RESEARCH ARTICLE

Vol: 2; Issue: 3

FORMULATION AND EVALUATION OF FLOATING MATRIX TABLET OF LEVOFLOXACIN HEMIHYDRATE

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Date Received:	Date of Accepted:	Date Published:
11-Feb-2014	15-Mar-2014	18-Mar-2014

Abstract:

The objective of the present work was to develop Gastro retentive dosage forms which would remain in the stomach and upper part or GIT for a prolonged period of time thereby maximizing the drug release at desired site within the time before GRDFs left the stomach and upper part of the GIT, has provoked a great deal of increased interest in the formulation of such drug as Floating drug delivery systems. Levofloxacin, (BCS class I) is a fluoro-quinolone anti-bacterial agent. The rationale for the formulation of floating matrix tablet are acidic solubility of levofloxacin, residence of *Halicobactor pylori* mainly in sub region of stomach and the overdosing associated adverse effect due to continuous intake of drug in acute infection. Floating tablet of levofloxacin hemihydrate was prepared by wet granulation method using different hydrophilic and hydrophobic polymers like guar gum, hydroxyl propyl methyl cellulose and Eudragit RS 100, sodium alginate, xanthan gum. Sodium bicarbonate and citric acid was used as gas generating agents. The FTIR spectra of the levofloxacin hemihydrate and Eudragit RS 100, guar gum, hydroxyl propyl methyl cellulose, sodium alginate, and xanthan gum alone and in combination show the compatibility of the drug and excipients. Formulations were optimized on the basis of in- vitro drug release in 0.1N HCL. It was found that the levofloxacin hemihydrate - Eudragit RS 100 (1:1) has given the best dissolution results. The optimized formulation evaluated for physical parameters such as weight uniformity, hardness, friability, drug content, in-vitro buoyancy and swelling index. The release mechanism of levofloxacin hemihydrate from the tablets was non-Fickian.

Keywords: Gastro retentive, Floating matrix tablet, Levofloxacin hemihydrate, Eudragit RS 100, In-vitro buoyancy, Non-Fickian

Introduction

Oral drug delivery is the most preferred and convenient option as the oral route provides maximum active surface area among all drug delivery system for administration of drugs. The attractiveness of these dosage forms is due to ineffectiveness of drugs and awareness to toxicity when administered by oral conventional method in the form of tablets & capsules [1]. Administration of drugs by this route offers ease administration and gastrointestinal physiology offers more flexibility in dosage form design than other routes [2]. These conventional dosage forms provide an immediate release of drug. Such immediate release products results in relatively rapid drug absorption and onset of accompanying pharmacodynamics effects. However, after absorption of drug from the dosage form is complete, plasma drug concentration decline

according to the pharmacokinetics profile of drug. Eventually, plasma drug concentrations fall below the minimum effective plasma concentration, resulting in loss of therapeutic activity. Before this point is reached another dose is usually given if a sustained therapeutic effect is desired [3]. Usually these conventional dosage forms produce wide range of fluctuation in drug concentration in the tissues and bloodstream with consequent undesirable toxicity and poor efficiency and less bioavailability. These factors lead to the concept of oral sustained release drug delivery systems [1].

Sustained release drug delivery systems are designed to achieve extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. The objective in designing sustained or sustained delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. So, sustained release dosage form is a dosage form that release one or more drugs continuously in a predetermined pattern for a fixed period of time, either systemically or to a specified target organ.

One of the most feasible approaches for achieving a prolonged and predictable drug delivery in the GI tract is to control the gastric residence time, by using gastro-retentive dosage forms (GRDFs). Gastro retentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs [4]. To formulate a successful gastro-retentive drug delivery system, several techniques are currently used such as floating drug delivery system, hydro-dynamically balanced systems (HBS), low-density systems, raft systems incorporating alginate gels, bio-adhesive or muco-adhesive systems, super porous hydrogels, high density systems, and magnetic systems [5].

Floating systems or Hydro-dynamically 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 floating system. After release of drug, the residual system is emptied from the stomach. This results in an increased Gastric retention time and a better control of the fluctuations in plasma drug concentration [6].

Levofloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria and show bactericidal activity. It enters in bacterial cells by a process of passive diffusion and interferes with DNA replication by inhibiting an enzyme complex called DNA gyrase[7].The purpose of the present research is to develop a pharmaceutically equivalent, stable, and quality improved floating tablet of levofloxacin hemihydrate to enhance its bioavailability and increase gastric resistance time by using various polymers such as guar gum, eudragit RS-100, xanthan gum, sodium alginate, and Hydroxy propyl methyl cellulose K4M.
Several approaches has been used to increase the gastric retention time of levofloxacin hemihydrates by formation of floating tablets with gum kondagogu, xanthum gum and HPMC K100M [8], HPMC K4M, HPMC K15M, HPMC K100M [9], HPMC and Carbopol 974P [10], HPMC K100M with different amounts [11], Gelucire 43/01 and HPMC [12], HPMC and ethyl cellulose [13], HPMC K100M, Xanthan gum [14], HPMC K4M and HPMC K100LV [15].

EXPERIMENTAL

MATERIALS

Levofloxacin Hemihydrate was obtained as a gift sample from Morepen Laboratories ltd, Solan, Badi. Hydroxy Propyl Methyl Cellulose was obtained from Alembic pharmaceutical ltd., Vadodara. Guar gum was obtained from Central drug house (P) ltd., New Delhi. Xanthan Gum was obtained from Vinubhai agencies pvt. Ltd. Mumbai. Eudragit RS 100 was obtained from Alembic pharmaceutical ltd., Vadodara. Sodium alginate was obtained from Central drug house (P) ltd., New Delhi. All other reagents and solvents used were of analytical grade.

METHODS

Preformulation studies:
Preformulation studies focus on those physiochemical properties of the drug that could affect performance and development of an efficacious dosage form. It is necessary to determine purity of API before formulation any dosage form. Preformulation studies are useful in determining the formulation components and physiochemical properties of new drug substance.

Description of drug
The sample of drug was observed for colour, state and odour.

Drug excipients compatibility study
Before formulating a dosage form it is very necessary to confirm that drug is not interacting with the polymer under certain experimental studies. Interacting among drug and polymer may affect the efficacy of final dosage form.

Drug and different excipients were taken in 1:1 ratio. The excipients used hydroxyl propyl methyl cellulose K4M, eudragit RS 100, guar gum, xanthan gum, sodium alginate. These studies performed from faculty of pharmaceutical sciences Jodhpur National University.

Standard calibration curve

1mg of levofloxacin was dissolved in 10ml 0.1 N HCl to give a solution of 100 µg/ml concentration and this served as the first standard stock solution. From this stock solution 5 ml was taken and diluted to 20 ml using buffer to get a solution of 25 µg/ml concentrations and this solution served as the second standard stock solution. From this second stock solution, the solution containing concentration of (i.e.) 2 ml (5µg/ml), 4 ml (10 µg/ml), 6 ml (15 µg/ml), 8 ml (20 µg/ml) were prepared [16].

Preparation of floating matrix tablet of levofloxacin hemihydrate

Seven different formulation of Levofloxacin Hemihydrate floating tablet prepared by wet granulation method using with different polymers in different ratios. Iso propyl alcohol is used as granulating agent. All the ingredients, previously passed through sieve no. 60 were weighed except magnesium stearate and talc. Levofloxacin Hemihydrate was mixed with required quantities of polymers (HPMC K4M), sodium bicarbonate, citric acid and lactose in mortar for 5 min. Isopropyl alcohol was added drop wise till suitable mass for granulation was obtained. The wet mass was granulated through sieve no. 10 and the wet granules were dried at 50°C for 30 minutes. The dried granules were passed through sieve no. 20 to make uniform sized granules, mixed with lubricants, magnesium stearate and talc. The granules equivalent to 500 mg of drug were weighed and compressed using Single punch machine

EVALUATION

1. Percentage yield

Thoroughly dried granules were collected and weighed accurately. The percentage yield was then calculated using formulae given below,

$$\text{Percentage Yield} = \frac{\text{Mass of granules obtained}}{\text{Total weight of drug, polymer \& excipients}} \times 100$$

2. Determination of drug content

20 tablets were weighed and powdered the powder weight equivalent to 100mg of Levofloxacin hemihydrate was dissolved in 100ml of 0.1N HCl and filtered. 5ml of this was diluted to 50ml with 0.1N HCl and drug content was estimated using UV-Visible spectrophotometer at 326nm.

$$\text{Drug content (\%)} = \frac{G_{act}}{G_{powder}} \times 100$$

3. In vitro Buoyancy Studies

The in vitro buoyancy was determined by floating lag time. The test for buoyancy was usually performed in USP dissolution apparatus containing 900ml 0.1 N HCl at 37^0 C as the testing medium. The time required for the tablet to rise to the surface and float was determined as Floating Lag Time (FLT) and the time period up to which the tablet remained buoyant is determined as Total Floating Time (TFT) [17].

4. In vitro dissolution test

The release of Levofloxacin hemihydrate from the tablet was studied using USP-Type II paddle apparatus. Drug release profile was carried out in 900 ml of 0.1N HCl maintained at 37 ± 0.5°C temperatures at 100 rpm. 5 ml of samples were withdrawn at regular time intervals. The samples was replaced by its equivalent volume of dissolution medium and was filtered through 0.45 µm Whatman filter paper and analyzed at 326 nm by UV spectrophotometer.

TABLET PREPARATION FOR OPTIMIZED FORMULATION:

Evaluation Test of Optimized Formulation

1) Pre-compression parameters

Bulk density

The bulk density of the formulated granules was evaluated using a bulk density apparatus. It is expressed in gm/ml and is given by

$$\text{Bulk Density } (\rho_b) = \frac{\text{Mass of the granules (M)}}{\text{Volume of the bulk powder } (V_b)}$$

Tapped density

It is the ratio of total mass of powder to the tapped volume of powder. The tapped volume was measured by tapping the powder to constant volume. It is expressed in gram/ml and is given by [18]

$$\text{Tapped Density } (\rho_t) = \frac{\text{Mass of the granules (M)}}{\text{Tapped Volume of the powder } (V_t)}$$

Compressibility Index and Hausner Ratio

The Compressibility index and Hausner's ratio are measures of the propensity of a powder to be compressed and the flow ability of granule. Carr's index and Hausner's ratio were calculated using following formula

$$\text{Carr's Index (I)} = \frac{\rho_t - \rho_b}{\rho_t} \times 100$$

$$\text{Hausner's ratio} = \frac{\rho_t}{\rho_b}$$

Where, ρ_t – Tapped density of the powder
ρ_b – Bulk density of the powder

Angle of repose
Angle of repose was determined by Neumann's method and calculated using the formula, for unlubricated as well as lubricated granules.

$$\tan \theta = \frac{h}{r}$$

$$\theta = \tan^{-1} \frac{h}{r}$$

Where, h = height of pile, r = radius of the pile base [19].

2. Post compression parameters

Shape of Tablets
Compressed tablets were examined under the magnifying lens for the shape of the tablets.

Tablet Dimensions:
Thickness and diameter of tablets were measured using Vernier Calipers. It was determined by checking ten tablets from formulation.

Hardness
Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Pfizer hardness tester. It was expressed in kg/cm^2 [18] [20].

Friability
It is performed as per I.P. specification. Maximum loss of weight (from a single test or from the mean of the three tests) not greater than 1.0 per cent is acceptable for most tablets [21].

Uniformity of Weight
It is performed as per I.P. specification. 20 tablets selected for the test.

Swelling index
The floating tablets were weighed individually (designated as W0) and placed separately in glass beaker containing 200 ml of 0.1 N HCl and incubated at 37°C±1°C. At regular 1-h time intervals until 24 h, the floating tablets were removed from beaker, and the excess surface liquid was removed carefully using the tissue paper. The swollen floating tablets were then re-weighed (Wt), and % swelling index (SI) was calculated using the following formula [17].

$$\text{Swelling Index } (\%) = \frac{W_t - W_0}{W_0} \times 100$$

In Vitro Dissolution

The dissolution study was carried out on optimized formulation using USP apparatus type-II. The dissolution medium was 900 ml 0.1N HCl kept at 37±1ºC. The basket was rotated at 50 rpm. Samples of 5 ml were withdrawn at specified time intervals and analysed spectrophotometrically at 326 nm.

Release kinetics
Release kinetic models, which described the overall release of drug from the dosage forms.

Zero-order model

$$Q_t = Q_0 + K_0 t$$

First order model

$$\text{Log } C = \log C_0 - Kt/2.303$$

Higuchi model

$$Q = K_H \times t^{1/2}$$

Korsmeyer-Peppas model

$$Q/Q_0 = Kt^n$$

Where, K_0 to K_H were release rate constants, Q/Q_0 was fraction of drug released at time t, K was a constant and n was diffusion constant that indicates general operating release mechanism. For Fickian (diffusion controlled), $n \leq 0.5$; for non- Fickian (anomalous) release, 'n' value is in between 0.5 to 1.0; for zero order release, n=1.0; for super case transport II, $n > 1.040$. Based on the slope and the R^2 values obtained from the above models the mechanism of drug release was decided [22]

RESULT & DISCUSSION

Description of drug
Various properties of drug related with physical appearance, state, and solubility given in table no. 1.

Drug excipients compatibility study
The possible interaction between drug and excipients were studied by IR spectroscopy. Below spectra shows the peaks of pure drug sample and polymers as compared to standard drug sample that is i.e. no chemical reaction occurs between polymers and drug samples as shown in Figure 1-4.

FTIR was performed on Levofloxacin hemihydrate with all polymers. The IR spectra showed all the principal IR absorption peak of Levofloxacin hemihydrate 3200cm-1, 1442cm-1, 1080cm-1. FTIR of drug and all polymers shows that all the peaks of drug and carrier as it is and drug is present in free form. This indicates that there is no interaction in between drug and the entire polymer employed in formulation.

Analytical Method for levofloxacin hemihydrate using standard calibration curve
Analytical methods were developed for analysis of

Levofloxacin Hemihydrate in powder mixtures, formulations and in solutions of different pH values using UV Spectroscopy. The method obeyed Beer's law and was found suitable for the study. Standard calibration curve of Levofloxacin Hemihydrate in different solvents of varying pH are shown in Figure 5.

Table 1- Description of Drug

S. No.	Properties	Inference
1	Colour	Slight yellow
2	State	Powder
3	Solubility	Slightly soluble in methanol; sparingly soluble in acetic acid and chloroform; soluble in dilute sodium hydroxide solution
4	Taste	Bitter

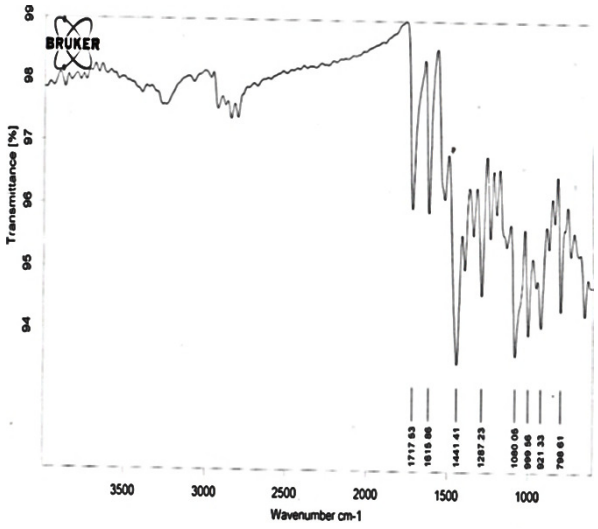


Figure 1: FTIR Spectrum of Levofloxacin Hemihydrate with HPMC and Eudragit RS100 (Immediate)

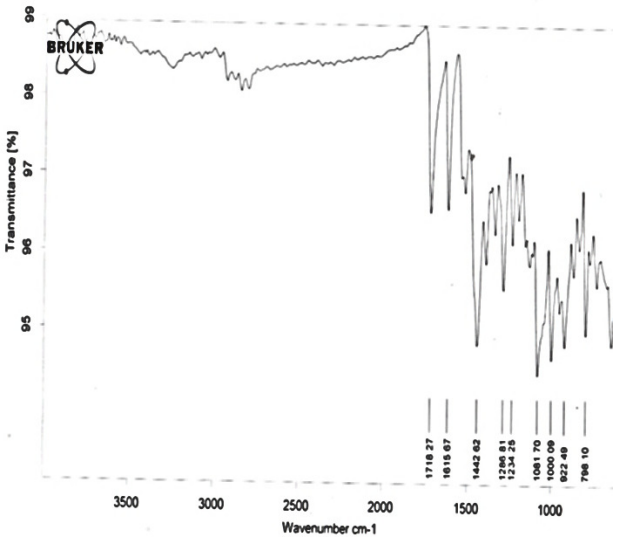


Figure 2: FTIR Spectrum of Levofloxacin Hemihydrate with HPMC and Eudragit RS100 (After 15 days)

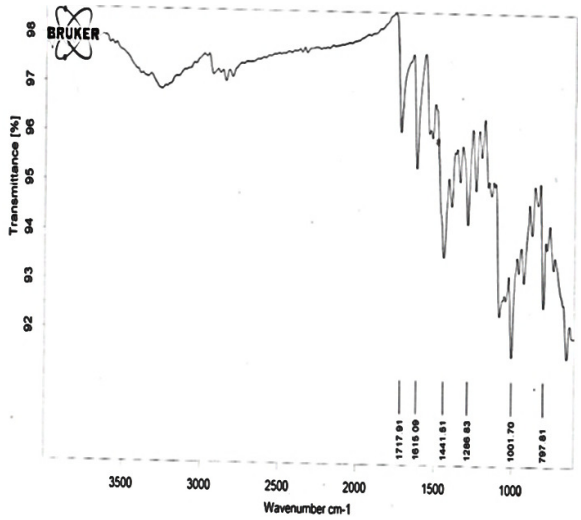


Figure 3: FT IR Spectrum of Levofloxacin Hemihydrate with Xanthan Gum and Guar Gum (Immediate)

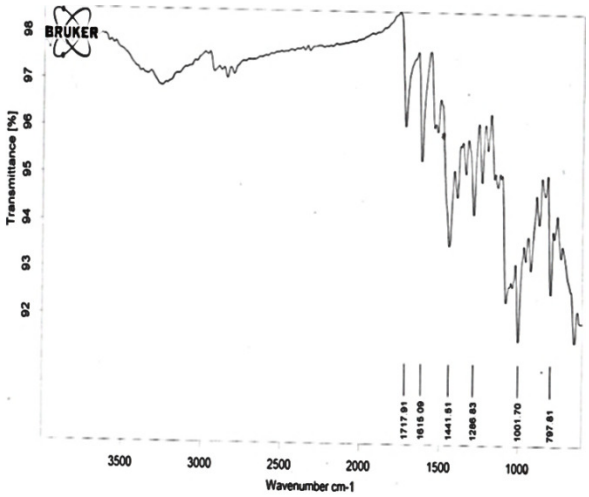
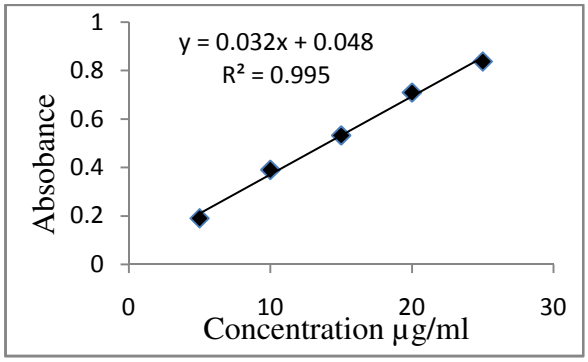


Figure 4: FT IR Spectrum of Levofloxacin Hemihydrate with Xanthan Gum and Guar Gum (After 15 days)



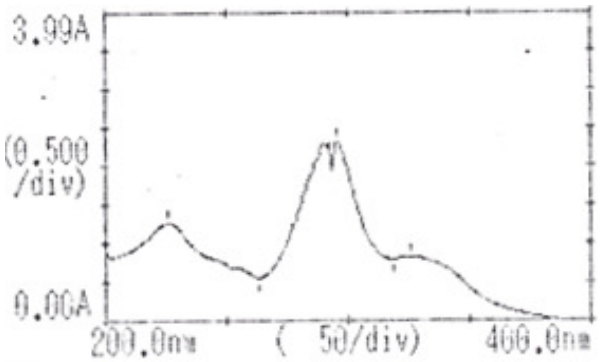


Figure 5- Levofloxacin Hemihydrate calibration curve and UV scan in 0.1 N HCl buffer at 326 nm λ_{max}

Formulation batches:

Table 2- Development of different formulations containing, varying proportions of polymers

Formulation Code	**F_1**	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**	**F_7**
Levofloxacin Hemihydrate	250	250	250	250	250	250	250
HPMC K4M	75	100	100	120	75	100	-
Eudragit RS100	-	-	-	30	75	50	-
Guar gum	75	-	-	-	-	-	75
Xanthan gum	-	50	-	-	-	-	75
Sodium alginate	-	-	50	-	-	-	-
Sodium bi carbonate	70	70	70	70	70	70	70
Citric acid	15	15	15	15	15	15	15
Magnesium stearate	5	5	5	5	5	5	5
Talc	10	10	10	10	10	10	10
Total Weight	**500mg**						

EVALUATION TESTS

1) Percentage yield

Percentage yield of different formulation was determined by weighing the granules after drying. The percentage yield of different formulation showed in table 3 was in range of 65.8- 86.1% as shown in Table. The maximum percentage yield was found in F_5.

Table 3: Percentage yield of the prepared granules

Formulation Batch	Initial Weight of Ingredients (mg)	Theoretical Yield (mg)	Yield of Formulation (mg)	% Yield
F_1	500	500	360.5	72.1
F_2	500	500	405.7	81.1
F_3	500	500	398.1	79.6
F_4	500	500	329.2	65.8
F_5	500	500	430.5	86.1
F_6	500	500	384	76.8
F_7	500	500	416.5	83.3

2) Determination of Drug Content:

Table 4: Drug content of formulation batches

Formulation Batch	Drug Content
F_1	95.87%
F_2	96.23%
F_3	96.33%
F_4	97.73%
F_5	98.36%
F_6	94.12%
F_7	93.09%

Only F_5 formulation complied with the test of levofloxacin hemihydrate content uniformity according to Indian Pharmacopoeia (Table 4), as beside these all formulations fall outside the limit of 98.5-101 %.

3) In vitro buoyancy studies

Table 5: Floating lag time of formulation batches

Formulation Code	Floating lag time (in min.)	Total Floating Time (hours)
F_1	5 min.	> 24
F_2	6 min. 20 sec.	> 24
F_3	4 min.	> 24
F_4	15 min. 20 sec.	> 24
F_5	16 min.	> 24
F_6	15 min. 15 sec.	> 24
F_7	8 min.	> 24

All the Intragastric floating (IGF) tablet formulations were prepared by effervescent approach. From the results, it was observed that floating effervescent tablets float after a certain time and remain buoyant up to 24 hrs without disintegration. The formulations with hydrophilic polymers (F_1, F_2, F_3, and F_7) showed less buoyancy lag time when compared to formulations with hydrophobic polymers (F_4, F_5, F_6). The formulation with combination of hydrophilic and hydrophobic polymers (F_4, F_5, and F_6) showed optimum buoyancy lag time (Table 5). The presence of hydrophobic polymers decreased the solubility of the formulation. Thus with an increase in the concentration of the hydrophobic polymer floating lag time was found to be increased due to decrease in the solubility.

4) In vitro release study

Table 6- In vitro Dissolution Profile of Levofloxacin Floating Tablet in 0.1 N HCl

Cumulative % Release at Different Time Intervals							
Time	**F_1**	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**	**F_7**
5 min.	4.15	3.56	1.25	6.48	2.10	4.56	6.47
10 min.	6.45	4.57	3.57	7.63	3.91	5.89	8.47
15 min.	8.67	6.45	4.45	9.15	4.95	7.42	9.19
30 min.	10.78	8.76	5.76	11.05	9.45	10.14	11.39
45 min.	15.55	12.78	10.78	13.87	12.50	13.01	13.63
60 min.	23.77	15.09	16.09	17.56	15.32	16.73	15.25
90 min.	29.89	20.77	29.88	22.45	20.08	21.58	26.45
120 min.	31.45	26.89	32.90	26.76	23.62	24.19	30.74
3 hrs.	35.36	31.45	38.45	31.45	29.64	31.11	39.67
4 hrs.	57.99	40.01	40.36	36.23	31.29	34.81	45.78
5 hrs.	60.78	64.99	59.12	38.21	33.88	37.38	59.24
6 hrs.	65.89	71.78	63.78	59.03	55.94	57.62	67.15
7 hrs.	76.03	85.89	69.84	70.48	59.47	60.41	76.79
8 hrs.	85.54	95.03	80.46	79.01	65.45	79.15	93.34
10 hrs.	96.98	95.03	94.14	97.38	74.92	91.15	93.34
12 hrs.	96.98	95.03	94.14	97.38	83.82	91.15	93.34

In vitro dissolution studies of all the formulations of floating tablets were carried out in 0.1N HCl solution. It was observed that the type of polymer influences the drug release pattern. These polymers showed sustained release and gastric retention of drug.
Formulations with hydrophilic polymer (F_1, F_2, F_3, and F_7) showed high release of drug when compared to formulations with combination of hydrophobic polymer (F_4, F_5, and F6) showed in table 6. The hydrophilic polymer solubilized more and drug release was high. The hydrophobic polymer solubilized less which retards the drug release to a greater extent. The plot of cumulative percentage drug release V/s time (hr) for all formulations were plotted in Figure 4 respectively.

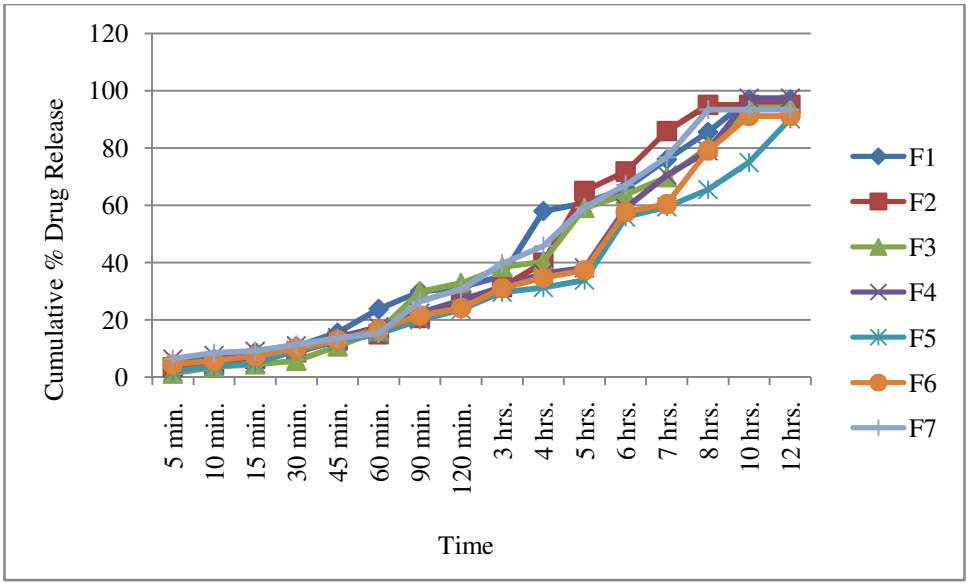


Figure 6- Comparative Dissolution Profile Data of all Formulations

As per as the percentage yield, drug content and dissolution studies are concerned, it indicated that F_5 formulation gives best percentage yield, drug content and shows best dissolution release. By the result observation, it can conclude that F_5 formulation should be a better candidate for floating tablet with best output. So evaluation test of F_5 formulation was performed.

FORMULATION AND EVALUATION TEST OF FINAL FORMULATION:

1. Physical evaluation of prepared granules

Table 7: Physical evaluation of prepared granules containing Levofloxacin hemihydrate and Eudragit RS 100

S. No.	Evaluation	HPMC K4M: Eudragit RS 100(1:1)
1.	Angle of repose	28.18±1.48
2.	Bulk density	0.62
3.	Tapped density	0.71
4.	Compressibility	12.68±0.20
5.	Hausner ratio	1.14±0.0

The values of all physical evaluation tests of tablets are shown in Table 7. Bulk density was 0.62 gm/ml and tapped density value 0.71 g/ml indicates good flow property. Hausner ratio was found to be 1.14. Carr's index was 12.68 % these indicate that the prepared granules exhibited good flow properties. From the results obtained, the angle of repose was 28.18 ±1.48, it indicates excellent flow property.

2. Formulation of tablets of Levofloxacin Hemihydrate with Eudragit RS 100 (1:1)

Tablets of final formulation prepared with wet granulation method using the various ingredients listed in table no. 8 in different quantity as needed.

Table 8: Composition of the Floating Tablet of Levofloxacin Hemihydrate

Formulation Code	F_5
Levofloxacin Hemihydrate	250
HPMC K4M	75
Eudragit RS100	75
Sodium bi carbonate	70
Citric acid	15
Magnesium stearate	5
Talc	10
Total Weight	500mg

Evaluation of final formulation floating tablets

Table 9: Evaluation of prepared tablet

S.No.	Evaluation	HPMC K4M: Eudragit RS 100(1:1)
1.	Average weight (gm.)	0.493±0.0077
2.	Friability (%)	0.46%
3.	Hardness (kg.)	8±1.63
4.	Thickness (cm.)	1.24±0.069
5.	Drug Content	97.44%±0.0092

The tablets prepared were flat faced round with 8mm diameter. All the tablets passed weight variation test as the % weight variation was within the Pharmacopoeias limits of ±5% of the weight. All tablet formulations had acceptable hardness (Table 9). Selected formulation meets the requirements of friability test, hence they are expected to show durability and withstand abrasion in handling, packaging and shipment. The optimized hardness for formulation was such that the tablets would be sufficiently hard to resist breaking during normal handling and yet soft enough to disintegrate after swallowing. Tablet thickness was almost uniform in all the formulations. Formulation complied with the test of levofloxacin hemihydrate content uniformity according to Indian Pharmacopoeia.

Swelling index

Table 10- Results of Swelling Index Studies of Levofloxacin Floating Tablets

Swelling index (%) at Different Time Intervals												
Time (hrs.)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
F5	24	30	38	45	56	63	69	76	81	87	91	95

The swelling index was calculated with respect to times. As time increases, the swelling index was increased, because weight gain by tablet increased proportionally with rate of hydration. The optimized formulations F_5 show maximum swelling index (table 10) hence retarded the release of the drug for a greater time. Swelling index in curve shape shown in figure 7.

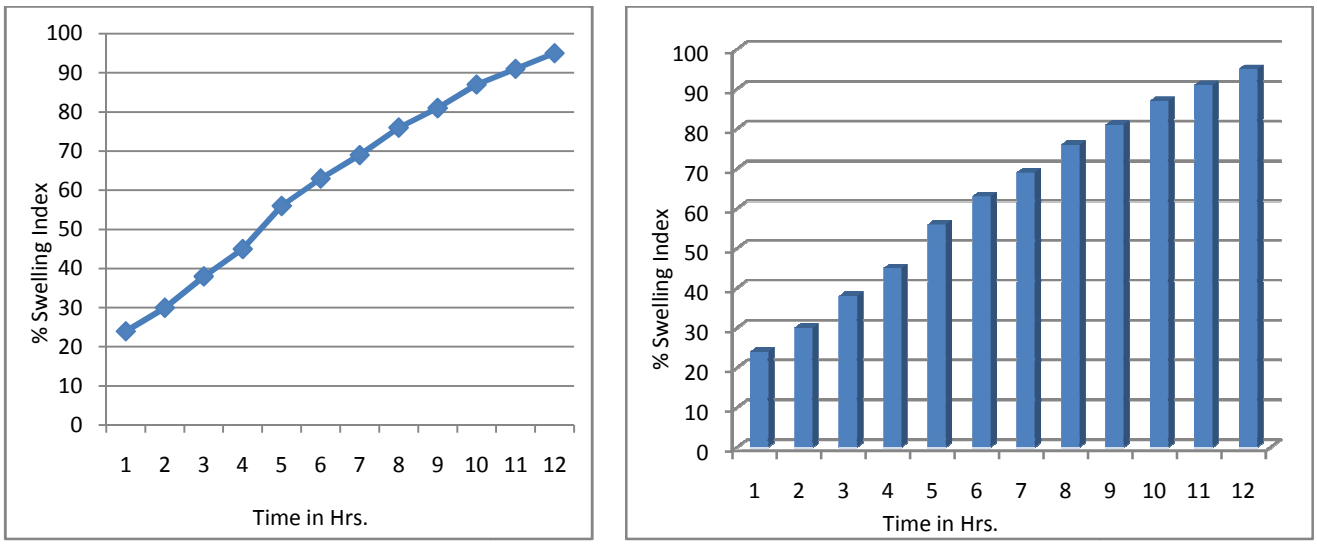


Figure 7: % Swelling Index

In vitro dissolution profile of final formulation

In vitro dissolution study was carried out for floating tablet in 0.1N HCl. The release rate profile was plotted as the percentage levofloxacin hemihydrate dissolved from the floating tablet, verses time. This showed that increase the concentration of hydrophobic polymer give sustained release. The dissolution profile and curve of levofloxacin hemihydrate from F_5 floating tablet presented in table 11 and figure 8.

Table 11: Dissolution of final formulation:

Time	Cumulative % Release
5 min.	2.09
10 min.	4.03
15 min.	6.19
30 min.	11.05
45 min.	15.91
60 min.	22.18
90 min	29.04
120 min	34.89
3 hr.	42.48
4hr.	47.48
5hr.	53.73
6hr.	56.87
7hr.	60.75
8hr.	70.65
10hr.	79.92
12hr.	92.34

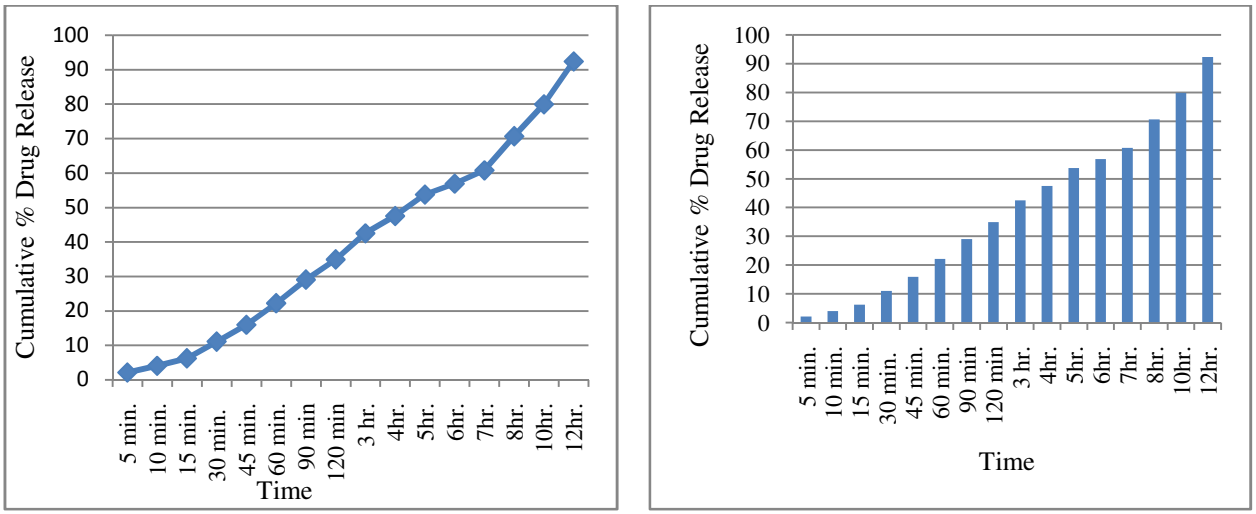


Figure 8: Dissolution Profile of final formulation

Release kinetics

The in vitro release data obtained from Formulation F_5 was fitted to kinetic models. In case of zero order ($Q_t = Q_0 + K_0 t$) the graph was plotted in cumulative percent of drug released versus time and in first order release kinetics (Log C= log C_0- Kt/2.303) the graph was plotted in log cumulative percent of drug remaining versus time. For Higuchi model kinetics ($Q= K_H \times t^{1/2}$) the graph was plotted in cumulative percent of drug released versus squre root of time, and for Korsmeyer-Peppas model ($Q/Q_0 = Kt^n$) the graph was plotted in log cumulative percent of drug released versus log time. The release of levofloxacin from the tablets was diffusion controlled as indicated by highest r^2values in Higuchi model shown in table 12. The n values obtained from the Korsmeyer-Peppas model showed that the release mechanism was non-Fickian.

CONCLUSION

The research was undertaken with the aim to formulate and evaluate the sustained release floating tablets of levofloxacin hemihydrate using hydrophilic and hydrophobic polymers by wet granulation method. The addition of gel forming polymer (HPMC K4M) and gas generating agent sodium bicarbonate were used to achieve the in-vitro buoyancy. From results obtained, it was concluded that the formulation of sustained release floating tablet of levofloxacin hemihydrate containing a combination of both polymers hydrophilic (HPMC K4M) and hydrophobic (Eudragit RS 100) in ratio of 1:4 as ideal or optimized formulation for 12 hours release. It was noticed from the study that increases in the polymer concentration retard the drug release from floating tablet. The micrometric characterizations of the powder blend were in favourable range. The tablets formulated were in acceptable hardness, disintegration time and in vitro release. Thus this can be concluded from the work that such combination can further be used for the development of levofloxacin hemihydrate floating tablet.

ACKNOWLEDGMENT

The author is thankful for the cooperation and facilities provided by the institute with kind permission of **Prof. Sanjeev Thacker**, Director/Principal, Seth G.L. Bihani S. D. College of Technical Education, Sri Ganganagar (Raj). The author is also grateful to the Morepen Laboratories, Chandigarh, Alembic pharmaceutical ltd., Vadodara and Vinubhai agencies pvt. ltd, Mumbai, Central drug house (P) ltd. New Delhi for exgratis samples of, levofloxacin hemihydrate Eudragit RS-100, Xanthan gum and Sodium alginate and guar gum respectively.

Table 12: Release kinetics of levofloxacin from tablet formulations

Zero order (r^2)	First order (r^2)	Higuchi equation (r^2)	Korsmeyer-peppas (r^2)	
			(r^2)	n
0.988	0.8084	0.9563	0.9678	0.691

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