FORMULATION AND EVALUATION OF CONTROL RELEASE GASTRO RETENTIVE FLOATING TABLET OF LEVOFLOXACIN

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ABSTRACT:

The present study concerns the formulation and evaluation of floating tablets of Levofloxacin, which enhance the gastric residence time and drug bioavailability after oral administration. Levofloxacin is a synthetic chemotherapeutic agent used to treat bacterial infections. Formulations were prepared using various polymers like Xanthan Gum, Guar Gum and Karaya Gum by wet granulation technique. Various formulation batches were evaluated for various parameters like weight variation, thickness, hardness, friability, floating lag time, content uniformity and *in-vitro* drug release. The study has revealed that the release rate from floating tablets depends on type and concentration of polymer. The formulations F3 prepared with Xanthan gum (35%) showed higher drug release rate i.e. 98.16% ± 0.9 over an extended period of 12 hours. Hence F3 was considered as best formulations. It is concluded that Levofloxacin floating tablets can be formulated with Xanthan gum, Gaur gum and Karaya gum polymers to achieve gastro retention and controlled release by employing wet granulation technique.

KEYWORDS: Levofloxacin, Gastro retentive, Floating tablet, Guar gum, Xanthan gum and Karaya gum

INTRODUCTION:

Oral controlled drug delivery system have a great potential of solving problems associated with conventional multiple dosing system like strict adherence to timely dosing, flip flop plasma concentration, various side effects due to systemic accumulation of drug. In recent years scientific and technological advancements have been made in the research and development of controlled release oral drug delivery systems by overcoming physiological adversities like short gastric residence time and unpredictable gastric emptying time (Shallusandhan *et al* 2015; Enrico C Nista *et al* 2006).

Gastro Retentive Dosage Form (GRDF):

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 (GRT), i.e. gastro retentive dosage form (GRDF or GRDDS). GRDFs extend significantly the period of time over which the drugs may be released. They not only prolong dosing intervals, but also increase patient compliance beyond the level of existing controlled release dosage form.

Floating Drug Delivery Systems (FDDS) have a bulk density lower than gastric fluids and thus remain buoyant in the stomach for a prolonged period of time, without affecting the gastric emptying rate. While the system is floating on the gastric contents, the drug is released slowly at a desired rate from the system. After the release of the drug, the residual system is emptied from the stomach. This results in an increase in the GRT and a better control of fluctuations in the plasma drug concentrations. Based on the mechanism of buoyancy, two distinctly different technologies i.e. effervescent system and non-effervescent system have been utilized in development of FDDS.

Methods for preparing floating dosage form: Following approaches can be used for preparing floating dosage forms:

- Using gel-forming hydrocolloids such as hydrophilic gums, gelatin, alginates, cellulose derivatives, etc.
- Using low-density enteric materials such as methacrylic polymer, cellulose acetate phthalate.
- By reducing particle size and filling it in a capsule.
- By forming carbon dioxide gas and subsequent entrapment of it in the gel network.
- By preparing hollow micro-balloons of drug using acrylic polymer and filled in capsules.
- By incorporation of inflatable chamber, this contained in a liquid e.g. solvent that gasifies at body temperature to cause the chambers to inflate in the stomach.

MATERIALS AND METHODS:

Materials

Levofloxacin was a gift sample from Dr.Reddy's Pvt. Ltd, Hyderabad. The polymers like Xanthun gum, Karaya gum and Guar gum were procured from Genuine chem.co, Mumbai, India.

Methods:

Preparation of standard curve of Levofloxacin in 0.1N HCl:

The stock solutions was freshly prepared by dissolving 100mg of Levofloxacin in a 100ml volumetric flask and then made up the solution up to the mark for obtaining the solution of strength 1000 µg/ml (stock I). 10 ml of this solution was diluted to 100ml with 0.1N HCl to obtain a solution of strength 100 µg/ml (stock II). From this secondary stock required concentrations 1, 2, 3, 4, 5, 6 and 7 µg/ml was prepared. The absorbance was measured at 294 nm using a UV spectrophotometer.

Fourier Transform Infra-Red spectroscopy (FTIR):

Drug excipients studies hold great importance in designing a formulation. In any drug formulation, it is very essential to analyze the possible interactions between the active compound and the excipients, because the choice of any excipients should be correlate with an efficient the drug delivery, to their compatibility with the same API and also with the stability of the final product. Levofloxacin powder was mixed with different excipients in the ratio of 1:1 and the resulting physical mixture was kept in sealed glass vials. These vials were placed at different temperatures conditions for 3 weeks. Therefore the content of each vial were observed for any change in the physical characteristics. The observation is recorded. Then afterwards those samples were scanned with FTIR over a wave number range from 4000 Cm^{-1} to 400 Cm^{-1}.

Preformulation studies:

Levofloxacin was used with Xanthan gum, Guar gum and Karaya Gum varying concentration of polymers to formulate the floating tablet by using wet granulation method. Sodium bi-carbonate was used to achieve in-vitro buoyancy, PVP was used as binding agent added to achieve desired hardness of tablet, and lactose was used as a diluent in the preparation of tablets. Same quantity of drug was added in each powder blend. The powder blend was then mixed well by using mortar and pestle for 15 to 30 minutes adding to binder solution, and then each mixture was passed through sieve no.16. Finally Talc and magnesium stearate were added and mixed thoroughly, and then each granule blend was stored in polythene bag individually. The batch size for each powder blend was 100 tablets. The granules blend then evaluated for the properties such as loose bulk density, tapped bulk density, carr's compressibility index, hausner's ratio and angle of repose (Sreenivasa reddy N *et al* 2010).

Angle of Repose:

The frictional force in the powder can be measured by the angle of repose. Angle of repose is calculated by fixed funnel method. In this method, the funnel was fixed to a stand so that the lower tip of the funnel was 2.5 cm above the surface; a graph paper was placed on a flat

surface. The blend was allowed to fall freely on the graph paper through the funnel, till the tip of the heap was noted and from this angle of repose was determined.

Angle of repose θ can be calculated the equation as follows:

$$\text{Tan } \theta = h/r \text{ ……..1}$$

Where, h = height of the heap in cm.

r = radius of the heap in cm.

Bulk Density:

Density is defined as weight per unit volume. Bulk density P_b is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of low bulk density. Here the smaller particles shift between the large particles resulting in heavy powder of high bulk density. Apparent bulk density (P_b) was determined by pouring blend into a graduated cylinder. The bulk volume (V_b) and weight of the powder (M) was determined. The bulk density was calculated by using the following formula

$$P_b = M / V_b \text{ …….2}$$

Where,

P_b = Bulk Density

M = Weight of sample in gm

V_b = Final volume of blend in cm^3

Tapped Density:

It is defined as the ratio of total mass of the powder to the tapped volume of powder. The volume was measured by tapping the powder for 500 times. Then the tapping was done for 750 times and the tapped volume was noted. If the difference between the two volumes is less than 2%, this volume is considered as final tapped volume. The tapped density was calculated by using the following formula

$$P_t = M / V_t \text{ ……..3}$$

Where,

P_t = Tapped Density

M = Weight of the sample in gm

V_t = Tapped volume of blend in cm^3

Compressibility Index and Hausner's ratio:

In recent years, the compressibility index and the closely related Hausner's ratio have become the simple, fast, and popular methods of predicting powder flow characteristics. 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. The compressibility index and the Hausner's ratio are determined by measuring the bulk volume/bulk density and tapped volume/tapped density of a powder by following equations.

$$\text{Carr's index} = \frac{\text{Tapped desnity} - \text{Bulk density}}{\text{Tapped density}} \times 100 \quad \ldots\ldots\ldots\ldots\ldots 4$$

$$\text{Hauser's Ratio} = \text{Tapped Density} / \text{Bulk Density} \ldots\ldots\ldots\ldots\ldots 5$$

In a variation of these methods, the rate of consolidation is sometimes measured rather than, or in addition to, the change in volume that occurs on tapping. For the compressibility index and the Hausner's ratio, the generally accepted scale of flow ability is described by carr's.

Formulation of Levofloxacin floating tablets:

Levofloxacin (250mg) was mixed with the required quantities of polymers (Xanthan Gum, Guar Gum and Karaya Gum) (25%, 30%, 35%, 40%), sodium bicarbonate and lactose in a mortar. A binder solution was prepared by taking accurate quantity of (5%) PVPK-30 and dissolved in isopropyl alcohol (IPA). The binder solution was then added to the dry blend gradually with constant kneading to form a homogeneous mass. The dough mass was passed through sieve no.16 and the granular mass was allowed to dry at room temperature. The granules were passed through sieve no.24. The lubrication of granules has been done by the addition of with magnesium Stearate and talc and compressed into then each powder blend was stored in polythene bag individually. The batch size for each powder blend was 100 tablets. After evaluation of powder blends accurately weighed 600 mg powder was fed manually in to Tablets using a 12-station tablet compression machine using a 12-mm standard flat-face die punch set Compression force was kept constant for all formulations. Composition of each tablet is as shown in TABLE I. Then the tablets were evaluated for different properties such as appearance, thickness, hardness, friability, weight variation, floating behavior, drug content and *in-vitro* drug release (P Subhash Chandra Bose *et al* 2011).

TABLE I: Composition of Different Floating Tablets Formulation of Levofloxacin

Formulation Code	D (mg)	X (mg)	G (mg)	K (mg)	S (mg)	L (mg)	IPA (ml)	PVP k30 (mg)	Talc (mg)	MS (mg)
F1	250	150	-	-	60	92	Q.S	30	12	6
F2	250	180	-	-	60	62	Q.S	30	12	6
F3	250	210	-	-	60	32	Q.S	30	12	6
F4	250	240	-	-	60	2	Q.S	30	12	6
F5	250	-	150	-	60	92	Q.S	30	12	6
F6	250	-	180	-	60	62	Q.S	30	12	6
F7	250	-	210	-	60	32	Q.S	30	12	6
F8	250	-	240	-	60	2	Q.S	30	12	6
F9	250	-		150	60	92	Q.S	30	12	6
F10	250	-		180	60	62	Q.S	30	12	6
F11	250	-		210	60	32	Q.S	30	12	6

D-Levofloxacin, X-Xanthan gum, G-Guar gum, K-Karaya gum, S- Sodium bicarbonate, L-Lactose (Filler), IPA-Isopropyl Alcohol, PVP k30 -Polyvinyl pyrrolidone, M S - Magnesium Stearate, Q.S = Quantity Sufficient. All the formulations contained 2% of talc, 1% of magnesium stearate.

Evaluation of floating tablets:

Evaluation was performed to assess the physicochemical properties and release characteristics of the developed formulations. Following parameters were evaluated (Robinson JR *et al* 1987).

Appearance: The tablets were visually observed for capping, chipping and lamination.

Tablet thickness: The thickness in millimetres (mm) was measured individually for 10 pre weighed tablets by using vernier calliper. The average thickness and standard deviation were reported.

Weight variation: To find out weight variation 20 tablets of each formulation were weighed individually using an electronic balance, average weight was calculated and individual tablet weight was then compared with average value to find the deviation in weight. Specifications of % weight variation allowed in tablets as per Indian Pharmacopoeia.

Tablet hardness: For each formulation, the hardness of 10 tablets was determined using the Monsanto hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading was set to be zero kg/cm^2. Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted in kg/cm^2.

Friability: Friability is the measure of tablet strength. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of preweighed tablets was placed in Roche friabilator which was then operated for 100 revolutions. The tablets were then dedusted and reweighed. A loss of less than 1 % in weight is generally considered acceptable. Percent friability (% F) was calculated as follows,

% Friability = (Initial weight - Final weight / Initial weight) x 100…….6

Content uniformity: The formulated Levofloxacin floating tablets were assayed for drug content. From each batch of prepared tablets, ten tablets were collected randomly and powdered. A quantity of powder equivalent to weight of one tablet was transferred in to a 100 ml volumetric flask, 0.1N HCL was added and then the solution was subjected to sonication for about 2 hours. The solution was filtered and suitable dilutions were prepared with 0.1 N HCL. Same concentration of the standard solution was also prepared. The drug content was estimated by recording the absorbance at 294 nm by using UV-Visible spectrophotometer.

In-vitro buoyancy studies:

Here, the tablets were placed in a 100-ml beaker containing 0.1N HCl as shown in FIGURE 1. The time required for the tablet to rise to the surface and float was determined as floating lag time and total duration of time by which dosage form remained buoyant is called Total Floating Time (TFT).

Procedure: The tablet was placed inside the dissolution vessel. 5ml of sample were withdrawn at time intervals of 0.5hr, 1hr, 2hr, 3hr, 4hr, 6hr, 8hr, 10hr and 12hr. The volume of dissolution fluid adjusted to 900 ml by replacing 5ml of dissolution medium after each sampling. The release studies were conducted with 3 tablets, & the cumulative drug release mean values were plotted versus time. Each sample was analysed at 294 nm using double beam UV and Visible Spectrophotometer against reagent blank. The drug concentration was calculated using standard calibration curve (Sheth PR *et al* 1984).

A B C D

Figure 1: Floating lag time (A= initially at 0 sec, B= at 3min, C= at 8 hr, D= at 12 hr)

Mechanism of drug release:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Kinetics of In-vitro Drug Release:

To study the release kinetics of *in-vitro* drug release, data was applied to kinetic models such as zero order, first order, higuchi and korsmeyer- peppas.

RESULTS AND DISCUSSION:

Gastro retentive floating tablets of Levofloxacin were successfully formulated by using low density polymers like Xanthan gum, Guar gum, Karaya gum. All the formulation was subjected to standard evaluation tests.

Preparation of standard curve of Levofloxacin by using 0.1N HCl: The λ_{max} of Levofloxacin in 0.1N HCl was scanned and found to have the maximum absorbance at 294 nm. Standard graph of Levofloxacin in 0.1N HCl was plotted and a good correlation was obtained with R^2 value of 0.998.

FTIR Spectroscopy: An FT infrared (FT-IR) spectroscopy study was carried out to check the compatibility between the drug Levofloxacin and the polymers Xanthan gum, Guar gum and Karaya used for the preparation of Levofloxacin floating tablets. The FT-IR was performed for drug, polymers, and physical mixture of drug and polymers. The spectra obtained from FT infrared spectroscopy studies at wavelength from 4000 cm^{-1} to 450 cm^{-1}. Major functional groups present in Levofloxacin show characteristic peaks in FTIR spectrum. The major peaks are identical to functional group of Levofloxacin. Hence, the sample was confirmed as Levofloxacin. The above FTIR spectra shows the peaks of major functional groups of Levofloxacin, these peaks are nearly unchanged in spectras of Levofloxacin with Guar gum, Levofloxacin with Xanthan gum, Levofloxacin with Karaya gum as compared

with Levofloxacin. So from the above spectras it can be concluded that there is no interaction between Levofloxacin and polymers used in formulation of floating tablet.

Evaluation of powder blend of Levofloxacin (Preformulation studies): The powder blends were prepared by mixing of various ingredients and used for characterization of various flow properties of powder as mentioned in TABLE II.

a) *Angle of repose:* The flow properties of powder were analysed by observing the angle of repose which was found between 26.56°±0.78 to 30.11°±0.04, for all formulations (F1 to F4 with xanthan gum, F5 to F8 with guar gum and F9 to F12 with karaya gum). Those results were indicating a good flow property.

b) *Bulk Density (BD):* As show in the TABLE II, powder blends of formulations have the bulk density ranged between 0.40±0.03 to 0.51±0.06 (gm/cm^3). It shows granules having good flow properties.

c) *Tapped bulk density (TBD):* The powder blends of formulations have the tapped bulk density ranged between 0.45±0.09 to 0.60±0.05 (gm/cm^3).These values are indicate good packing characteristics.

d) *Carr's Compressibility Index:* The Carr's index for all the formulations was found to be in the range of 10.76% to 15.53% indicating that the powders have a good compressibility.

e) *Hausner's Ratio:* As shown in the TABLE II, the Hausner's ratio for all the formulations was found to be <1.25, indicating granules having good flow properties.

TABLE II: Evaluation of Powder Blend of Levofloxacin (Preformulation Studies)

Formulation Code	**Angle of repose (θ)***	**Bulk density (gm/cm3)***	**Tapped Density (gm/cm3)***	**Carr's index (CI)***	**Hausner's ratio (HR)***
F1	22.56±0.78	0.45±0.07	0.49±0.03	10.76±0.03	1.08±0.92
F2	26.68±0.06	0.51±0.06	0.58±0.05	12.06±0.07	1.13±0.90
F3	28.68±0.05	0.50±0.03	0.58±0.05	13.79±0.09	1.16±0.89
F4	30.39±0.01	0.43±0.05	0.51±0.04	14.0±0.05	1.18±0.94
F5	26.68±1.09	0.40±0.09	0.45±0.09	11.11±0.05	1.19±0.84
F6	27.42±0.67	0.43±0.08	0.50±0.04	12.13±0.06	1.16±0.95
F7	28.56±0.08	0.51±0.03	0.58±0.08	12.06±0.08	1.13±0.96
F8	29.71±0.06	0.44±0.02	0.50±0.07	12.02±0.04	1.13±0.93
F9	29.24±0.05	0.51±0.05	0.60±0.05	15.53±0.04	1.17±0.97

F10	30.11±0.04	0.45±0.02	0.53±0.06	15.09±0.05	1.17±0.99
F11	29.21±0.08	0.44±0.04	0.52±0.04	15.38±0.09	1.18±0.92
F12	27.01±0.04	0.40±0.03	0.45±1.05	11.11±0.05	1.12±0.96

*All the values are expressed as a mean ± SD, n=3

Evaluation of Controlled Release Floating Tablet:

The results of all the evaluation parameters are shown in TABLE III (N Sreenivasa Rao *et al* 2011)

i. *Appearance:* The tablets were observed visually and did not show any defect such as capping, chipping and lamination.

ii. *Physical characteristic:* The physical characteristic of Levofloxacin floating tablets (F1 to F12) such as thickness, hardness, friability, weight variation and drug content were determined and results of the formulations (F1 to F12) found to be within the limits specified in official books.

iii. *Thickness:* Thickness and diameter specifications may be set on an individual product basis. Excessive variation in the tablet thickness can result in problems with packaging as well as consumer acceptance. There were no such visible variations in the thickness of tablets within each formulation indicating uniform behavior of granules throughout the compression process. The thickness of the tablets of all formulations was found to be within the range of 4.14±0.27 mm to 4.27±0.35 mm.

iv. *Tablet Hardness:* A difference in tablet hardness reflects difference in tablet density and porosity. In which turn are supposed to result in different release pattern of the drug by affecting the rate of penetration of dissolution fluid at the surface of the tablet and formation of gel barrier and also effecting the floating lag time. The hardness of tablets was found to be in the range of 5.30±0.09 kg/cm^2 to 5.45±0.05 kg/cm^2. This indicates good tablet strength

v. *Percent Friability:* Percentage friability of all the formulations was found between 0.47± 0.06% to 0.68±0.05%. This indicates good handling property of the prepared Floating tablet.

vi. *Weight Variation:* A tablet is designed to contain a specific amount of drug. When the average mass of the tablet is 600 mg the pharmacopoeial limit for percentage deviation is ±5% (601.13± 5.05 to 607.25 ± 4.25). The percentage deviation from average tablet weight for all the tablet was found to be within the specified limits and

hence all formulations complied with the test for weight variation according to the pharmacopoeial specifications.

vii. *Drug content:* The content of active ingredients in the formulation was found to be between 99.92%±0.32 to 101.74%±1.36 w/w, which is within the specified limit as per Indian Pharmacopoeia 1996 (i.e. 90-110% w/w).

viii. *In-vitro buoyancy studies:* Results are shown in TABLE IV. In this study, penetration of water into tablets with low viscosity Karaya gum was slow, causing delayed gel formation and subsequent increase in the floating lag time and decreased total floating duration compared to the tablets prepared with Xanthan gum and Guar gum. F3 showed the best floating lag time of 290 ± 2 s. With the exception of formulations F1 to F12, all the formulated tablets were buoyant for more than 12 hr.

TABLE III: Evaluation Parameters of Controlled Release Floating Tablet

Formulation Code	**Weight Variation (mg)**	**Friability (%)**	**Thickness** (mm)**	**Hardness*** (kg/cm^2)**	**Drug Content* (%)**
F1	602.23±2.07	0.58±0.03	4.21±0.18	5.41±0.06	100.93±0.34
F2	607.25±4.25	0.56±0.06	4.14±0.27	5.32±0.07	99.97±0.39
F3	601.79±2.63	0.65±0.05	4.17±0.09	5.30±0.09	101.74±1.36
F4	605.76±1.49	0.58±0.03	4.21±0.15	5.31±0.06	100.03±0.97
F5	606.82±3.41	0.68±0.05	4.27±0.16	5.40±0.04	99.92±0.33
F6	601.29±2.34	0.64±0.05	4.24±0.05	5.41±0.05	99.98±0.32
F7	610.03±2.97	0.52±0.08	4.25±0.14	5.44±0.06	99.96±0.35
F8	603.34±2.14	0.48±0.09	4.25±0.18	5.36±0.04	99.98±0.36
F9	605.78±1.82	0.56±0.04	4.21±0.19	5.45±0.05	100.05±0.39
F10	602.34±2.13	0.52±0.02	4.16±0.14	5.44±0.06	99.92±0.32
F11	601.59±2.29	0.47±0.06	4.20±0.18	5.44±0.04	99.95±0.37
F12	604.54±3.84	0.52±0.05	4.27±0.35	5.42±0.08	99.78±1.36

* All the values are expressed as a mean ± SD, n=3, **n=5, ***n=6.

TABLE IV: Floating Lag Time and Total Floating Time

Formulation Code	Floating Lag Time (sec)	In vitro Total Floating Time (Hrs)
F1	305±6	>12
F2	315±4	>12
F3	290±2	>12
F4	330±7	>12
F5	275±8	>12
F6	294±6	>12
F7	315±3	>12
F8	323±7	>12
F9	325±5	>12
F10	330±4	>12
F11	328±9	>12
F12	356±8	>12

In-Vitro Dissolution Studies

The *In vitro* dissolution study of formulations F1, F2, F3 and F4 that containing 25%,30%,35% and 40% of xanthan gum respectively, were able to controlled the drug release for 10,11 and 12hr respectively done in 0.1N HCl and the percent of drug release from formulation were 97.76%, 96.37%, 98.16% and 88.28% respectively. Formulation F3 obtained the desired drug release profile and floated with a lag time of 290 sec, for these reasons it was considered as the best formulation among four the formulation.

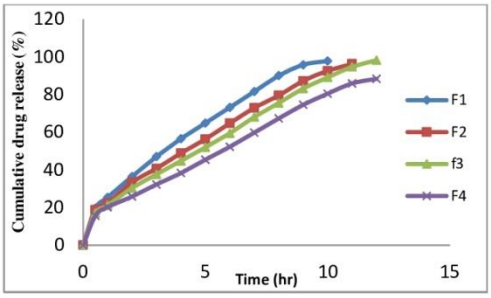

Figure.2. Plot of % Cumulative drug release vs. time in hrs (F1-F4)

Invitro dissolution study of formulations F5, F6, F7 and F8 were also done in 0.1N HCl and the percent drug released was calculated. These four formulations prepared with Guar Gum containing 25%, 30%, 35% and 40% and the percent of drug release from formulation were 97.10% (9hr), 98.15% (11hr), 91.95% (12hr) and 82.28% (12hr) respectively. Formulation F7 obtained the desired drug release profile and floated with a lag time of 323 sec, for these reasons it was considered as the best formulation among four the formulation.

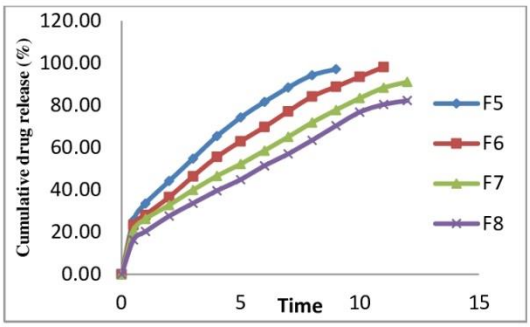

Figure.3. Plot of % Cumulative drug release vs. time in hrs (F5-F8)

Invitro dissolution study of formulations F9, F10, F11, F12 were also done in 0.1N HCl and the percent drug released was calculated. These four formulations prepared with Karaya gum low viscosity polymer containing 25%, 30%, 35% and 40% and the percent of drug release from formulation were 97.45% (8hr), 99.01% (10hr), 94.81%(11hr) and 90.78%(12hr) respectively. Formulation F12 obtained the desired drug release profile and floated with a lag time of 356 sec, for these reasons it was considered as the best formulation among four the formulation in all the formulations, polymer concentration greatly affected the release of the drug. The drug release rate was inversely proportional to the polymer concentration present in the matrix.

From the above evaluation parameters it was concluded that the formulation F3 having a high percentage of drug release in a sustained manner, so the formulation F3 was selected as the best formulation.

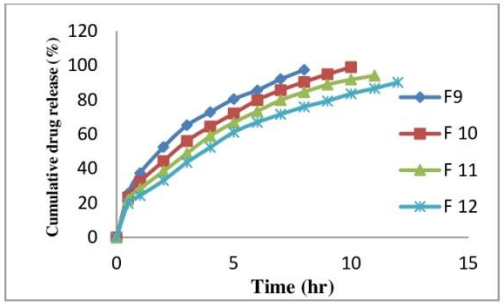

Figure.4. Plot of % Cumulative drug release vs. time in hrs (F9-F12)

In vitro release kinetics studies Data Analysis (Curve Fitting Analysis)

To study the release kinetics of Levofloxacin floating tablets, the goodness-of-fit method was applied and different kinetic equations were applied to interpret the release rate from matrices. The linear nature of curves obtained for zero-order and first order, or Higuchi model and Korsemeyer-Peppas model as demonstrated by very close and higher R^2 values suggests that the release from the formulations may follow any one of these models.

All the kinetic *invitro* dissolution profiles were fitted into zero, first, Higuchi, release was Peppas equation. All the floating tablets showed highest linearity with Higuchi equation followed by Zero order and first order, According to Peppas equation the plots of all formulations showed highest linearity. The release exponent "n" values are having indicating. The controlled release device *n* is the release exponent indicative of the drug release mechanism. For tablets of a known geometry (in this case a slab) $n = 0.5$ means Fickian diffusion, $0.5 < n < 1.0$ non-Fickian diffusion, and $n = 1.0$ case II diffusion. Regarding the *n* values calculated for the studied tablets (TABLE V), in most cases a non-Fickian mechanism was found to be predominant, which indicated that water diffusion as well as polymer rearrangement played an essential role in drug release.

TABLE V: *In Vitro* Release Kinetics of Levofloxacin Effervescent Floating Tablets Mean ± S.D (n=3)

Formulation Code	R2				N
	Zero order	First order	Higuchi	Korsemeyer-Pappas	
F1	0.965	0.9305	0.9909	0.9907	0.539
F2	0.9754	0.9482	0.9835	0.9808	0.508
F3	0.9808	0.956	0.9997	0.9859	0.623
F4	0.9949	0.9619	0.9764	0.9833	0.539
F5	0.9414	0.9492	0.9976	0.9916	0.682
F6	0.9576	0.9678	0.9859	0.9852	0.634
F7	0.9576	0.9678	0.9859	0.9852	0.578
F8	0.9747	0.9687	0.9853	0.984	0.648
F9	0.9969	0.9418	0.9971	0.9964	0.589
F10	0.9294	0.9858	0.9976	0.9987	0.549
F11	0.9336	0.99	0.9973	0.9988	0.543
F12	0.9364	0.9968	0.9954	0.9849	0.505

CONCLUSION:

It is concluded that hydrophilic polymers could be a better choice for formulating controlled release floating tablets of Levofloxacin. The investigated controlled release floating tablet was showing good drug release upto 12 hours which indicated the ability to maintaining a constant plasma drug concentration for prolong time. The study also revealed that the release rate of drug was retarded by increasing concentration of polymer, and hence the results confirmed that the release rate of levofloxacin from the prepared floating tablets was depend on the type and concentration of various polymers. It has been confirmed in this investigation that the tablets prepared with Xanthan gum, Guar gum and Karaya gum retarded the release rate of drug. The formulations F3 prepared with Xanthan gum (35%) showed higher drug release rate respectively over an extended period of 12 hours. Hence F3 was considered as best formulations. Finally, it is concluded that Levofloxacin floating tablets can be formulated with Xanthan gum, Gaur gum and Karaya gum polymers to achieve gastro retention and controlled release by employing wet granulation technique.

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