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Original Research Paper

FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF LEVOFLOXACIN USING NATURAL POLYMER

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ABSTRACT

The objective of this study was to develop matrix tablets of levofloxacin for sustained release. Xanthan gum, guar gum, karaya gum used as natural polymers and study the effect of various formulation factors such as polymer proportion and effect of filler type on the in vitro release of the drug. Levofloxacin Matrix tablets were prepared by direct compression technique with average weight of drug of 250 mg. The prepared tablets were evaluated for weight variation, friability, hardness, thickness and in vitro dissolution studies. All the granules of formulations showed compliance with pharmacopoeial standards. From the In vitro dissolution studies it is clear that by increasing the amount of drug release is decreased as the concentration of polymer increased, drug release was found to be retarded. The formulation F7 is selected as the optimized formulation by in vitro drug release for 12 hrs with the release of 99.26%. The kinetic treatment showed that mechanism of drug tablets of levofloxacin follows non fickian transport mechanism which having n < 1 and by the stability studies there is no significant difference in the drug content. By the stability studies there is no significant difference in the drug content.

Keywords: Levofloxacin, Xanthan gum, In vitro dissolution studies, Sustained release matrix tablets.

INTRODUCTION

Sustained drug delivery system was aimed to release the medication in a prolonged rate to maintain plasma drug levels. The drugs having shorter half life are suitable for the sustained drug delivery system. The main objective in designing sustained delivery system is to reduce dosing frequency and thereby increasing the action. The drug molecules shows better sustained drug release profile in matrix systems by different mechanisms. The introduction of matrix tablet as a sustained release had made a new phase for the novel drug delivery system. Hydroxypropyl methylcellulose was the mostly used hydrophilic polymer to prolong the drug release pattern due to its gelling property, rapid hydration, and robust mechanism, choice in viscosity grades, nonionic nature, reproducible release profile, cost effectiveness and good compressibility property.[1] Sustained release system implies to the pharmaceutical dosage form formulated for retardation of release of therapeutic agent such that its appearance in the systemic circulation was delayed or prolonged and its plasma profile was sustained in duration. The onset of pharmacologic action was delayed and duration of therapeutic effect also delayed.[1,2] The aim of this work is to

formulate a sustained release matrix tablets using natural gums as a matrix forming materials. Levofloxacin Hydrochloride was selected as a model drug. Due to the low biological half life it requires frequent administration. Hence sustained or prolonged release dosage forms are formulated to reduce the dosing frequency thereby improving patient compliance. Main objective of the work is to formulate sustained or prolonged dosage form by adopting direct compression method using natural gums (Guar gum, Karaya gum and Xanthan gum) as a retarding material at different concentrations. All the formulations are evaluated for hardness, friability, thickness, weight uniformity, content uniformity and *in-vitro* dissolution studies and followed by stability and kinetics study for the best formulation among them.

MATERIALS AND METHODS

Levofloxacin was a generous gift from Micro Lab's Ltd., Lactose, Magnesium stearate, Talc from Thomas Baker Pvt. Ltd., Mumbai, Xanthan Gum, Guar gum, Karaya Gum from Lobba Chemie, Mumbai.

Methods

Drug: Polymer Interactions

Fourier Transform Infrared Spectroscopy

It was important to check any kind of interaction between drug and polymer. It was done using Fourier Transformed Infrared Spectroscopy.IR spectra of pure Levofloxacin and polymers were taken separately. Then to know if there is any interaction between drug and polymer, IR spectra of physical mixture of Levofloxacin and polymers were taken in combination

Determination of λ_{max} (UV-Spectroscopy)

Stock solution (1000µg/ml) of *levofloxacin* was prepared in 0.1N HCl. This solution was apparently diluted with same solvent to obtain concentration of 100 µg/ml. The resultant solution was scanned in the range of 200-400 nm on double beam UV-spectrophotometer.

Preparation of standard curve of levofloxacin by 0.1N HCl and 7.4 pH phosphate buffer

In 0.1N HCl:

85 ml of conc. hydrochloric acid was diluted up to 1000 ml with distilled water, gives 1N solution. 10 ml of resulting solution was further diluted up to 100 ml with distilled water gives 0.1 N HCl. Stock solution was prepared by dissolving 100.0 mg of Levofloxacin in 100.0 ml of 0.1 N HCl solutions, which was further diluted to give the solutions of concentration 5, 10, 15, 20 and 25 µg/ml respectively. Absorbance of these solutions were measured on UV spectrophotometer at 233 nm and plotted against the concentration to give the standard curve.

In 7.4 pH phosphate buffer

Accurately weighed quantity of 27.218g of potassium dihydrogen phosphate was dissolved in distilled water and diluted with distilled water up to 1000 ml. 50ml of above solution was taken in a 200 ml volumetric flask, 39.1 ml of 0.2 M NaOH was added to the solution and then diluted with distilled water upto volume.Stock solution was prepared by dissolving 100.0 mg of Levofloxacin in 100.0 ml of 7.4 pH Phosphate buffer solutions, which was further diluted to give the solutions of concentration 5, 10, 15, 20 and 25 µg/ml respectively. Absorbance of these solutions were measured on UV spectrophotometer at 233 nm and plotted against the concentration to give the standard curve.

Preparation of levofloxacin sustained release tablets [6]

Various batches of Sustained release tablets of levofloxacin were prepared by direct compression technique with each batch containing 100 tablets with 250 mg of drug. All the ingredients were thoroughly mixed. Then the powder was passed through sieve mesh 20 to get uniform size of particles. Then it was lubricated by adding magnesium stearate. The above powder was compressed with the help of 8 x 8 mm punch size, by keeping average weight 400 mg. After compression the tablets were evaluated for weight variation, hardness, thickness, friability, dissolution, and assay test were determined. The composition of each formulation is given in following table 1.

Evaluation of Powder Blend

Flow properties by angle of repose[3]

A funnel was kept vertically in a stand at a specified height above a paper placed on a horizontal surface. The funnel bottom is closed and 10 gm of sample powder is filled in funnel. Then funnel was opened to release the powder on the paper to form a smooth conical heap, is found by measuring in different direction. The height of the heap was measured by using scale. The value of angle of repose is calculated by using the following formula:

Tan θ = h/r, θ = $\tan^{-1}$ h/r

Where, **h**- height of the heap, **r**-radius of the heap For most pharmaceutical powders, the angle of repose values range from 25 to 45, with lower values indicating better flow characteristics. Values of angle of repose = 30 usually indicate a free flowing material and angle =40 suggest a poorly flowing materials.

Bulk density[4]

A known quantity of powder was poured into the measuring cylinder carefully level the powder without compacting, if necessary and read the unsettled apparent volume, V_0, to the nearest graduated unit. Calculate the bulk density, in gm per ml, by the formula,

Bulk Density = m / V_0,

Where **m** - Unsettled, **V_0** - apparent volume

Tapped density[5]

Cylinder dropping distance: 14± 2 mm at a normal rate of 300 drops / minute. Unless otherwise specified, tab the cylinder 500 times initially and measure the tapped volume, Va, to the nearest graduated unit. Repeat the tapping an additional 750 times and measure the tapped volume, Vb, to the nearest graduated unit. If the difference between the two volumes is less than 2%, Vb is the final tapped volume, Vf. Repeat in increments of 1250 taps, as needed, unit the difference between succeeding measurements is less than 2%. Calculate the tapped density, in gm per ml, by the formula:

Tapped Density = Vb /Vf

Where **Vb** – tapped volume, **Vf** – final tapped volume

Generally replicate determinations are desirable for the determination of this property.

Measurement of powder compressibility

The compressibility Index and Hausner Ratio are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of inter particulate interactions. In a free flowing power, such interactions are generally less and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater inter particle interactions, and a greater difference between bulk and tapped densities will be observed. These differences are reflected in the compressibility Index and the Hausner Ratio Calculated by the formula:

Compressibility Index was calculated using following equation.

Compressibility index = [(Dt-Db)/Dt] x100

Where **Dt** = tapped density, **Db** = bulk density

Hausner's ratio[6]

Hausner Ratio was calculated using the formula,

Hausner Ratio = Dt/Do

Where Dt = tapped density, **Do** = bulk density

Evaluation of Sustained Release Levofloxacin Matrix Tablets

Weight variation test[7]

Twenty tablets were randomly selected and weighed to determine the average weight and were compared with individual tablet weight. The percentage weight variation was calculated as per Indian Pharmacopoeial Specification. Tablets with an average weight more than 400 mg should not be more than ±5 %.

Friability test[6]

Weighed amount of 20 dedusted tablets were subjected to rotating drum of friability test apparatus. The drum rotated at a speed of 25 rpm. The apparatus was operated for 4 minutes and reweighed the tablets. Friability was calculated by the following formula.

F =100 (W_0-W)/W_0

Where **W_0** = Initial weight, **W** = Final weight

Hardness test[7]

The hardness of tablets was carried out in Monsanto hardness tester. The result was complies with IP specification.

Thickness test[6]

The control of physical dimension of the tablets such as sizes and thickness is essential for consumer acceptance and to maintain tablet to tablet uniformity. The dimensional specifications were measured using screw gauge. The thickness of the tablet is mostly related to the tablet hardness can be uses as initial control parameter.

Drug content[8]

The amount of drug per tablet needs to be monitored from tablet to tablet, and batch to batch is to evaluate tablets potential for efficacy. To perform the test, ten tablets from each batch were weighed and powdered. Powder equivalent to the average weight of the tablet was accurately weighed and transferred into a 100 ml volumetric flask and dissolved in a suitable quantity of distilled water. The solution was made up to the mark and mixed well. A portion of the sample was filtered and analyzed by a UV spectrophotometer at 293 nm.

In Vitro dissolution studies:

Medium : 0.1M HCl and Phosphate buffer p^H 7.4.
Apparatus : USP II (Basket)
Speed : 100 rpm
Time : 1 hour to 12 hours
Temperature : 37°C ± 0.5° C
λ max : 293 nm.

The *in-vitro* release of Levofloxacin from formulated tablets was carried out in acid buffer pH 1.2 for 2 hours and then continued in phosphate buffer pH 7.4 for 10 hours. The studies were performed in USP dissolution apparatus II, at 37 ± 0.5° C and 100 rpm speed. Samples were taken at hourly interval and analyzed for Levofloxacin content at 293.0 nm by using UV–Visible spectrophotometer. (Model No. UV 3000$^+$, LAB INDIA Pvt Ltd).

Kinetic Treatment of Data of Dissolution Profiles of Levofloxacin Tablets

Dissolution kinetic model

Model dependent methods are based on different mathematical functions, which describe the dissolution profile. Once a suitable function has been selected the dissolution profiles are evaluated depending on the derived model parameters mentioned in the table 2.Where, Q_t is amount of drug dissolved in time t, Q_0 is the initial amount of drug in the solution, K_0 is zero order release constant, $K_1$is first order release rate constant, K_h is Higuchi dissolution constant and K_s is constant incorporating surface volume relation.

Stability studies

The stability study aims at determining the result of aging and storage under various conditions and the effect on the release characteristics and chemical stabilities. Stability studies were carried out to evaluate the stability of F7 formulation on sustained release tablets of levofloxacin storing at 45 °C±2 °C after 45 days.

RESULTS AND DISCUSSION:

Drug-Polymer Interaction/Compatibility Study Using FTIR

The different peaks of drug, polymer and their physical mixture indicate all groups and characteristics of the drug were not altered. There is no significant interaction in drug and polymer given in table 3. Physical mixture of drug and polymer was characterized by FTIR spectral analysis (figures 2, 3, 4 and 5) for any physical as well as chemical alteration of drug characteristics. From results, it was concluded that there was no interference in the functional group as the principle peaks of Levofloxacin were found to be unaltered in the drug polymer physical mixture as shown in the graphs 1-4.

Spectrophotometric characterization

Determination of λ_{max} of Levofloxacin

A solution of 10 µg/ml of Levofloxacin was scanned in the range of 200 to 400 nm. The drug exhibited the λ_{max} at 293 nm in 0.1 N Hydrochloric acid and has good reproducibility shown in graph 5.

Standard calibration curves of Levofloxacin

From the scanning of drug in 0.1N HCl, and Phosphate buffer pH 7.4 it was concluded that the drug had λ_{max} of 293.0 nm and which was exactly

similar as reported. From the standard curve of 0.1 N HCl and Phosphate buffer pH 7.4 it was observed that the drug obeys Beer-Lambert's law in concentration range of 0 – 30µg / ml in the medium as shown in table 4 and graphs 6,7.

Pre compression parameters

The powder characteristics of various batches of sustained release tablets. Various formulations shown good flow properties. Results of Bulk density (0.36 – 0.39), Tapped density 0.41 – 0.48), Compressibility index (12.06 – 20.63), Angle of repose ($24^0.14'$ – $28^0.41$) shows satisfactory results, which is required for better bioavailability indicated in the table 5.

Post compression parameters

In each batch, it was concluded that the tablets of all batches had desirable physical characteristics. Results of thickness of various batches of prepared formulations, (3.46-3.54mm), Hardness (5.7 –6.3 kg / sq cm.) and Friability (0.51 – 0.85 %) indicates that the tablets having sufficient strength to withstand physical abrasion. Tablets of all batches pass the weight variation test and uniformity in content was as per the limits prescribed in IP shown in post compression parameters (table 6).

In vitro dissolution studies

Table 7 and graph 8 indicate the dissolution data of various batches of Levofloxacin HCl sustained release tablets. The percentage drug release from batch F1 to F13 vary from 88.46 to 99.26%. From the data it is clear that by increasing the amount of polymer in the formulation, the amount of drug release is decreased. Based on the dissolution studies F7 was selected as an optimized batch because it shown maximum drug release at the end of 12 hours.

Study of drug release kinetics

For understanding the mechanism of drug release and release rate kinetics of the drug from dosage form, the *in-vitro* drug dissolution data obtained was fitted to various mathematical models such as zero order, First order, Higuchi matrix and Korsmeyer Peppa's model. The values were compiled in table 8.The diffusion coefficients (n) values ranged between 0.756 and 0.941. The observed diffusion coefficient values were indicative of the fact that the drug release from the formulation follows non-Fickian transport mechanism. From graph 9 and table 8 the optimized formulation F7 follows korsemeyerpeppa's model and non fickian transport (<1).

Stability studies of optimized formulation

According to ICH guidelines, 45 days stability study at 4^0C ±2^0C, 27^0C ±2^0C and 45^0C ±2^0C for 45 days at RH 75±5% of optimized formulation (F7) was carried out. It showed negligible change over time for parameters like appearance, drug content, dissolution and assay etc., No significant difference in the drug content between initial and formulations stored at 4^0C ±2^0C, 27^0C ±2^0C and 45^0C ±2^0C for 45 days at RH 75±5% for 45 days shown in table 9.

CONCLUSION

Levofloxacin sustained release tablets were formulated by using natural polymers such as Xanthan gum, Guar gum and Karaya gum. Infrared spectra of the drug reveal that there is no significant interaction between drug and polymers. Preformulation studies were done initially and the results were found within the limits. The evaluation tests results are found to be within pharmacopoeial specifications. From *in-vitro* dissolution study it is concluded that the formulation of sustained release tablet of Levofloxacin containing Guar gum, Karaya gum and Xanthan gum in 40 mg proportions were taken as ideal or optimized formulation of sustained release tablet for 12 hours release as it fulfills all the requirement of sustained release tablet. Kinetic studies were observed as Non-fickian release mechanism of drug through polymeric membrane was found through diffusion and rate of diffusion is controlled by swelling of polymer. From the stability studies, it was concluded that no significant difference in the drug content between initial and formulations stored at 4^0C ±2^0C, 27^0C ±2^0C and 45^0C ±2^0C for 45 days at RH 75±5% for 45 days in optimized formulation F7.

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Table 1: Composition of levofloxacin sustained release tablets

Ingredients	Levofloxacin	Xanthan Gum	Guar Gum	Karaya Gum
F1	250	120	-	-
F2	250	-	120	-
F3	250	-	-	120
F4	250	20	40	60
F5	250	40	60	20
F6	250	60	20	40
F7	250	40	40	40
F8	250	20	60	40
F9	250	40	20	60
F10	250	60	40	20
F11	250	60	60	-
F12	250	60	-	60
F13	250	-	60	60

Table 2: Mathematical models used to describe drug dissolution curves

Sr. No.	Models	Equation
1	Zero Order	$Q_t = Q_0 + K_0 t$
2	First Order	$\ln Q_t = \ln Q_0 + K_1 t$
3	Higuchi	$Q_t = K_h t^{1/2}$

Table 3: FTIR spectral analysis

Functional group	Characteristic Peaks (cm^{-1})	Observed Peaks (cm^{-1})
COOH	3267	3315.74
C-CH_3	2359	2360.95
C=O	1624	1625.08
C-N	1294	1271.13
F (Halogen)	1085	1084.03

Table 4: Calibration curve data of levofloxacin in 0.1N HCl and 7.8 pH phosphate buffer

S. No.	Concentration	Absorbance in 0.1N HCl	Absorbance in 7.4 pH phosphate buffer
1	0	0	0
2	5	0.114	0.101
3	10	0.229	0.19
4	15	0.334	0.281
5	20	0.439	0.369
6	25	0.544	0.459
7	30	0.654	0.556

Table 5: Characteristics of Final Powder blend

Formulations	Bulk Density (g/ml)* (± SD)	Tapped Density (g/ml)* (± SD)	Compressibility Index (%)* (± SD)	Angle of Repose* (± SD)
F1	0.39±0.52	0.46±0.62	15.22±0.78	24.14±0.67
F2	0.39±0.43	0.47±0.78	17.88±0.33	27.25±0.48
F3	0.37±0.91	0.46±0.24	18.45±0.64	24.41±0.50
F4	0.36±0.35	0.42±0.62	14.29±0.80	25.73±0.45
F5	0.38±0.71	0.48±0.34	20.63±0.77	27.68±0.57
F6	0.39±0.12	0.45±0.93	15.22±0.42	28.21±0.90
F7	0.37±0.20	0.41±0.32	12.06±0.71	27.41±0.66
F8	0.37±0.43	0.46±0.74	19.3±0.49	28.41±0.32
F9	0.38±0.02	0.45±0.02	14.42±0.5	27.00±0.5
F10	0.37±0.20	0.41±0.32	12.06±0.71	27.41±0.66
F11	0.37±0.43	0.46±0.74	19.3±0.49	28.41±0.32
F12	0.38±0.02	0.45±0.02	14.42±0.5	27.00±0.5
F13	0.38±0.71	0.48±0.34	20.63±0.77	27.68±0.57

Table 6: Post compression parameters of Levofloxacin Sustained release tablets

Formulation	Thickness ± SD*	Hardness (kg/cm2) ± SD	Friability (%) ± SD*	Weight Uniformity (mg) ± SD*	Uniformity content ± SD
F1	3.48±0.14	6.0±0.28	0.85±0.29	Complies	98.56±0.25
F2	3.49±0.83	6.2±0.62	0.63±0.12	Complies	97.35±0.92
F3	3.49±0.67	5.8±0.40	0.53±0.10	Complies	98.73±0.37
F4	3.53±0.38	6.1±0.97	0.69±0.87	Complies	99.46±0.59
F5	3.49±0.14	6.1±o.14	0.67±0.19	Complies	100.74±0.94
F6	3.54±0.14	5.7±0.95	0.54±0.26	Complies	98.57±0.54
F7	3.54±0.21	6.3±0.36	0.51±0.66	Complies	100.25±0.23
F8	3.52±0.73	5.7±0.32	0.53±0.43	Complies	98.22±0.40
F9	3.46±0.20	6.1±0.48	0.72±0.19	Complies	99.38±0.37
F7	3.54±0.21	6.3±0.36	0.51±0.66	Complies	100.25±0.23
F8	3.52±0.73	5.7±0.32	0.53±0.43	Complies	98.22±0.40
F9	3.46±0.20	6.1±0.48	0.72±0.19	Complies	99.38±0.37
F10	3.54±0.21	6.3±0.36	0.51±0.66	Complies	100.25±0.23
F11	3.52±0.73	5.7±0.32	0.53±0.43	Complies	98.22±0.40
F12	3.46±0.20	6.1±0.48	0.72±0.19	Complies	99.38±0.37
F13	3.49±0.67	5.8±0.40	0.53±0.10	Complies	98.73±0.37

Table 7: *In Vitro* dissolution study of formulations F1 – F13

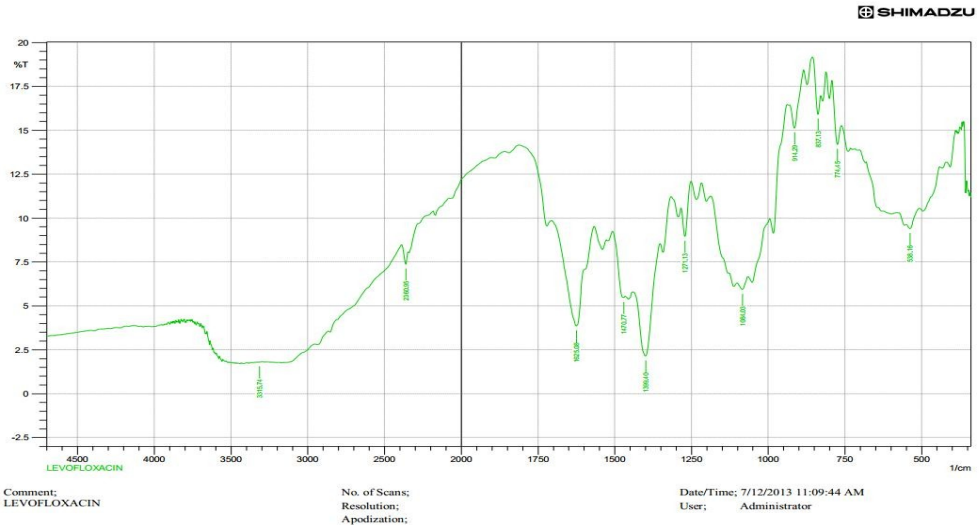
Time	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	13.96	11.42	12.99	16.19	14.64	15.96	10.13	13.32	15.42	16.42	11.99	13.54	9.54
2	27.14	24.49	28.12	25.46	21.96	23.89	20.11	20.21	22.96	26.44	17.25	19.25	12.96
3	37.92	35.16	36.26	30.25	29.16	31.12	27.58	28.36	30.19	31.24	21.29	24.56	17.48
4	49.97	46.58	48.73	39.58	39.14	36.96	35.64	34.65	35.46	39.54	27.65	31.84	24.41
5	58.12	54.14	59.01	48.42	46.98	49.03	45.12	44.51	49.47	48.25	34.18	38.11	31.24
6	66.49	64.92	65.96	59.48	54.46	57.86	53.14	53.57	58.54	60.21	39.72	46.21	35.67
7	74.54	72.12	74.14	65.26	63.54	63.21	60.28	61.49	64.31	68.56	47.66	51.47	41.68
8	87.58	84.65	86.99	71.62	69.54	70.58	69.74	66.42	69.54	76.15	56.79	60.75	50.1
9	92.42	91.75	92.37	79.16	77.76	78.46	76.59	75.34	77.54	82.45	67.24	70.69	60.9
10	98.61	97.07	98.35	88.14	85.56	87.14	85.64	86.47	89.26	89.65	77.15	77.58	68.46
11	---	---	---	95.26	92.45	93.9	92.54	91.69	94.12	92.65	88.19	86.17	79.58
12	---	---	---	96.84	94.57	95.14	99.26	92.73	95.06	97.56	91.25	93.35	88.46

Table 8: Dissolution kinetics of formulations F1-F13

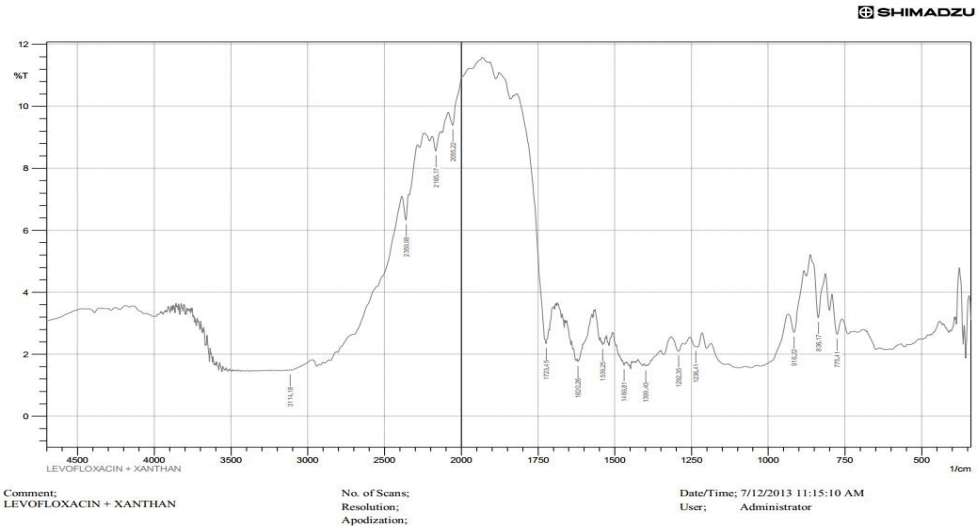
Formulation Code	Zero order	First order	Matrix	Peppas		Best fit model
	R	R	R	R	n	
F1	0.988	0.827	0.993	0.997	0.845	Peppa's
F2	0.993	0.871	0.991	0.996	0.920	Peppa's
F3	0.988	0.839	0.993	0.993	0.864	Higuchi
F4	0.989	0.877	0.982	0.991	0.756	Peppa's
F5	0.992	0.912	0.984	0.994	0.789	Peppa's
F6	0.989	0.903	0.981	0.990	0.761	Peppa's
F7	0.998	0.732	0.982	0.999	0.917	Peppa's
F8	0.993	0.914	0.977	0.992	0.830	Zero order
F9	0.987	0.901	0.977	0.987	0.782	Peppa's
F10	0.984	0.893	0.982	0.989	0.753	Peppa's
F11	0.986	0.856	0.927	0.964	0.865	Zero order
F12	0.995	0.864	0.953	0.978	0.811	Zero order
F13	0.983	0.849	0.920	0.967	0.941	Zero order

Table 9: Stability studies of Levofloxacin sustained release tablets of optimized formulation F7

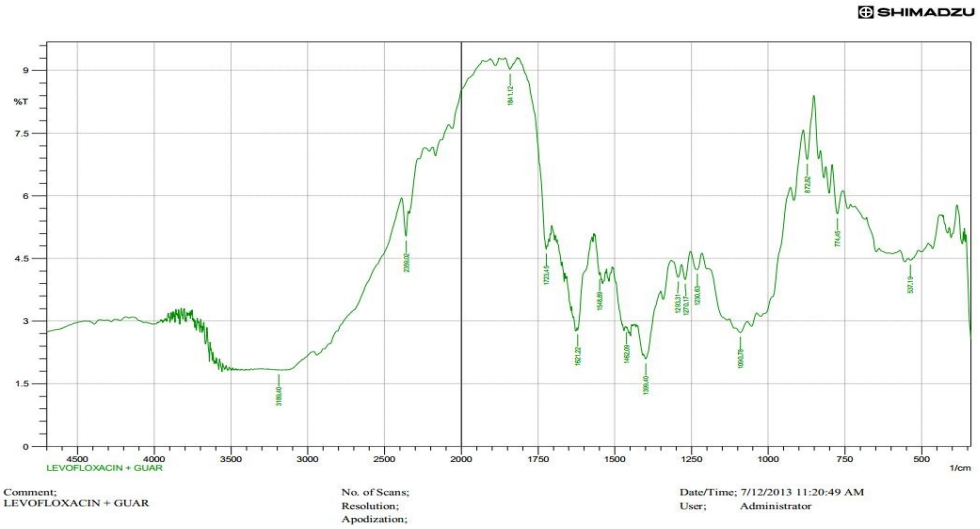
Parameters	After 15 days	After 30 days	After 45 days
Physical appearance	No change	No change	No change
Weight variation (mg)	404±3.34	402±2.55	402±4.23
Thickness (mm)	3.51±1.87	3.53±2.86	3.54±3.98
Hardness (kg/cm^2)	6.4±0.23	6.3±0.64	6.2±0.99
Friability (%)	0.51±0.05	0.53±0.08	0.53±0.06
Drug content (%/ tablet)	100.25±0.34	99.81±0.29	99.01±0.87



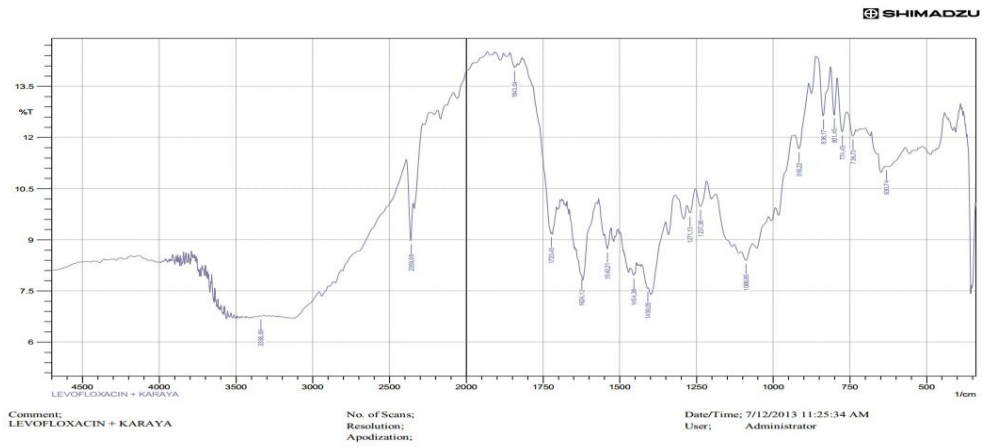
Graph 1: FTIR Spectral Analysis of Levofloxacin



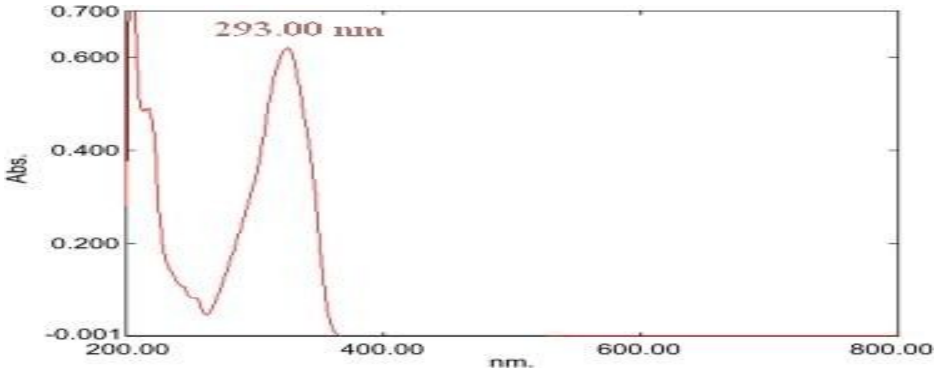
Graph 2: FTIR spectral analysis of physical mixture of drug and polymer (Levofloxacin +Xanthan Gum)



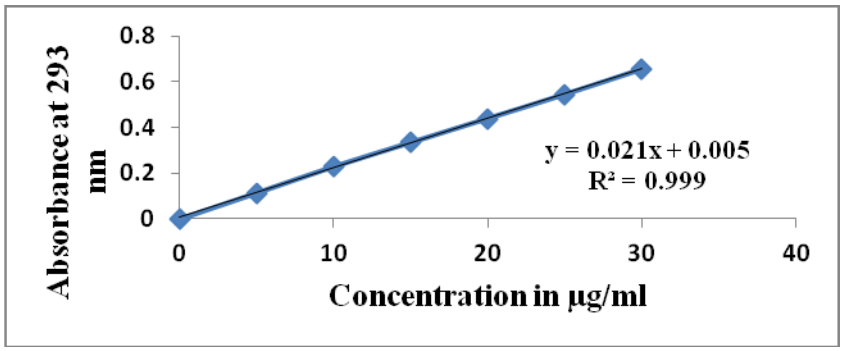
Graph 3: FTIR spectral analysis of physical mixture of drug and polymer (Levofloxacin +Guar gum)



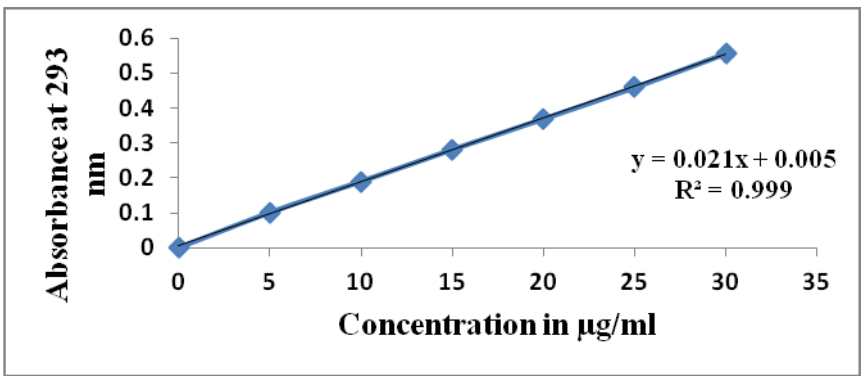
Graph 4: FTIR spectral analysis of Physical mixture of Drug and polymer (Levofloxacin + Karaya gum)



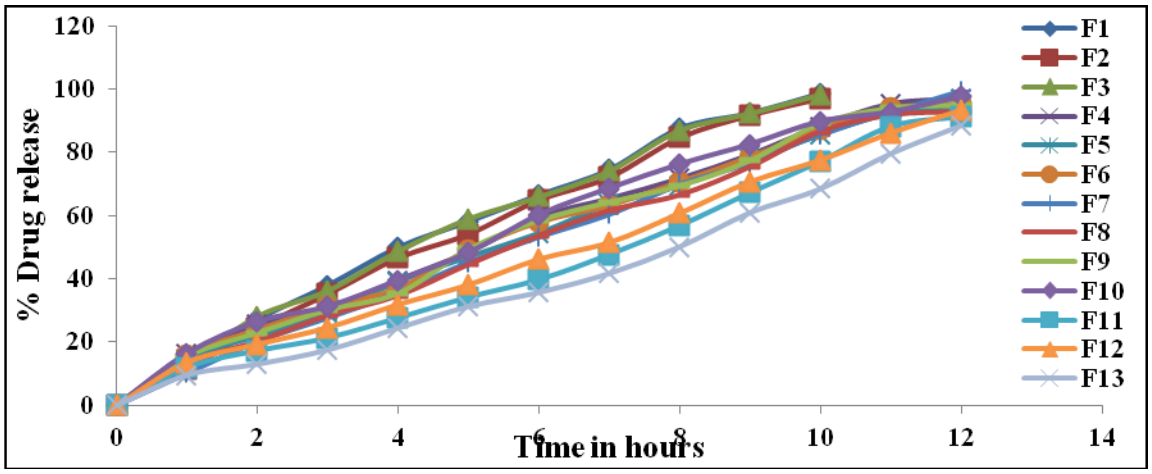
Graph 5: Absorption maxima of Levofloxacin



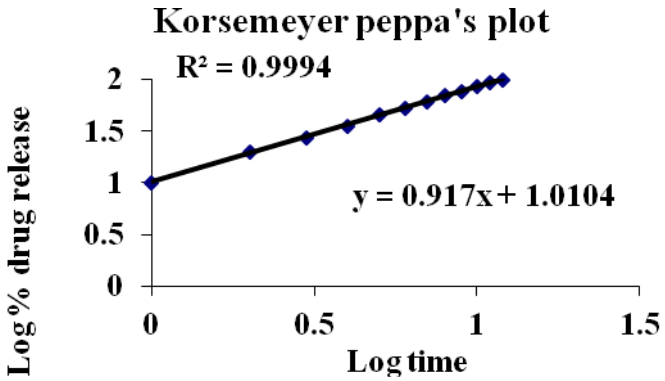
Graph 6: Calibration curve of Levofloxacin in 0.1N HCl at 293 nm



Graph 7: Calibration curve of Levofloxacin in 7.4 pH Phosphate buffer at 293 nm



Graph 8: *In Vitro* Dissolution study of formulations F1 – F13



Graph 9: Korsemeyerpeppa's plot of formulation F7

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