

Formulation and Evaluation of Floating Tablet Levofloxacin

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Abstract

Drifting medicate conveyance framework may be a framework to held the sedate within the stomach which is pertinent as it were for ineffectively solvent and less steady in intestinal liquids. It is premise on the thick on gastric liquids which is coast on gastric liquids. Coasting tablet Definitions of levofloxacin were arranged by basic mixing and punching with carbopol, HPMC K4M, sodium bicarbonate, citric corrosive and conversation for verbal application. Levofloxacin is an anti-microbial sedate having higher protein authoritative, hepatic digestion system moo verbal bioavailability and lower half life. The medicate requires a medicate conveyance framework that gives a arrangement of these issues and makes strides bioavailability. Arranged drifting clusters were characterized for compatibility ponder, pre compression and post compression assessment, % sedate substance, in-vitro sedate discharge. Major focal points of the framework incorporate ease of planning, tall % sedate discharge and long length over 12 hours. From this consider, it was concluded that drifting tablet batch F3 offers way better supported discharge in ceaseless way that supportive to preserve bioavailability for long length and decreases recurrence of dosage, too diminishes dosage.

Keywords: Drifting, tablets, leavofloxacin, Carbopol.

Introduction

➤ **Gastroretentive Drug Delivery Systems (GRDDS)**

Gastroretentive sedate conveyance frameworks (GRDDS) have been found to be a promising approach in conveying drugs to the stomach for a drawn out period time, possibly moving forward the adequacy of drugs in annihilating H. pylori. By drawing out the gastric home time, these frameworks can improve medicate accessibility, diminish dosing recurrence, and eventually progress quiet compliance. In expansion, the location of H. pylori disease, which is the gastric bodily fluid layer, is particular, can be focused on by GRDDS for ideal sedate conveyance. By expanding the sum of medicate conveyed to this location, higher concentrations can be accomplished, expanding the probability of bacterial destruction. Furthermore, GRDDS can moreover secure drugs from gastric chemicals and acidic conditions that can lead to medicate debasement, which may restrain the viability of customary medicate conveyance frameworks [1-2]

➤ **Floating Tablets**

Coasting tablets are a novel strategy for gastroretentive sedate conveyance, which is particularly advantageous for drugs with a limit retention window within the gastrointestinal tract. These tablets are designed to drift within the intestine for an expanded period of time, in this manner upgrading drug release and assimilation. Gastroretentive medicate conveyance systems (GRDDS) have been made to extend the length of medicine maintenance within the stomach, and coasting tablets are a well known approach due to their ease of definition and moo fetched. They are defined with different excipients such as foaming specialists, gas-generating specialists, and hydrophilic polymers, that make gas bubbles, which increment the tablet's buoyancy. These tablets have appeared promising comes about in expanding medicate bioavailability, diminishing dosing recurrence, and moving forward understanding compliance. In later a long time, broad inquire about has been carried out to optimize the formulations of drifting tablets and investigate their potential for conveyance of different drugs. This survey points to summarize later improvements within the planning and assessment of drifting tablets, their instruments of floatation, and their applications in sedate conveyance. Coasting tablets have developed as a promising approach for annihilation of *Helicobacter pylori* (*H. pylori*) diseases in stomach due to their interesting focal points. Firstly, they are simple to define utilizing ordinary strategies, making them a cost-effective choice for medicate conveyance. Besides, they permit for site-specific medicate conveyance, upgrading the nearby concentration of medicate and diminishing systemic side impacts. Thirdly, they enable prolonged conveyance of drugs, guaranteeing supported discharge and drawn out activity of the pharmaceutical [3].

➤ **Advantage of Floating Tablets in *H. pylori* Eradication**

Coasting tablets have developed as a promising strategy for the destruction of *H. pylori* diseases within the stomach due to their interesting benefits. Firstly, they are simple to define utilizing customary procedures, making them a cost-effective alternative for sedate conveyance. Furthermore, they permit for site-specific medicate conveyance, improving the nearby concentration of medicate and lessening systemic side impacts. Thirdly, they empower to control conveyance of drugs, guaranteeing maintained discharge and delayed activity of the pharmaceutical. Moreover, drifting tablets can be outlined to provide drugs for remaining stomach activity at a specific location, giving progressed medicate retention through expanded gastric maintenance time (GRT) and overabundance term of contact at its target location. This minimizes the bothering of gastrointestinal mucosa by drugs with a slow-release rate. Moreover, delayed discharging coasting measurement frame can cause tall disintegration of the sedate in gastric liquid, moving forward its assimilation and viability. Coasting tablets are also beneficial when there's incredible intestinal movement with a brief travel time, because it keeps up the sedate in a coasting condition within the stomach for superior viability. At last, their ease of organization and higher understanding compliance make them a favored alternative for sedate conveyance [4].

➤ **Formulation Strategies of Floating Tablets**

Effervescent Floating Tablets

The utilize of foaming operators and unstable fluids in drifting frameworks is known as bubbling drifting tablets. These frameworks regularly contain gas-generating specialists such as tartaric corrosive or citric corrosive, sodium bicarbonate, calcium carbonate, together with hydrophilic polymers. The foaming specialist responds with gastric fluid to discharge CO₂ gas, which is at that point captured within the

hydrocolloid framework. This handle gives buoyancy to the tablet and impacting the medicate discharge properties [5]. Drifting bubbling frameworks can be assist classified as single-layer, double-layer, or multiple-unit tablets. Single-layer tablets contain the foaming substance, sedate, polymer, and excipients, whereas in double-layer tablets, one layer contains the polymer, sedate and CO₂ gas-generating specialist, and the other layer contains an immediate-release sedate and excipients without CO₂ and polymer [6]. Foaming coating tablets have been detailed to extend gastric home time, neighborhood medicate conveyance, and drag out the sedate discharge. They too offer assistance minimize the bothering of the gastrointestinal mucosa by drugs with slow-release rate and progress sedate retention by expanding the GRT and the time of contact of the measurement regimen at its target location. In addition, the organization of prolonged-release coating dose frame, such as bubbling tablet, can keep up sedate in coating condition within the stomach range, which is especially invaluable beneath conditions of brief travel time due to incredible intestinal development that might lead to destitute retention [7]. The effortlessness of administration and higher quiet compliance are extra benefits of foaming coating tablets. This approach is known as effervescent-swelling system, which combines the benefits of both effervescence and swelling components to preserve drawn out gastric maintenance and maintained medicate discharge. The effervescent-swelling framework contains an bubbling specialist and a swellable polymer, which are planned to generate CO₂ gas and frame a gellike structure within the nearness of gastric liquid. The CO₂ gas produced from the foaming response is caught inside the swollen polymer framework, making a permeable structure that permits the dosage shapes to drift on the gastric substance. The effervescent swelling framework can be outlined as single-unit or multiple-unit dose shapes. Singleunit effervescent-swelling tablets are regularly arranged by mixing the medicate, foaming specialists, swellable polymer, and other excipients taken after by compression into tablets.

Non- Effervescent Floating Tablets

Non-effervescent medicate conveyance frameworks utilize gel-forming polymers or cellulose subsidiaries that have tall swelling properties. These polymers are mix with the sedate to make different frameworks such as HBS, single- and double-layer drifting tablets, and smaller scale balloons/hollow microspheres. HPMC, HPC, hydroxyethyl cellulose, sodium carboxymethylcellulose, carrageenan, agar, and alginic corrosive are illustrations of gelforming hydrophilic polymers found in HBS [08]. To make coating tablets, the substance and hydrophilic polymers are consistently combined. The polymer swells upon contact with gastric liquid, diminishing the bulk thickness of the tablet to 1 g/cm³, and the low-density framework coasts on the gastric liquid, subsequently amplifying the gastrointestinal home time (GRT). HPMC, polyethylene oxide, HPC, and cellulose acetic acid derivation phthalate are as often as possible utilized hydrophilic polymers in drifting tablets. Analysts have created bilayer coating tablets comprising of a sedate layer with prompt discharge and a layer with maintained discharge. The immediate-release layer contains a deteriorating specialist for fast sedate discharge, though the sustained-release layer contains a hydrophilic polymer to control the sedate discharge rate and deliver the tablet buoyancy. Multiple-unit, drug-loaded miniaturized scale balloons/microspheres are delivered by basic solvent vanishing or dissolvable dissemination strategies, and they coast within the encompassing discuss. Smaller scale inflatables are regularly made from low-methoxylated pectin, cellulose acetic acid derivation, polycarbonate, Eudragit S, calcium alginate & agar [9].

Material and Method

Material

S.NO	MATERIALS
1	HPMC K100M (Hydroxy propyl methyl cellulose)
2	HPMC K4M (Hydroxy propyl methyl cellulose)
3	Levofloxacin
4	Xanthan gum
5	Citric acid
6	Sodium Bi Carbonate
7	Microcrystalline Cellulose
8	Magnesium stearate
9	Guar gum

Table 1: List of materials used.

➤ EQUIPMENT

S.No.	Equipments.	Manufacturer.
1	Digital balance	Sieve Tec (CWC Series)
2	UV Spectrophotometer	Labindia-UV 3000 ⁺
3	Tablet punching machine	Proton mini press
4	Vernier calliper	Praga (TM)
5	Hardness tester	Swastika India
6	Friabilator	Praga (TM)
7	USP dissolution apparatus	Labindia Disso 2000

8	FT-IR Spectrometer	Shimadzu
9	Stability chamber	Rolex

Table 2: List of instruments used in the research work.

➤ **Formulation of levofloxacin floating tablets [17]**

Levofloxacin drifting tablets were defined utilizing HPMC K100M, HPMC K4M, xanthan gum, sodium bicarbonate, citric corrosive, microcrystalline cellulose, and magnesium stearate in Part-I (F1-F7), and HPMC K100M, Guar gum, HPMC K4M, , sodium bicarbonate, microcrystalline cellulose, citric corrosive and magnesium stearate in Part-II (F16-F30). citric corrosive and Sodium bicarbonate were utilized as coating specialists, whereas HPMC K100M, Guar gum, Xanthan gum and HPMC K4M served as discharge control polymers and covers. Magnesium stearate was utilized as a grease. The coordinate compression strategy was utilized for tablet planning. Levofloxacin and all other excipients, but the grease, were completely mixed and sieved to get a uniform molecule estimate. Along these lines, the grease and glidant were blended to the mix and blended for 15 minutes. The blend was at that point compressed employing a 10-station rotational tablet compression machine (PROTON Scaled down PRESS) with a standard flat-face punch of 9 mm breadth.

Ingredients [mg]	F1	F2	F3	F4	F5	F6	F7
Levofloxacin.	250	250	250	250	250.	250	250
HPMC K4 M.	60.	80	40	80	80	40	60
HPMC K100 M	45	45	60	60	30	45	60
Gouar gum	30	45	30	30	30	15	15
Sodium bicarbonate.	50	50.	50	50	50	50	50.
Citric acid	20	20	20	20	20.	20	20
Microcrystalline Cellulose	40	5	45	5	35	75	40.
Magnesium Stearate	5	5	5	5.	5	5	5
Total [mg]	500	500	500	500	500	500	500

Table 3: Formulation Table for Levofloxacin floating tablets using gour gum and HPMC polymers blend.

Expermental Work.

- **Preformulation Study**
- **Drug polymer Compatibility studies:**

Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) was used to study the compatibility of Levofloxacin with excipients.

➤ **Fourier transform infrared (FTIR) spectroscopy [10,11]**

FTIR spectra of Levofloxacin, excipients, and physical blends with a medicate to excipient proportion of 1:1 gotten within the wavelength extend of 500- 4,000 cm^{-1} utilizing an FTIR 8400S instrument (Shimadzu, Japan). For investigation, a little amount of the substance was set on a potassium bromide (KBr) salt plate. The tests were at that point uniformly and meagerly compressed employing a water powered press to guarantee reproducibility of the spectra gotten. The salt plate containing the test was embedded into the FTIR spectrometer and calibrated to optimize the signal-to-noise proportion. Infrared radiation was coordinated throughs the test, and the resulting absorption range was recorded. The crests watched within the assimilation range compared to the chemical bonds display within the test. The positions and power of these highlights were analyzed to recognize utilitarian bunches and characterize the chemicals of the tests .

➤ **Differential scanning calorimetry (DSC) [12,13]**

DSC measurements of Levofloxacin and physical mixtures with a drug-to-excipient ratio of 1:1 was conducted using a differential scanning calorimeter (DSC 204 F1 Phoenix®). Samples weighing 5 mg were put in aluminium pan and sealed. The pans, one containing the sample and the other empty serving as a reference, were loaded into the DSC instrument. The temperature was gradually varied at a controlled rate, starting from ambient temperature, and increasing up to 400 °C, with a heating rate 10 °C/min, all under a nitrogen atmosphere flowing at a rate of 50 ml/min. During the heating process, the DSC instrument measured the heat flow of the sample pan relative to the reference pan. The resulting DSC curve represented the heat flow as a action of temperature. This curve exhibited distinct features such as endothermic or exothermic peaks, which indicated changes in the thermal characters of the sample.

➤ **UV spectroscopy [14]**

UV spectroscopy estimations were assessed employing a Shimadzu UV-1800 spectrophotometer (Japan). A standard stock arrangement containing Levofloxacin at a concentration of 100 $\mu\text{g/ml}$ was arranged in 10% (v/v) acetonitrile. Diverse aliquots were examined from the stock arrangement and weakened to the 10 ml with the same dissolvable to get a arrangement of concentrations. These solutions were at that point checked employing a UV-visible spectrophotometer (Shimadzu-2450) within the wavelength range of 200-400 nm. The gotten UV-Vis spectra of Levofloxacin are appeared within the Figure... and summarized in Table... The absorbance maxima of Levofloxacin were watched at 295 nm [93].

➤ **Standard calibration curve of Levofloxacin in 1.2 pH buffer [15]**

For the Levofloxacin standard calibration bend in 1.2 pH buffer, 100 mg of immaculate Levofloxacin was precisely weighed and blended in 100 ml of 0.1N HCl. From this arrangement, 10 ml was advance weakened to the 100 ml check with the same dissolvable, coming about in a 100 $\mu\text{g/ml}$ Levofloxacin standard arrangement. Along these lines 2, 4, 6, 8,10 ml aliquots were taken from this arrangement and exchanged to 10 ml standard carafes, which were at that point filled with 0.1N HCl to get arrangements with concentrations of 2, 4, 6, 8,10 $\mu\text{g/ml}$. The absorbances of these tests were examined at 295 nm. A clear arrangement utilizing 0.1M HCl was utilized for investigation

➤ **Angle of repose [16]**

The fixed funnel method involves the use of a funnel is securely positioned with its tip at a pre-determined height h. In these methods, the funnel is placed 2 cm above a sheet of graph sheet is laid flat on a horizontal surface. By measuring the conical shape pile radius (r) in the bottom of the formed and using the equation, the angle of repose can be found:

$$\text{Angle of repose} = \tan^{-1} (h/r)$$

Where, h – height of the pile, and r is the radius of the bottom of the pile.

➤ **Tapped density and Bulk density.**

Both the Tapped thickness and Bulk thickness were measured. To decide these densities, 2 grams of the physical blend from each definition, which had been marginally shaken to break any agglomerates shaped was set into a 10 ml measuring barrel. The beginning volume was recorded, and after that the barrel was permitted to drop unreservedly from a tallness of 2.5 cm at 2-second interims, utilizing the wt. of the barrel itself. The tapping was continued until no another alter within the volume was famous TBD and LBD were calculated utilizing taking after equations:

LBD= Weight of the powder/ powder volume pressed.

TBD= Weight of the powder/Tapped volume pressed

➤ **Compressibility index**

The compressibility index of the prepared granule was determined by Carr's index following the equation,

$$\text{Carr's index (\%)} = [(TBD - LBD) * 100] / TBD$$

Where,

TBD= Weight of the powder/Tapped volume packed.

LBD= Weight of the powder/ volume packed.

Evaluation of floating tablets of Levofloxacin using HPMC K100M, HPMC K4M and gouar gum.

➤ **Visual Inspection**

The tablets were outwardly assessed to survey their surface surface and check for any absconds such as capping (Tablet crowns might part somewhat or totally.), cover (division of tablet layers), mottling (unequal colour dispersion), picking, and staying.

➤ **Weight Variation**

Twenty tablets were arbitrarily assessed from each bunch and exclusively weighed. Tablet weight normal group was calculated, and the rate deviation from the normal weight was decided for each tablet taking after IP 2010 rules.

➤ **Thickness**

The thickness of all batches was measured by a vernier calliper to evaluate the uniformity of tablet batches.

➤ **Hardness and Friability**

The degree of hardness of the floating tablet batch was measured in kg/cm² using a Monsanto hardness testing apparatus. Six tablets were randomly selected from each formulation and mean, and standard deviation measurements were calculated [103].

➤ **Friability Test**

The friability of the tablet group was evaluated utilizing Roche's Friabilator. A tablet weighing a indicated sum was put within the Friability device and pivoted for 100 transformations at 25 rpm. After the test, the tablets were cleaned to evacuate any following powder and weighed. The rate friability was dissected utilizing the equation:

% Friability = (Weight introductory - Weight last) / Weight beginning. The rate friability ought to be underneath 1% [103].

➤ **Floating Lag Time .**

The floating behavior of the tablets was assessed visually, in triplicate, utilizing the FLT method outlined by Rosa et al. [24]. Five separate floating tablets were positioned in flasks containing 400 ml of 0.1 N HCl. The duration taken for each tablet to rise from the bottom to the surface of the flask was recorded. The sample mean, standard deviation, and coefficient of variation were computed.

➤ **Swelling Index [18]**

The swelling behavior of the tablets was assessed in triplicate following the method outlined by Dorozynski et al. A tablet was placed in a glass beaker containing 200 ml of 0.1 N HCl maintained at 37± 0.5°C and weighed (W1). At regular intervals, the tablet was taken out, excess surface liquid was removed with filter paper, and the weight of the swollen tablet was measured again (W2). The swelling index (SI) was calculated using the following formula:

$$SI = (W2 - W1) / W1$$

➤ **In-vitro drug release profile [19]**

The release of levofloxacin was studied using USP Dissolution II (DS 8000, Lab India, India) in 900 millilitres of 0.1 N HCl maintained at 37 ± 0.5°C with a speed of 50 revolutions per minute. Aliquots of 5 millilitres were taken at specified predetermined time intervals and make replaced with a same volume of freshly produced medium. The resulted samples were evaluated using a UV-VIS double beam spectrophotometer at 295 nm (Elico SL 164, India). The release studies were done in triplicate, and the results were expressed as mean ± SD. The time required to release of the drug 90% from tablet (T90%) was calculated and recorded in the table.

Results

- Preformulation study for part i formulation
- Drug excipient Compatibility study by Fourier transform infra-red (FTIR) analysis.

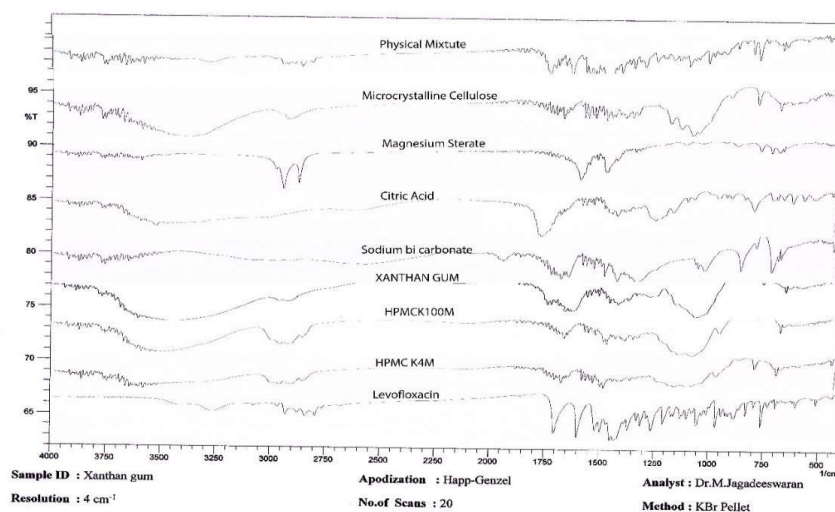


Fig 1: FTIR spectra of Levofloxacin, Excipients (individual) and Physical mixture

- Drug excipient Compatibility study by DSC analysis

The findings are illustrated in Figure 1. The FTIR spectrum of Levofloxacin (the pure compound) displays distinct peaks at 3266 cm⁻¹ corresponding to the carboxylic group, 2933 cm⁻¹ related to the stretching of alkanes, 1724 cm⁻¹ attributed to the carbonyl group stretch, and 1295 cm⁻¹ associated with the stretching of amines, along with a peak at 1100/1400 cm⁻¹ indicative of a halogen group (see Fig. 1). These results align with those reported by Numan R S et al., supporting the identification and purity of Levofloxacin. The physical mixture maintains the key peaks of the FTIR spectrum for the purified drug without any notable shifts. This indicates that there are no interactions between the drug and excipients or any incompatibilities during processing.

- Drug excipient Compatibility study by DSC analysis

Endothermic peaks of DSC thermograms Levofloxacin Showed a melting point 224.6°C [14]. The sharp endothermic at 222.7°C corresponds to the Levofloxacin melting point and was retained in all the thermograms of 1:1 w/w physical mixtures of the Levofloxacin and selected excipients. DSC experiments showed that Levofloxacin did not interact with any excipients and was stable during formulation.

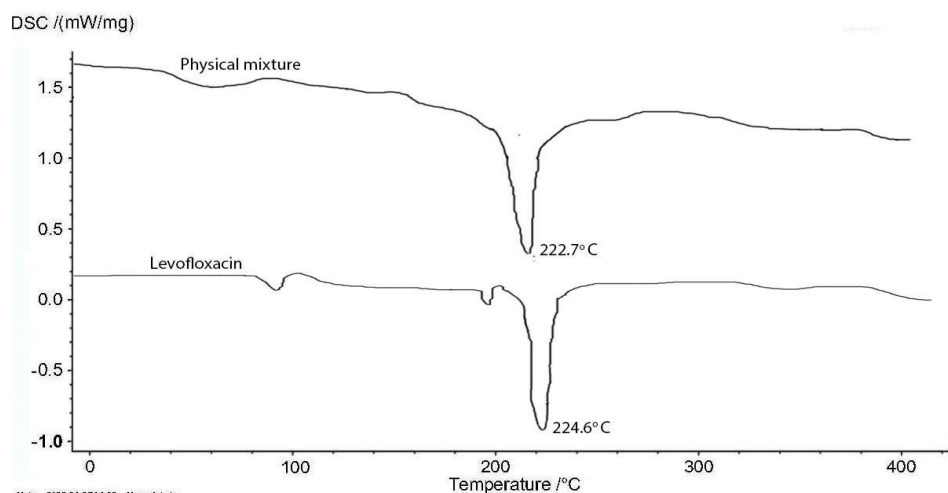


Fig 2: DSC thermograms for Levofloxacin and Physical mixture Result

➤ **Levofloxacin Standard calibration curve in 1.2 pH buffer**

S.No.	Concentration (mcg/ml)	Absorbance
1	0	0
2	2	0.168
3	4	0.309
4	6	0.416
5	8	0.551
6	10	0.709

Table 4: Levofloxacin Standard calibration curve in 1.2 pH buffer

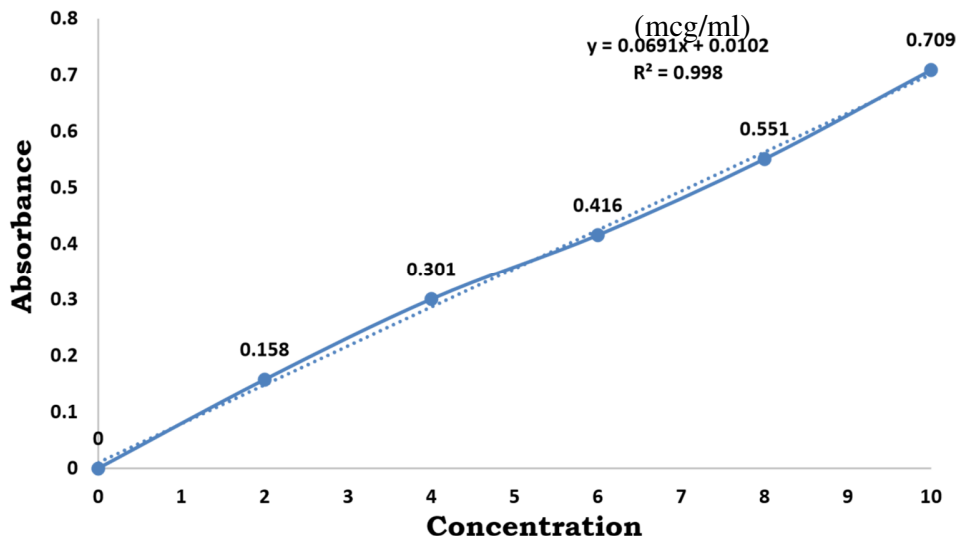


Fig 3: Standard calibration curve of Levofloxacin 1.2 pH buffer

➤ Evaluation of precompression parameters of drugs, polymers.

➤ Formulation [mg]	Parameters				
	Angle of repose [θ]	Loose Bulk Density [gm/cm ³]	Tapped Bulk Density [gm/cm ³]	Hausner's Ratio [HR]	Compressibility Index [%]
F1	26 ⁰ 53'' ± 0.54	1.05±0.03	1.33±0.04.	1.26±0.08	21.05±1.52
F2	28 ⁰ 84'' ± 1.24	1.05±0.05	1.31±0.02	1.25±0.03.	20.00±1.65
F3	29 ⁰ 12'' ± 1.68	1.05±0.07	1.17±0.08	1.11±0.09	10.52±0.92
F4	30 ⁰ 50'' ± 0.92	1.05±0.02	1.40±0.03.	1.33±0.10	25.00±1.85
F5	26 ⁰ 63'' ± 1.35.	0.95±0.06	1.26±0.09	1.33±0.04	25.00±1.23
F6	28 ⁰ 95'' ± 1.08	0.95±0.04	1.18±0.02	1.25±0.03	20.00±1.57
F7	25 ⁰ 74'' ± 0.83.	1.05±0.05	1.25±0.10.	1.18±0.10.	15.78±1.45

Table 5: Precompression parameters of Levofloxacin floating tablets formulation (F1-F7) powder blend

➤ **Evaluation of Post-compression parameters of Levofloxacin floating tablets formulation (F1-F7) powder blend**

Formulation	Thickness [mm]	Hardness [kg/cm ²]	Friability [%]	Weight variation [mg]
F1	3.17±0.14	4.81±0.12	0.83±0.05	500±0.22
F2	3.18±0.12	4.73±0.53	0.81±0.02	512±0.16
F3	3.16±0.12	4.55±0.40.	0.86±0.03	496±0.02
F4	3.14±0.11	4.67±0.33	0.83±0.01.	506±0.75
F5	3.20±0.10	4.71±0.17	0.81±0.08	521±0.46
F6	3.19±0.16.	4.58±0.28	0.82±0.06	486±0.85
F7	3.17±0.14	4.58±0.31	0.81±0.03	523±0.89

Table 6: Post-compression parameters of Levofloxacin floating tablet

➤ **Floating lag time Contour plot of Levofloxacin Floating tablets (HPMC K100M Vs HPMC K4M)**

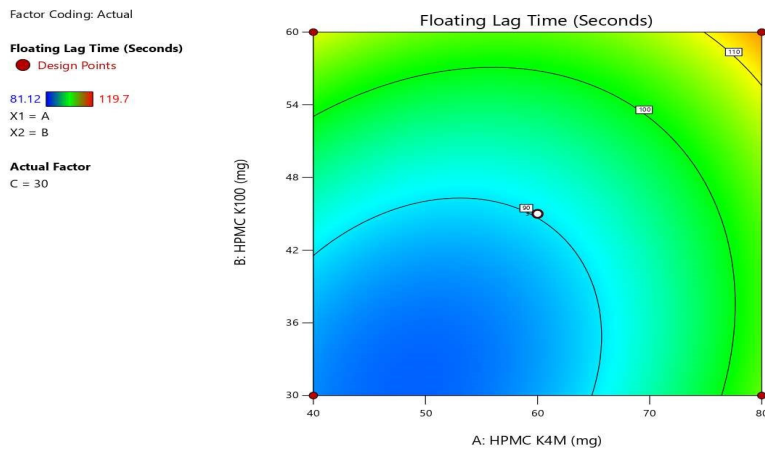


Fig4.Lag Time and 3D surface plot of Levofloxacin tablet.

➤ Swelling index Contour plot and 3D surface of Levofloxacin Floating tablets F1-F7

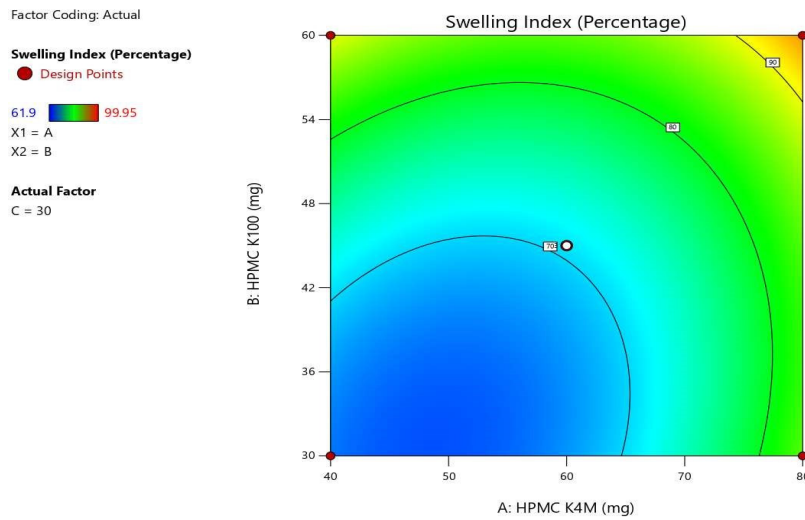
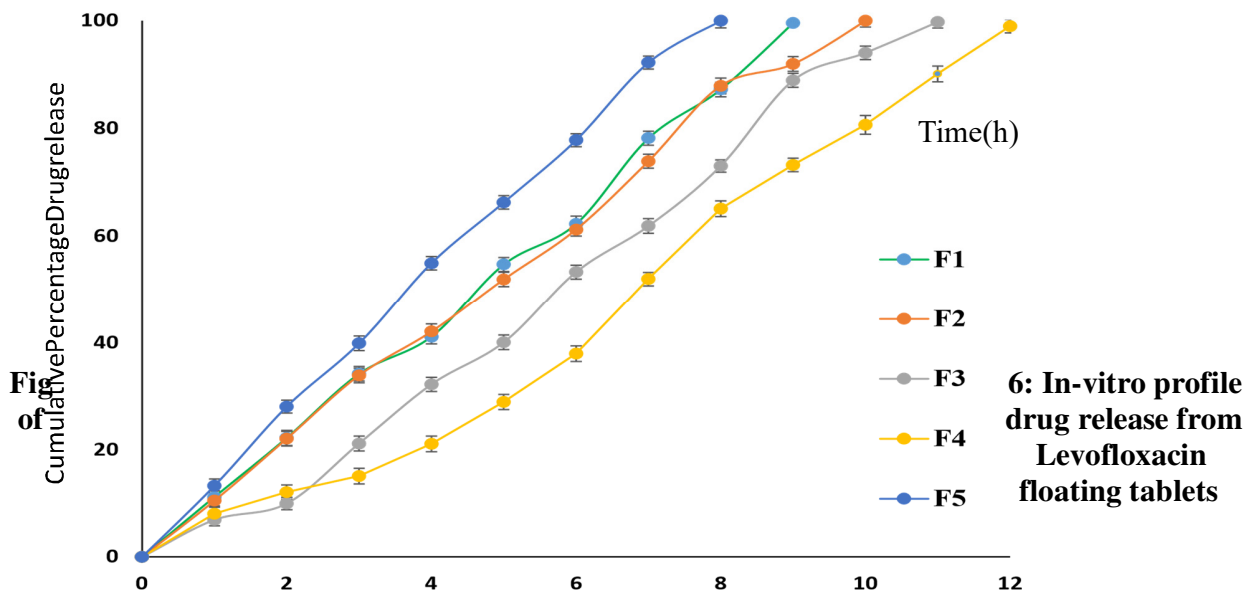


Fig 5: Swelling index Contour plot of Levofloxacin Floating tablets

➤ In-vitro profile of drug release from Levofloxacin floating tablets formulations.



6: In-vitro profile drug release from Levofloxacin floating tablets

➤ Conclusion

Floating tablet Formulations of levofloxacin were prepared by simple blending and punching with carbopol, HPMC K4M, sodium bicarbonate, citric acid and talk for oral application. levofloxacin is an antibiotic drug having higher protein binding, hepatic metabolism low oral bioavailability and lower half life. The drug requires a drug delivery system that provides a solution of these problems and improves bioavailability. Prepared floating batches were characterized for compatibility study, pre compression and post compression evaluation, % drug content, in-vitro drug release. Major

advantages of the system include ease of preparation, high % drug release and long duration over 12 hours. From this study, it was concluded that floating tablet batch F3 offers better sustained release in continuous manner that helpful to maintain bioavailability for long duration and reduces frequency of dose, also reduces dos

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