RESEARCH ARTICLE

Design, Development and Characterization of Gastroretentive Floating Tablet of Levofloxacin using Natural Polymer Peanut Husk

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ABSTRACT

In the present study, levofloxacin gastroretentive floating tablet (GRFT) was formulated using peanut husk powder as a natural release modifier for providing sustained drug delivery at the stomach to effectively treat infections. Preformulation studies such as UV analysis and drug excipients study using Fourier-transform infrared (FTIR) were performed. Peanut husk powder was prepared by crushing and grinding the dried peanut husk. The GRFT formulations (GRFT1- GRFT9) were formulated using the direct compression method with varied concentrations having peanut husk powder, HPMCK4M and carbapol 934, along with other ingredients. Formulations were characterized based on the pre-compressional parameter and post-compressional parameters. The results for GRFT5 were found to be best among all batches as it showed sustained %drug release of 89.52 ± 0.3% upto 12 hours and it revealed enhanced therapeutic performance of the drug. However, *in-vivo* study needs to be performed for a better comparison of data with *in-vitro* results.

Keywords: Levofloxacin, Gastroretentive, Floating tablet, Natural, Peanut.

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INTRODUCTION

Due to the adverse physicochemical properties of drugs, the oral bioavailability of drugs is low[1]. Delayed gastric residence of dosage form improves bioavailability as well as the solubility of drugs that are poorly soluble at high GI pH[2]. Many approaches are used to enhance gastric residence of oral dosage forms like bioadhesive drug delivery system and gastro retentive floating drug delivery system[3]. Gastroretentive dosage forms have turned up as an ideal technique to subdue these drawbacks. The objective is to extend the gastric residence time of the dosage forms for a prolonged time in order to obtain a sustained release of the drug[4].

Levofloxacin is a broad-spectrum antibiotic that is quickly and fully absorbed after its oral administration. For managing infections, its therapy need a constant amount of drug in systemic circulation for a sustained duration that can be attained by designing gastroretentive floating tablets[5].

MATERIALS AND METHODS

The drug levofloxacin (LF) was a gift sample obtained from Dr. Reddy's Pvt. Ltd., Hyderabad. HPMC K4M, magnesium stearate was obtained from Meditab Pvt. Ltd., Satara. Carbopol 934, sodium bicarbonate and talc from SD Fine Chemicals Ltd., Mumbai. Other solvents are of analytical grade.

Preformulation Studies

Determination of absorbance maxima of levofloxacin

The absorbance maxima of levofloxacin were measured by scanning its solution in 0.1 N HCl (100 µg/mL) using UV-visible spectrophotometer Model 1900 at a wavelength of 400 to 200 nm[6,7].

Preparation of standard curve of Levofloxacin (LF)

Standard cure of pure drug LF was prepared in 0.1 N HCl and further dilution was done to obtain 2,4,6,8,10 µg/mL and the absorbance was noted at 294 nm.[6]

Drug excipient compatibility (DEC) study

DEC study was done by FTIR. FTIR of levofloxacin, HPMC K4M, carbapol 934, peanut husk powder and GRFT5 were recorded between 600 and 4000 cm^{-1} using the potassium bromide pellet technique.[8]

Formulation Development

Preparation of peanut husk powder

The seeds of peanuts were obtained from a local market and were oven-dried at 40°C for 3 hours. The surface layer of the seeds was removed by crushing. Then husk was converted into

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Table 1: Formulation development of GRFT of levofloxacin

Ingredients (mg)	*Formulations (n = 3)*								
	GRFT1	*GRFT2*	*GRFT3*	*GRFT4*	*GRFT5*	*GRFT6*	*GRFT7*	*GRFT8*	*GRFT9*
Levofloxacin	250	250	250	250	250	250	250	250	250
Peanut husk powder	35	35	-	35	70	70	175	-	-
HPMC K4M	130	-	130	65	65	65	-	130	65
Carbapol 934	-	130	65	35	35	-	65	-	130
Sodium bicarbonate [$NaHCO_3$]	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0
Citric acid [$C_6H_8O_7$]	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
Magnesium stearate [$Mg(C_{18}H_{35}O_2)_{2]}$	10	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10	10

fine powder form by using a grinder and it was passed through sieve 80 and stored in a desiccator for further use.[9]

Preparation of gastroretentive floating tablet (GRFT) of levofloxacin

GRFT of levofloxacin was formulated by direct compression.[10] Gas-generating agents in the formulation were sodium bicarbonate [NaHCO3], peanut husk powder, HPMC K4M and carbapol 934 were used as rate-controlling polymers. All ingredients were accurately weighed and uniformly blended in the amount mentioned in Table 1. All materials, including levofloxacin, were uniformly mixed after passing through filter #80. Further, magnesium state and talc were used as a lubricating agent in a blend and it was compacted into a tablet shape using an 8 mm flat-faced punch.[9,11]

Determination of pre-compression parameters

Various pre-compression parameters were evaluated as per the standard method already mentioned.[12-14]

Evaluation parameters of GRFT[15,16]

The formulated GRFT of LF was evaluated for thickness, hardness, friability and weight variations test as per the standard method described in IP. Further, the GRFT was also evaluated for swelling index (SI), floating lag time (FLT), floating time (FT) and drug content%. *In-vitro* drug release (% DR) was calculated by USP Type-II dissolution testing apparatus and was analyzed using a UV-visible spectrophotometer at 294 nm. The stability study was performed at 40 ± 2°C/75 ± 5% RH for 3 months. Samples were withdrawn at intervals of 0, 30, 90, and 180 days period and the stability of the tablet was determined.

RESULTS AND DISCUSSION

The absorbance maxima of levofloxacin in 0.N HCl was found to be 294 nm and it was found to be matched with the standard. The standard curve of LF was plotted in 0.1 N HCl and a correlation coefficient was generated with R^2 value of 0.995. FTIR spectrums of levofloxacin, HPMC K4M, carbapol 934, peanut husk powder and GRFT5 are shown in Figures 1 to 5, respectively. Results of the study indicated no change in the characteristic peak of the drug and it revealed that there was no in compatibility found between the drug and excipients.

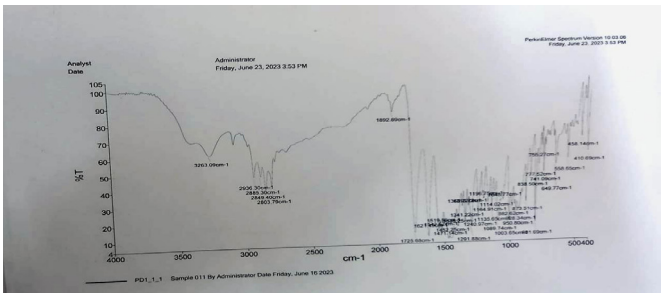

Figure 1: FTIR spectrum of levofloxacin

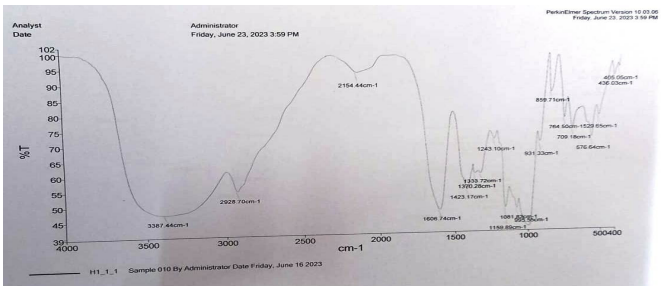

Figure 2: FTIR spectrum of HPMC K4M

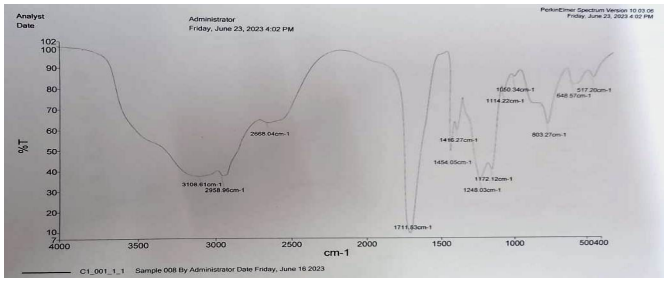

Figure 3: FTIR spectrum of carbapol 934

Peanut husk powder was prepared and it was found to have good powder characteristics. GRFT of Levofloxacin was formulated and all the formulations were further subjected

Table 2: Data of results of flow property (n=3)

Formulation batch	*Angle of repose (Degree)*	*Bulk density (g/mL)*	*Tapped density (g/mL)*	*Carr's index (%)*	*Hausner's ratio*
GRFT1	25 ± 0.3	1.33 ± 0.01	1.56 ± 0.03	14.36 ± 0.05	1.17 ± 0.01
GRFT2	27 ± 0.1	1.36 ± 0.02	1.59 ± 0.04	16.27 ± 0.02	1.20 ± 0.01
GRFT3	26 ± 0.4	1.32 ± 0.03	1.61 ± 0.03	18.73 ± 0.03	1.23 ± 0.02
GRFT4	25 ± 0.3	1.37 ± 0.02	1.58 ± 0.04	14.01 ± 0.06	1.16 ± 0.01
GRFT5	29 ± 0.3	1.35 ± 0.06	1.57 ± 0.05	13.78 ± 0.04	1.15 ± 0.01
GRFT6	26 ± 0.4	1.29 ± 0.05	1.58 ± 002	13.01 ± 0.03	1.13 ± 0.02
GRFT7	28 ± 0.3	1.36 ± 0.04	1.56 ± 0.06	12.87 ± 0.02	1.13 ± 0.02
GRFT8	27 ± 0.1	1.38 ± 0.06	1.57 ± 0.02	13.08 ± 0.02	1.15 ± 0.01
GRFT9	28 ± 0.2	1.37 ± 0.07	1.59 ± 0.05	13.43 ± 0.04	1.16 ± 0.03

Table 3: Data of results of thickness, hardness, friability test and weight variation (n = 3)

Formulation batch	*Thickness (mm)*	*Hardness (kg/cm^2)*	*Friability (%)*	*Weight variation (%)*
GRFT1	3.25 ± 0.02	4.1 ± 0.02	0.642 ± 0.03	0.915 ± 0.06
GRFT2	3.42 ± 0.03	4.3 ± 0.01	0.619 ± 0.02	1.231 ± 0.02
GRFT3	3.51 ± 0.02	4.2 ± 0.03	0.598 ± 0.01	1.964 ± 0.01
GRFT4	3.64 ± 0.04	4.4 ± 0.02	0.662 ± 0.04	1.387 ± 0.04
GRFT5	3.82 ± 0.03	4.5 ± 0.01	0.567 ± 0.02	1.115 ± 0.03
GRFT6	3.74 ± 0.04	4.3 ± 0.02	0.581 ± 0.03	1.831 ± 0.02
GRFT7	3.65 ± 0.02	4.1 ± 0.02	0.713 ± 0.02	1.455 ± 0.05
GRFT8	3.49 ± 0.03	4.3 ± 0.03	0.591 ± 0.04	0.918 ± 0.04
GRFT9	3.73 ± 0.04	4.4 ± 0.02	0.712 ± 0.03	0.945 ± 0.09

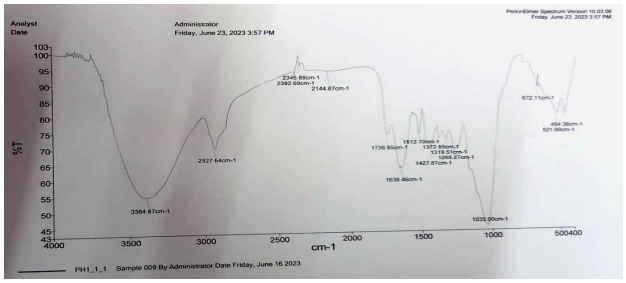

Figure 4: FTIR spectrum of peanut husk powder

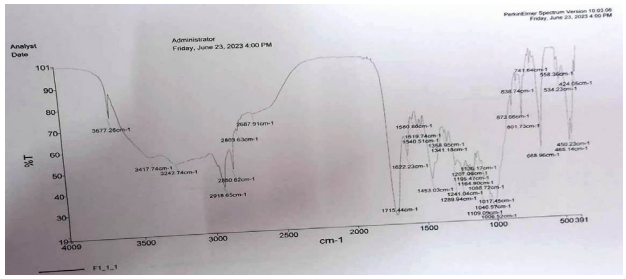

Figure 5: FTIR spectrum of GRFT5

to characterization on the basis of various parameters. Pre-compression results are given in Table 2. It suggested the good flow properties of the final powder blend. Various evaluation parameters, thickness, friability and weight variations for the tablets were mentioned in Table 3. %Swelling index, floating lag time and drug content% was mentioned in

Table 4: Data of results of SI, FLT, FT and drug content (n = 3)

Formulation batch	*SI (%)*	*FLT (seconds)*	*FT (hours)*	*%DC*
GRFT1	74.32 ± 0.3	310 ± 0.9	>12	97.21 ± 0.02
GRFT2	74.81 ± 0.2	318 ± 0.8	>12	97.73 ± 0.03
GRFT3	75.38 ± 0.2	298 ± 0.9	>12	96.56 ± 0.01
GRFT4	78.77 ± 0.2	325 ± 0.7	>12	97.25 ± 0.04
GRFT5	79.82 ± 0.4	280 ± 0.5	>12	99.45 ± 0.02
GRFT6	76.34 ± 0.3	299 ± 0.8	>12	98.01 ± 0.06
GRFT7	73.97 ± 0.8	320 ± 0.9	>12	97.49 ± 0.04
GRFT8	76.46 ± 0.3	326 ± 0.8	>12	98.67 ± 0.05
GRFT9	78.79 ± 0.2	319 ± 0.9	>12	95.31 ± 0.03

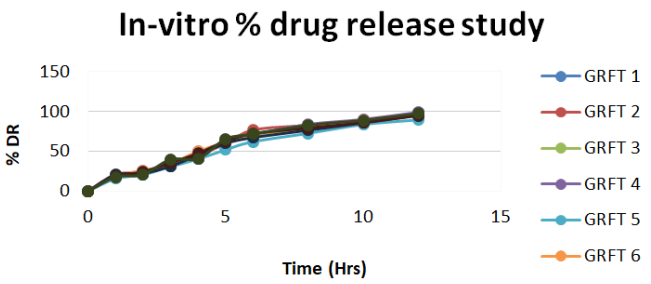

Figure 6: *In-vitro* %drug release studies

Table 5: Data of results of *in-vitro* drug release studies (n = 3)

Time (Hours)	*In-vitro %drug release data*								
	GRFT1	*GRFT2*	*GRFT3*	*GRFT4*	*GRFT5*	*GRFT6*	*GRFT7*	*GRFT8*	*GRFT9*
0	0	0	0	0	0	0	0	0	0
1	19.31 ± 0.1	20.78 ± 0.2	18.26 ± 0.1	17.39 ± 0.2	15.47 ± 0.1	19.7 2 ± 0.1	20.43 ± 0.2	18.16 ± 0.3	17.58 ± 0.1
2	25.24 ± 0.1	22.83 ± 0.3	24.18 ± 0.2	20.74 ± 0.3	20.59 ± 0.2	25.27 ± 0.1	22.19 ± 0.1	24.26 ± 0.2	20.76 ± 0.1
3	34.65 ± 0.3	31.21 ± 0.1	35.95 ± 0.2	39.64 ± 0.1	30.78 ± 0.2	34.26 ± 0.2	31.25 ± 0.2	35.39 ± 0.1	39.5 6 ± 0.2
4	49.38 ± 0.2	45.27 ± 0.2	47.36 ± 0.3	40.19 ± 0.2	40.23 ± 0.2	49.91 ± 0.1	45.43 ± 0.3	47.35 ± 0.2	40.81 ± 0.2
5	61.65 ± 0.4	59.37 ± 0.4	62.64 ± 0.2	65.27 ± 0.2	51.87 ± 0.1	61.25 ± 0.3	59.91 ± 0.2	62.47 ± 0.2	65.29 ± 0.1
6	72.52 ± 0.4	76.76 ± 0.2	70.92 ± 0.1	71.15 ± 0.3	62.07 ± 0.2	70.85 ± 0.3	67.26 ± 0.1	71.98 ± 0.1	71.64 ± 0.3
8	80.13 ± 0.2	82.78 ± 0.1	79.45 ± 0.3	83.92 ± 0.1	72.56 ± 0.3	80.79 ± 0.2	76.45 ± 0.2	79.36 ± 0.2	82.72 ± 0.4
10	88.52 ± 0.1	89.35 ± 0.2	87.91 ± 0.2	90.14 ± 0.2	83.73 ± 0.4	88.82 ± 0.1	85.76 ± 0.2	86.16 ± 0.3	89.07 ± 0.2
12	98.43 ± 0.2	98.21 ± 0.3	97.87 ± 0.3	99.11 ± 0.3	89.52 ± 0.3	95.34 ± 0.2	94.96 ± 0.3	95.34 ± 0.2	97.46 ± 0.3

Table 4. %drug release [DR] results were presented in Table 5 and Figure 6. Among all 9 batches, GRFT 5 was found to be best as it showed the sustained drug release of 89.52 ± 0.3% up to 12 hours. There was no significant change in the stability of GRFT was observed based on the results of obtained data when determined after 3 months at 40°C ± 2°C/75 ± 5% RH.

CONCLUSION

Levofloxacin faces the problem of therapeutic performance as it reaches a high pH of GI tract. To overcome this problem GRFT of levofloxacin was prepared using natural polymer (peanut husk powder) by direct compression method. All the formulation ingredients were found to be compatible with each other. GRFT formulations were evaluated on the basis of various parameters and it was also found stable. Based on the results, GRFT5 was found to show best among all batches.

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