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Formulation and evaluation of effervescent floating tablet of Levofloxacin against *H.pylori* infection

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ABSTRACT

The purpose of the present study was to develop a gastric floating drug delivery system (GFDDS) containing Levofloxacin against the H.pylori infection using gas-forming agents, like sodium bicarbonate, citric acid and hydrocolloids, like Hydroxypropyl ethylcellulose (HPMC) and Carbopol 974P. The prepared tablets were evaluated in terms of their pre compression parameters, physical characteristics, in vitro release, buoyancy, floating lag time (FLT), total floating time (TFT) and swelling index. The formulations were optimized for the different viscosity grades of HPMC, Carbopol 974P and its concentrations and combinations. Stability study was also performed after storage at 40°C/75% RH for three months. All the formulations showed good floating lag time i.e. less than 3 mins. The batch containing combination of HPMC K4M, HPMC K100M and Carbopol 974P (i.e. L12) showed total floating lag time more than 24 hrs. The batch L12 showed the highest swelling index among all the prepared batches (i.e. 95%). The batch L12 was chosen as the optimized batch since it was also stable for three months during stability study.

Keywords: gastric floating drug delivery system, total floating time, HPMC, Carbopol 974P, stability study.

INTRODUCTION

The real challenge in the development of a controlled drug delivery system is not just to sustain the drug release but also to prolong the presence of the dosage form in the stomach or the upper small intestine until all the drug is completely released in the desired period of time [1–2]. The

residence of a drug delivery system in the upper part of the gastrointestinal tract (GIT) can be accomplished by several drug delivery systems, such as intragastric floating systems [3-5], swelling and expandable systems [6], bioadhesive systems [7], modified shape systems [8], high density systems [9], delayed gastric emptying systems [10] and low density super porous systems [11]. FDDS, also called hydrodynamically balanced system, is an effective technology to prolong the gastric residence time in order to improve the bioavailability of the drug. This technology is suitable for drugs with an absorption window in the stomach or in the upper part of the small intestine, drugs acting locally in the stomach and for drugs that are poorly soluble or unstable in the intestinal fluid. FDDS have a bulk density lower than the gastric fluid and thus 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 [12]. Levofloxacin, the model drug for this study, is a fluoroquinolone anti biotic with *in vitro* activity against a wide range of gram-negative and gram-positive microorganisms. The antibacterial action of Levofloxacin results from inhibition of DNA gyrase and topoisomerase IV, essential enzymes that are involved in the replication, transcription, and repair of bacterial DNA. The recommended adult oral dosage of Levofloxacin is ranging from 250 mg to750 mg daily. The solubility of the compound is pH dependent. The maximum aqueous solubility (272 mg/mL) occurs at pH 6.7. It is also freely soluble at pH below 5.8. The bioavailability of Levofloxacin is 99% [13,14]. It is one of the drugs with absorption window, so its primary site of absorption is the stomach region. Research is also going on the various delivery approaches for Levofloxacin. It is one of the important anti biotics in ophthalmic dosage form which is prepared as an ophthalmic insert [15]. Cheow *et al* has reported Levofloxacin nanoparticles against *E.coli* [16]. Recently, Levofloxacin is proved to be one of the potential drugs against *H.pylori* infection, responsible for duodenal ulcers and various cytotoxic complications [17]. *H.pylori* resides mainly in stomach region, specifically in the sub-region of the mucous layer in stomach [17]. It is also reported that a stomach specific locally targeted dosage form would be more effective against *H.pylori* compared to the conventional one [17]. So it demands prolonged and constant drug conc. at that particular site to eradicate the infection. This leads to the formulation of clinically acceptable sustained-release dosage forms of Levofloxacin. The gastroretentive drug delivery systems can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract. The local delivery of Levofloxacin by this approach will also promote a fast and effective eradication of *H.pylori* rather than a conventional tablet containing Levofloxacin.

In the work reported here, floating tablet was prepared containing gas-forming agents, like sodium bicarbonate, citric acid and hydrocolloids, like Hydroxypropyl ethylcellulose (HPMC) and Carbopol 974P. It was evaluated mainly for floating lag time (FLT), total floating time (TFT) and *in vitro* drug release.

MATERIALS AND METHODS

Materials:

Levofloxacin was purchased from Mediwin Pharmaceutical, Ahmedabad. HPMC K4M and HPMC K100M were gifted by Colorcon Asia Pvt. Ltd., Goa, India. Carbopol 974P was kindly supplied by Maruti chemicals, Ahmedabad, India. Concentrated hydrochloric acid (HCL) was kindly supplied by Purvi Chemicals, Ahmedabad, India. All other chemicals were of analytical grade.

Methods:

Preparation of Floating Tablets of Levofloxacin

The ingredients were weighed accurately and mixed thoroughly. Granulation was done with a solution of PVP K-30 in sufficient Isopropyl alcohol. The granules (16#) were dried in conventional hot air oven at 60^0C. The dried granules were sized through 22#/44#, lubricated with magnesium stearate (2%w/w) and Aerosil (1%w/w) and compressed into tablets using an 8-station rotary tablet machine. The tablets were yellowish in colour, round and flat. The hardness of the tablets was kept constant. Twelve formulations were prepared and coded them from L1 to L12. The detail of composition of each formulation is given in Table 1.

Table: 1 Composition of different floating tablet formulations of Levofloxacin

Ingredients (mg)	L1	L2	L3	L4	L5	L6	L7	L8	L9	L10	L11	L12
Levofloxacin	250	250	250	250	250	250	250	250	250	250	250	250
HPMC K4M	130	97.5	65	32.5	---	---	---	---	---	---	65	32.5
HPMC K100M	---	---	---	---	130	97.5	65	32.5	---	---	65	65
Carbopol 974P	---	---	---	---	---	---	---	---	97.5	65	---	21.5
Citric acid	65	65	65	65	65	65	65	65	65	65	65	65
Sodium bicarbonate	130	130	130	130	130	130	130	130	130	130	130	130
Lactose	23	55.5	88	120.5	23	55.5	88	120.5	55.5	88	23	34
PVP K 30	32.5	32.5	32.5	32.5	32.5	32.5	32.5	32.5	32.5	32.5	32.5	32.5
Magnesium stearate	13	13	13	13	13	13	13	13	13	13	13	13
Aerosil	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5
Total weight	650	650	650	650	650	650	650	650	650	650	650	650

Compatibility study of Levofloxacin with other polymers

The compatibility study of Levofloxacin with other polymers was done by using Fourier Transform Infrared spectroscopy (FT-IR). FT-IR spectra of pure drug and mixture of drug and polymers were measured using FT-IR instrument using KBr disk method.

Evaluation of Levofloxacin Tablets

The flow properties of granules (before compression) were characterized in terms of bulk density [18], tapped density, Carr's index [19], Hausner ratio and Angle of repose [19].

Physical evaluation of Levofloxacin floating tablets

Two tablets from each formulation were randomly selected and organoleptic properties such as colour, odour, and shape were evaluated. Thickness and diameter of ten tablets were measured using vernier calipers. The prepared floating tablets were evaluated for uniformity of weight using 20 tablets [20], hardness [21], and friability using 10 tablets.

Determination of % Swelling Index[5]

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, was calculated from the following equation:

$$\% \text{ SI} = \frac{\text{Weight of tablet Initial weight at time (t)} - \text{Initial weight of tablet}}{\text{Initial weight of tablet}} \times 100$$

In vitro buoyancy studies

In vitro buoyancy studies were performed for all the twelve formulations as per the method described by Rosa et al [22]. The randomly selected tablets from each formulation were kept in a 100 ml beaker containing 0.1 N HCl (pH 1.2). 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).

In vitro dissolution studies

The release rate of Levofloxacin from floating tablets was determined using USP 24 Dissolution Testing Apparatus 2 (paddle type-Make: DBK, Ahmedabad). The dissolution test was performed using 900 ml of 0.1N HCl, pH 1.2 at 37°C ± 0.5°C and 50 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µm Whatman filter and diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 294 nm wavelength (λmax) using a UV/Visible spectrophotometer (Shimadzu UV-1700). The % cumulative drug release was plotted against time to determine the release profile.

Kinetic treatment of dissolution profiles

The drug diffusion through most types of polymeric systems is often best described by Fickian diffusion, but other processes in addition to diffusion are important. There is also a relaxation of the polymer chains, which influences the drug release mechanism. This process is described as non-Fickian or anomalous diffusion. Release from initially dry, hydrophilic glassy polymers that swell when added to water and become rubbery show anomalous diffusion as a result of the rearrangement of macromolecular chains. The thermodynamic state of the polymer and the penetrant concentration are responsible for the different types of the diffusion. A third class of the diffusion is Case II diffusion, which is a special case of non-Fickian diffusion. A simple, semi-empirical equation given by Korsmeyer and Peppas [23] (Eq. 1) was used to analyze data of controlled release of drugs from polymer matrices.

$$\mathbf{M_t/M_\infty = kt^n} \text{ ---------- (1)}$$

Where M_t is amount of drug release at time t, M_∞ is total amount of drug present in formulation, *k* is release rate constant depend on geometry of dosage form and *n* is diffusion exponent indicating the mechanism of drug release.

Table: 2 Diffusion exponent and solute release mechanism for cylindrical Shape

Diffusion exponent (n)	Overall solute diffusion mechanism
0.45	Fickian diffusion
0.45 < n < 0.89	Anomalous (non Fickian) diffusion
0.89	Case II transport
n > 0.89	Super case II transport

Comparison with marketed product

The promising formulation was compared with marketed product of Levofloxacin. The evaluation parameter tested and compared was in-vitro dissolution profile.

Stability studies [24]

The promising formulation was tested for a period of three months at 40^0C with 75% RH, for their drug content and other parameters.

RESULTS AND DISCUSSION

The interaction of Levofloxacin with the polymers used was studied using FT-IR spectroscopy method and it was found that drug had not any interaction with the polymers as revealed from figure 1 and table 3. So the drug is compatible with the polymers.

Compatibility study of Levofloxacin with other polymers

Figure: 1 FT-IR spectra of (a) Levofloxacin (b) Levofloxacin + HPMC (Physical mixture) (c) Levofloxacin + Carbopol (Physical mixture)

a) Levofloxacin

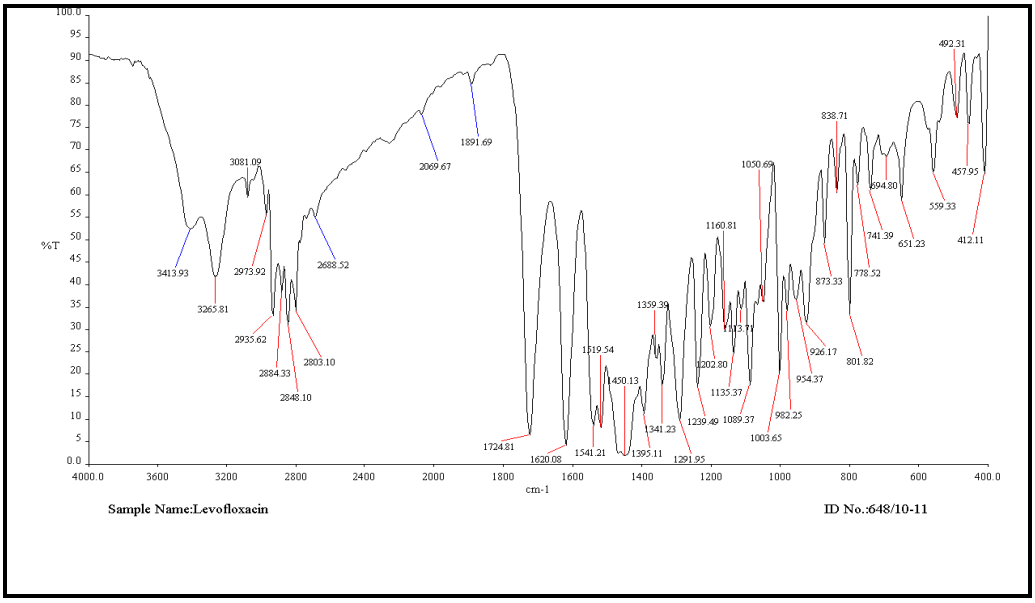
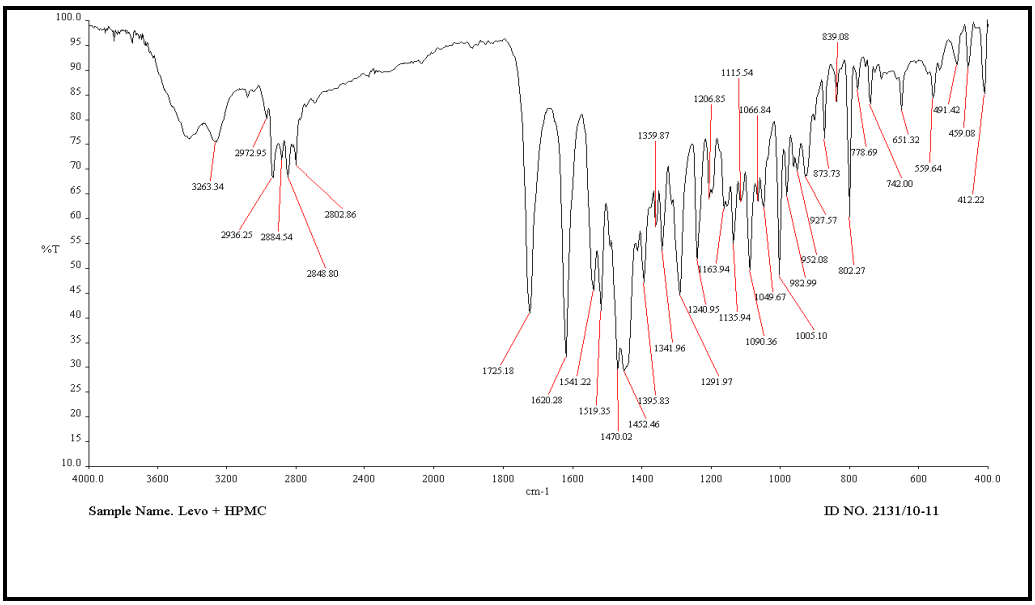


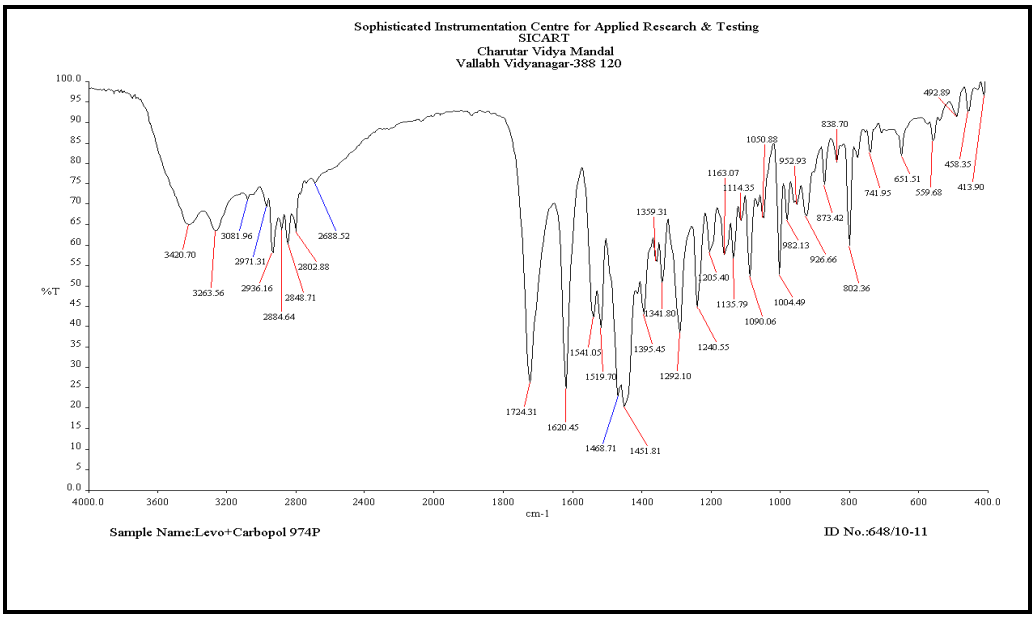
Table: 3 FT-IR Absorption data of Levofloxacin with polymers in physical mixture (4000-400 cm^{-1})

Functional Group	Carbonyl C=O	Aromatic C-H	O-H group of Carboxyl (-COOH) moiety
Levofloxacin	1724.81 cm^{-1}	2935.62 cm^{-1}	3265.81 cm^{-1}
Levofloxacin +HPMC (Physical mixture)	1725.81 cm^{-1}	2936.25 cm^{-1}	3263.34 cm^{-1}
Levofloxacin + Carbopol (Physical mixture)	1724.31 cm^{-1}	2936.16 cm^{-1}	3263.56 cm^{-1}

b) Levofloxacin + HPMC (Physical mixture)



c) Levofloxacin + Carbopol (Physical mixture)



Pre compression parameters of Levofloxacin granules

The formulations showed good flow property and Carr's index (Table 4). The bulk density and tapped density of the prepared granules ranged from 0.449 to 0.588 and 0.594 to 0.720 respectively. Hausner ratio ranged from 1.17 to 1.45 and the Carr's index ranged from 17.13 to 27.75. Angle of repose ranged from 25.8^0 to 30.5^0. The results of angle of repose indicates good flow property of the granules and the value of Carr's index further showed support for the flow property.

Table: 4 Results of Pre compression Flow Properties of Granules of Levofloxacin

Batch	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index (%)	Hausner ratio (H_R)	Angle of repose (θ)
L1	0.503	0.685	17.83	1.36	29.2^0
L2	0.484	0.698	18.71	1.44	30.3^0
L3	0.449	0.654	21.44	1.45	30.5^0
L4	0.477	0.660	23.52	1.38	29.6^0
L5	0.543	0.711	17.13	1.30	28.4^0
L6	0.567	0.705	18.33	1.24	27.3^0
L7	0.588	0.720	22.24	1.22	26.8^0
L8	0.461	0.661	27.75	1.43	29.9^0
L9	0.488	0.685	24.84	1.40	29.7^0
L10	0.456	0.633	27.51	1.38	29.5^0
L11	0.476	0.594	25.22	1.24	27.5^0
L12	0.532	0.657	19.45	1.17	25.8^0

Post compression parameters of Levofloxacin tablets

All formulations remained yellowish, smooth, flat faced circular with no visible cracks. The thickness and diameter of tablets was measured by vernier calipers and was ranged between 4.3±0.02 mm to 4.5±0.02 mm and 12.6 to 12.7 mm respectively. The hardness of the tablets was measured by Monsanto tester and was in between 5.0 to 6.0 kg/cm^2. The friability was measured by Friabilator and was found to be 0.413% to 0.689%, which is an indication of satisfactory mechanical resistance of the tablets. The results are shown in Table 5. All the formulations showed values within the prescribed limits for tests like hardness, friability and weight variation which indicate that the prepared tablets are of good standard quality.

Table: 5 Results of Post Compression Properties of Levofloxacin Floating Tablets

Batch	Diameter (mm)	Thickness (mm)	Hardness (kg/cm^2)	% Friability	Weight variation (mg)
L1	12.7	4.5±0.01	5.5	0.543	650±0.85
L2	12.6	4.3±0.03	6.0	0.520	647±0.64
L3	12.65	4.4±0.01	5.0	0.658	647±0.58
L4	12.65	4.3±0.01	5.5	0.456	650±0.35
L5	12.7	4.5±0.01	6.0	0.445	647±0.26
L6	12.7	4.5±0.02	5.5	0.488	650±0.35
L7	12.6	4.4±0.01	5.0	0.503	648±0.25
L8	12.65	4.5±0.01	5.0	0.689	648±0.55
L9	12.7	4.3±0.02	5.5	0.644	651±0.36
L10	12.7	4.5±0.01	5.5	0.555	651±0.66
L11	12.7	4.4±0.03	6.0	0.413	648±0.45
L12	12.7	4.5±0.01	6.0	0.472	650±0.2

Swelling Index studies

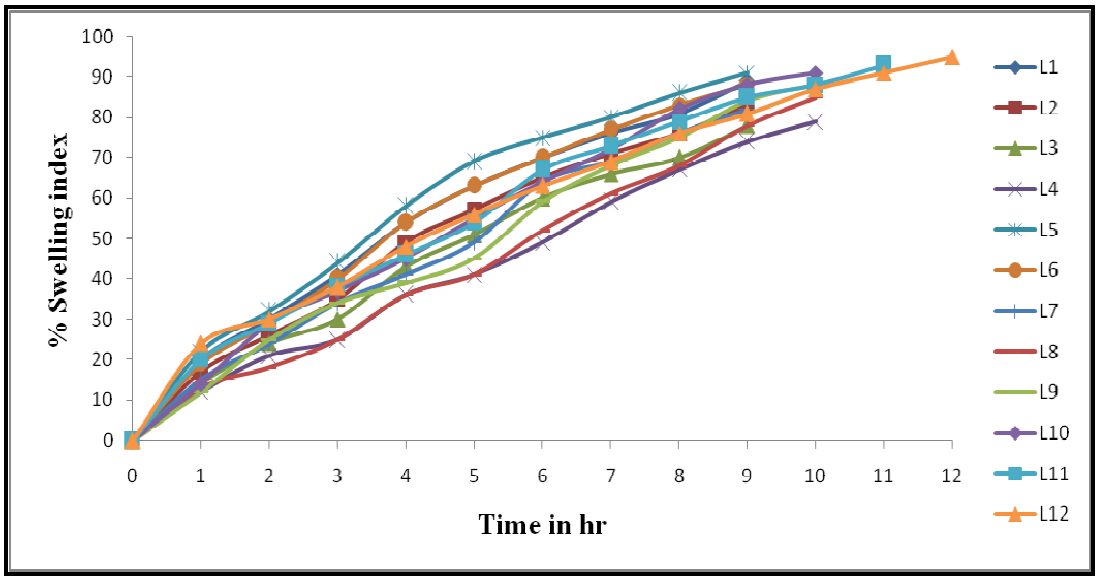
Tablets composed of polymeric matrices build a gel layer around the tablet core when they come in contact with water. This gel layer governs the drug release. Kinetics of swelling is important because the gel barrier is formed with water penetration. Swelling is also a vital factor to ensure floating and drug dissolution. To obtain floating, the balance between swelling and water acceptance must be restored [25,26]. The swelling index of floating tablets of L1 to L12 is shown

in Table 6 and in Figure 2. Tablets containing Carbopol 974P (L9 and L10) showed less swelling index at the beginning but higher swelling index was observed at the end of 12 h. While HPMC K4M and HPMC K100M (L1 to L8) swelled rapidly at the beginning in 0.1 N HCl. Tablets containing combination of Carbopol 974P, HPMC K4M and HPMC K15M (L12) showed constant increasing in swelling index upto 12 h. Combination of HPMC K4M and HPMC K100M resulted in a higher swelling index compared with HPMC K100M alone. The HPMC grade also affects the swelling and hydration with considerably higher swelling index for HPMC K100M than HPMC K4M. HPMC K4M exhibited lower swelling index, but there was no decrease in swelling rate [27]. Further, no significant effect of effervescing agents on swelling indices was observed.

Table: 6 Results of Swelling Index Studies of Levofloxacin Floating Tablets

Batch	Time in hrs												
	0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
L1	0	20	30	41	54	63	70	76	81	89	---	---	---
L2	0	17	26	35	49	57	65	71	76	83	---	---	---
L3	0	14	24	30	43	51	60	66	70	78	---	---	---
L4	0	12	21	25	36	41	49	59	67	74	79	---	---
L5	0	22	32	44	58	69	75	80	86	91	---	---	---
L6	0	19	29	40	54	63	70	77	83	88	---	---	---
L7	0	15	24	34	41	49	64	69	76	82	---	---	---
L8	0	13	18	25	36	41	52	61	68	78	85	---	---
L9	0	12	25	34	39	45	59	68	75	84	88	---	---
L10	0	14	29	37	45	55	64	72	82	88	91	---	---
L11	0	20	29	38	46	54	67	73	79	85	88	93	---
L12	0	24	30	38	48	56	63	69	76	81	87	91	95

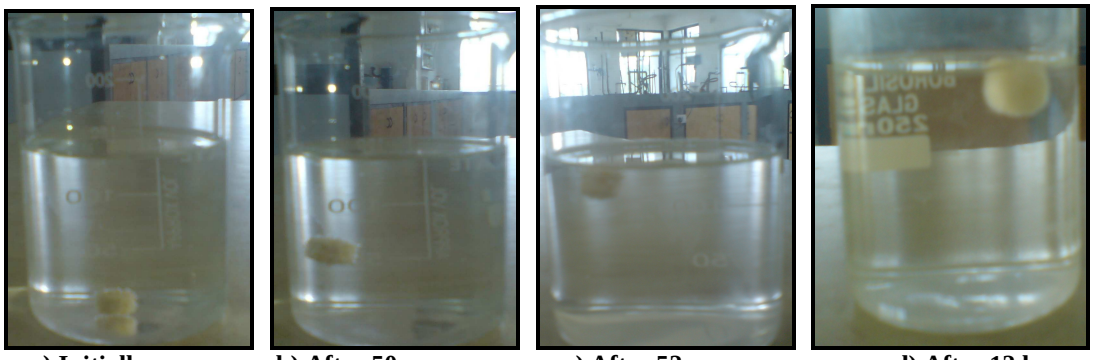
Figure: 2 Swelling Index profile of Levofloxacin Floating Tablets



In vitro buoyancy studies

All the tablets were prepared by effervescent approach. Sodium bicarbonate was added as a gas-generating agent. Sodium bicarbonate induced carbon dioxide generation in presence of dissolution medium (0.1 N HCl). The combination of sodium bicarbonate and citric acid provided desired floating ability and therefore this combination was selected for the formulation of the floating tablets. It was observed that the gas generated is trapped and protected within the gel, formed by hydration of polymer (HPMC), thus decreasing the density of the tablet below 1 and tablet becomes buoyant. All the batches of tablets were found to exhibit short floating lag times due to presence of sodium bicarbonate and citric acid. The tablets with low-viscosity grade HPMC K4M exhibited short floating lag time and floated for longer duration as compared with formulations containing high viscosity grade HPMC K100M. This indicated that the molecular weight distribution or viscosity of the gel-forming polymer HPMC influenced the *in vitro* buoyancy. Reduction in HPMC level in the formulations prolonged the floating lag time and shortened the total floating time. With reference to buoyancy studies results it can be concluded that the batch containing HPMC K4M polymer showed good floating lag time (FLT) and total floating time (TFT) when compared to batch containing HPMC K100M polymer. The results of *in vitro* buoyancy studies are tabulated in table. Fig shows the floating sequence of the batch L12.

Figure: 3 Floating sequence of batch L12 at different timings



a) Initially **b) After 50 secs.** **c) After 52 secs.** **d) After 12 hrs.**

Table: 7 Results of *In vitro* Buoyancy study of Levofloxacin Tablets

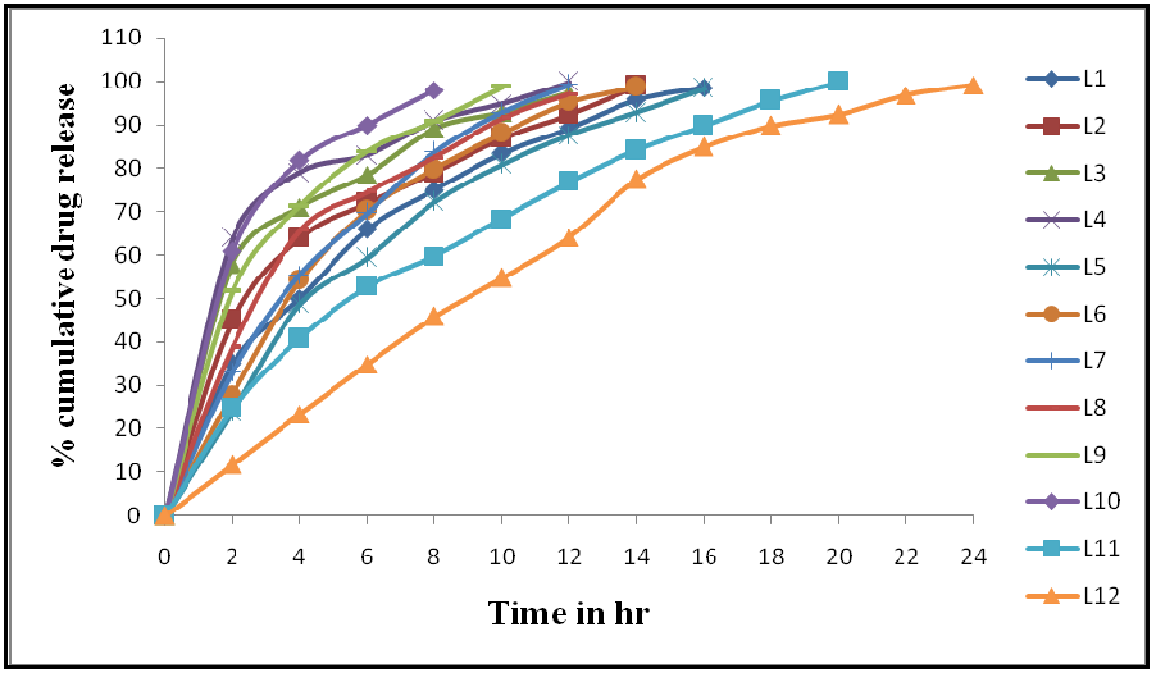
Batch	Floating lag time(s)	Total floating time (hrs.)
L1	48	>16
L2	54	>15
L3	68	>13
L4	85	>12
L5	76	>17
L6	92	>15
L7	125	>14
L8	137	>12
L9	128	>7
L10	130	>8
L11	59	>21
L12	52	>24

In vitro dissolution studies

In vitro dissolution studies of all the formulations are shown in Table 8 and figure 4. It was observed that the type of polymer influences the drug release pattern. A significantly higher rate and extent of drug release was observed from the batches based on HPMC K4M. Varying amount of HPMC K4M affects the drug release. Drug release from HPMC K100M was lesser owing to its high viscosity and also due to less permeability of water to HPMC K100M. Moreover the HPMC containing tablets L1-L8 could not bear their matrix shape until 24 h and drug released before 24 h. The drug release from floating tablets composed of Carbopol 974P (L9 and L10) was less than tablets containing different grades of HPMC. Although combination of and HPMC K4M and HPMC K100M sustains the drug release for a longer time. As expected, the drug release rate was dependent on the viscosity grade and the concentration of the polymer used. Tablets containing combination of HPMC and Carbopol 974P (L12) showed constant drug release up to 24 hr. This controlled release of drug from L12 could be attributed to the formation of a thick gel structure that delays drug release from the tablet matrix.

Thus a formulation L12 was selected as the promising formulation, containing combination of sodium bicarbonate (130 mg) and citric acid (65 mg) with HPMC K4M (32.5 mg), HPMC K100M (65 mg) and Carbopol 974P (21.5 mg), as it achieved optimum *in vitro* buoyancy, floatability of more than 24 hrs as well as controlled and sustained *in vitro* drug release.

Figure: 4 *In vitro* Dissolution profile of batches L1-L12



Kinetic treatment of dissolution profiles

Highest R^2 was observed in Korsmeyer-Peppas model (Table 9) and the n value was found to be 0.0632 which indicates Fickian (diffusion) drug release.

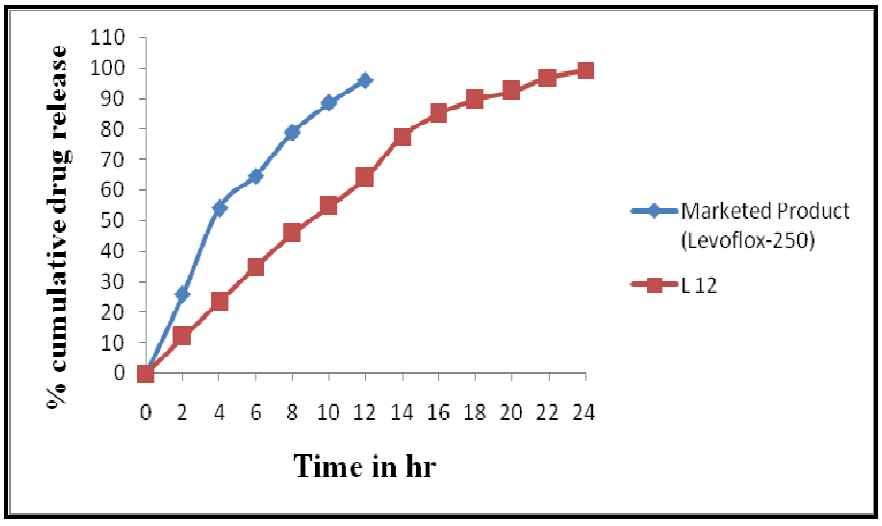
Table: 8 *In vitro* Dissolution profile of batches L1-L12

Batch	% Cumulative drug release at every 2 hrs												
	0	**2**	**4**	**6**	**8**	**10**	**12**	**14**	**16**	**18**	**20**	**22**	**24**
L1	0	35	50	66	75	83.5	89.2	95.7	98.5	----	----	----	----
L2	0	45	64	72	79	86.9	92.3	98.9	----	----	----	----	----
L3	0	58	71	78.4	89.1	92.8	97.4	----	----	----	----	----	----
L4	0	64	79	83.0	90.9	94.8	99.8	----	----	----	----	----	----
L5	0	24	48.7	59.4	72.3	80.9	87.6	92.7	98.4	----	----	----	----
L6	0	28	54.2	70.3	79.8	88.0	95.2	98.7	----	----	----	----	----
L7	0	33.1	55.5	69.7	83.7	92.7	99.2	----	----	----	----	----	----
L8	0	38.8	65.7	74.5	82.5	91.5	97.1	----	----	----	----	----	----
L9	0	51.7	71.2	83.9	90.7	98.6	----	----	----	----	----	----	----
L10	0	60.8	81.7	89.9	97.9	----	----	----	----	----	----	----	----
L11	0	24.7	40.8	52.7	59.8	68.4	76.8	84.1	89.7	95.5	99.8	----	----
L12	0	11.8	23.4	34.8	45.9	54.8	64.1	77.4	84.9	89.7	92.4	96.8	99.1

Table 9 Result of model fitting to optimized formulation (L12)

Model	R^2
Zero order	0.9735
First Order	0.9785
Higuchi	0.9691
Korsmeyer-Peppas	0.9868
Hixson Crowell	0.9554
Weibull	0.9868

Figure: 5 Comparison of *in vitro* dissolution profiles of L12 and Marketed Product



Comparison with marketed product

The promising formulation (L12) as found by evaluation studies was compared with marketed product (Levoflox-250®,Cipla Ltd., India) The comparative *in vitro* dissolution study of optimized formulation (L12) and marketed product are presented in Figure 4.The result showed that the optimized formulation L12 has better control over release rate in comparison to the

commercial product. The marketed product released the drug 96% in 12 hours whereas the optimized formulation L12 released the drug 64.1 % in 12hrs. and the optimized formulation L12 remained floatable in the stomach for 24 hours and give the maximum released 99.1% at 24th hour.

Stability study of optimized formulation (L12)

The optimized floating tablets (L12) were selected for stability study on the basis of *in vitro* buoyancy and *in vitro* drug dissolution studies. The tablets were investigated at 40°C/75% RH for 3 months. From the data, the formulation is found to be stable under the conditions mentioned above since there was no significant change in the percentage amount of drug content (Table 10). Thus, it was found that the floating tablets of Levofloxacin (F12) were stable under these storage conditions for at least 3 months.

Table: 10 Stability study (40 °C/75%RH) of Optimized Formulation (L12)

Evaluation parameters	Initially	After 3 months
Weight variation (mg.)	650±0.2	650±0.2
Hardness (kg/cm^2)	6.0	5.7
% Friability	0.472	0.490
Floating lag time (sec)	52	49
Total floating time (h.)	>24	>24
In vitro % Cumulative drug release (after 24 h.)	99.3	98.1

CONCLUSION

The addition of gel-forming polymer HPMC K4M, HPMC K100M, Carbopol 974P and gas-generating agent sodium bicarbonate was essential to achieve in vitro buoyancy. Addition of citric acid, to achieve buoyancy under the elevated pH of the fed stomach, caused an enhancement in drug release. Polymer swelling is crucial in determining the drug release rate and is also important for flotation. A lesser FLT and a prolonged floating duration could be achieved by varying the amount of effervescent and using different polymer combinations. The in vitro drug release profiles obtained for tablets (L12) made with combinations of HPMC K4M, HPMC K100M, Carbopol 974P showed lesser FLT (<60 s) and a prolonged floating duration (>24hrs) with controlled and sustained release of Levofloxacin. Good stability was observed for 3 months. So the formulation can be scaled up to validate its industrial applicability and can become a promising gastroretentive drug delivery system against *H.pylori* infection.

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