulations was found to be less than 0.5 ($n < 0.5$), so it suggested that the drug release from the beads followed fickian (case I) diffusion.

Stability Studies: At various time intervals, samples were evaluated for the stability studies. There were no more difference in the drug content and the floating properties at the various sampling intervals. The *in vitro* drug release profiles were super imposable which confirms the stability of the product.

Scanning Electron Microscopy: The beads (both blank and drug loaded) were spherical and the external surface was smooth with slightly rougher surface / shrinkage which could be due to drying. The internal surface of the blank beads shows sponge-like nature with little droplets of entrapped oil which imparts buoyancy to the beads. In the drug loaded beads the internal surface is slightly spongy due to the drug and rate controlling polymer are uniformly dispersed in the polymer matrix [18].

CONCLUSION: The aim of the present study was to develop a delivery system wherein the retention of Ofloxacin could be achieved for increasing local action in gastric region against *Helicobacter pylori*. Therefore the present investigation is concerned with the development of rice bran oil entrapped zinc pectinate beads containing Ofloxacin, which after oral administration were designed to prolong the gastric residence time, thus to increase the bioavailability of the drug.

Various formulations of floating beads of Ofloxacin were developed using polymers like LMP alone and mixture of LMP with rate controlling polymers such as GG, KG and XG. The beads were prepared by emulsion gelation method. Rice bran oil was used to impart buoyancy to the beads due to its low density and beads formulated with mixture of LMP and GG (F1) showed the highest drug release compared to other formulations. The selected formulation showed no more changes in drug content, floatability or *in vitro* drug release profile after storage at 75 ± 5%, RH at 40 ± 2 °C during stability study for two months. Thus, the objective of the present work of formulating a dosage form of Ofloxacin by using a low density oil and different proportions and combinations of release rate controlling polymers has been achieved with success.

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