ISSN: 2455-8109

International Journal of Farmacia (IJF)

IJF |Vol.11 | Issue 2 | Apr - Jun -2025

www.ijfjournal.com

DOI : https://doi.org/10.61096/ijf.v11.iss2.2025.55-65

Research

Direct Compression Approach To Formulate And Evaluate Oro-Dispersible Tablets Containing Gatifloxacin Using Natural Superdisintegrants

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Published on: 08 May 2025

Published by:
DrSriram Publications

Abstract

Orally dispersible tablets (ODTs) quickly break down or dissolve in the mouth without the need for water. The demand for orally disintegrating tablets (ODTs) has experienced a significant surge, leading to a substantial expansion of this field within the pharmaceutical business and academics. Orally dissolving tablets are becoming increasingly popular compared to regular tablets since they are convenient to administer and suitable for patients. This study aims to create orally dispersible tablets of Gatifloxacin (GTF) utilizing natural superdisintegrants. The preparations were made by the direct compression approach. The optimal flow properties, such as angle of repose, bulk density, and tapped density, were demonstrated by the amalgamation of all the formulations. The produced tablets exhibited favorable post-compression characteristics and successfully met all quality control evaluation criteria according to the I.P limits. The F1 formulation exhibited the highest drug release, specifically 98.75%, within a 20-minute timeframe. Therefore, it is regarded as the optimum formulation. Out of all the formulations, the F1 that uses plantago ovata as a superdisintegrant satisfies all the requirements. In comparison to other formulations, it has demonstrated exceptional in vitro disintegration and dissolution. The study came to the conclusion that GTF may be successfully made into dispersible tablets since it meets all the requirements for a dispersible tablet and can serve as a substitute for the traditional tablets that are currently on the market.

Keywords: Gatifloxacin, Orodispersible tablet, Plantago ovata, Tragacanth, Acacia, Starch.

INTRODUCTION

The Centre for Drug Evaluation and Research (CDER) and the United States Pharmacopoeia (USP) have approved the use of oral disintegrating (OD) tablet technique. According to the USFDA, a oral disintegrating tablet is a solid drug that dissolves on the tongue when it comes into contact with the tongue, usually in a matter

of seconds. The term "Oro Dispersible Tablet" has been added to the European Pharmacopoeia to describe tablets that are meant to be taken orally and quickly dissolve before being ingested. In the patient's mouth, these dosage forms quickly dissolve or crumble in 15 to 3 minutes without the need for water or chewing. When it comes to drug delivery, oro-dispersible tablets are unique and have a number of benefits over conventional oral solid dosage formulations. This tablet medications are made to dissolved rapidly in the oral cavity, despite the fact that they can be described by a number of names[1, 2]. There were some work done on orodispersible drug delivery formulations such as, bilastin[3], aceclofenac[4], valsartan and nebivolol[5], salbutamol sulfate[6], flucloxacillin[7].

Plantago ovate (psyllium) is a white to pale white powder that has no smell or flavour and flows freely. Slightly soluble in ethanol (95%). It swells in water (volume up to 300 times). Used as a disintegrant in tablets and capsules formulations at a conc. of 2-8%. To prevent caking, it is advisable to store it in a well sealed container, protecting it from significant fluctuations in temperatures and moisture[8, 9]. Tragacanth and starch is also used as disintegrants[10, 11]. Gatifloxacin is a fluoroquinolone antibiotic that is a white to slight yellow crystalline powder. Stored in well closed container in cool dry place, protect from light.[12] The aim of the present research is to formulate oral dispersible tablets containing Gatifloxacin (GTF) by direct compression technique.

MATERIALS & METHODS

Chemicals

Gatifloxacin was obtained as a gift sample from Karnataka Antibiotics, Bangalore. Plantago ovata obtained from Mother herbs, Delhi. Starch is purchased from Loba chemicals, Delhi. Tragacanth, acacia and lactose were purchased from Spectrum reagents and chemicals, Cochin. Magnesium stearate and talc from S.D. Fine Chemicals, Mumbai. All the used reagents and chemicals were of analytical reagent grade, unless otherwise stated.

Compatibility studies for drug with the excipient

The medication and disintegrant compatibility investigations were conducted using FT-IR spectrophotometers. Gatifloxacin, plantago ovata, tragacanth, acacia, and starch all had spectra that were recorded. Using the potassium bromide (KBr) disc procedure, the samples were made. The powder was compressed to create the KBr disc, and the scanning range was maintained between 4000 and 450 cm−1.

Manufacturing Dispersible Tablets [13, 14, 15]:

Plantago ovata (psyllium), tragacanth, acacia, and powdered starch were added to different superdisintegrants and disintegrants in concentrations of 5%, 10%, and 15% to create dispersible tablets of GTF using the direct compression method. Tables 1–4 provide the formulation's makeup. After the components were well combined, sieve number 22 was used.

Table 1: Formulation of dispersible tablet of GTF. (F1-F3)

Ingredients mg/ tab	F1	F2	F3
Gatifloxacin	200mg	200mg	200mg
Lactose	117.5mg	105mg	92.5mg
Plantago ovate	12.5mg	25mg	37.5mg
Talc	10mg	10mg	10mg
Mg Stearate	10mg	10mg	10mg

Table 2: Formulation of dispersible tablet of GTF. (F4-F6)

Ingredients mg/ tab	F4	F5	F6
Gatifloxacin	200mg	200mg	200mg
Lactose	117.5mg	105mg	92.5mg
Tragacanth	12.5mg	25mg	37.5mg
Talc	10mg	10mg	10mg
Mg Stearate	10mg	10mg	10mg

Table 3: Formulation of dispersible tablet of GTF. (F7-F9)

Ingredients mg/ tab	F7	F8	F9
Gatifloxacin	200mg	200mg	200mg
Lactose	117.5mg	105mg	92.5mg

Acacia	12.5mg	25mg	37.5mg
Talc	10mg	10mg	10mg
Mg Stearate	10mg	10mg	10mg

Table 4: Formulation of dispersible tablet of GTF. (F10-GT12)

Ingredients mg/ tab	F10	F11	F12
Gatifloxacin	200mg	200mg	200mg
Lactose	117.5mg	105mg	92.5mg
Starch	12.5mg	25mg	37.5mg
Talc	10mg	10mg	10mg
Mg Stearate	10mg	10mg	10mg

Evaluation of post compression parameters for prepared Tablets[16]

A comprehensive analysis was conducted on the physicochemical parameters of the proposed tablet formulation, encompassing drug content, hardness, thickness, friability, and weight change.

In vitro Dissolution Study[17]

Lab India's model DS-800, a modified USP XXIII dissolving test apparatus, was used for the in-vitro release investigations. A dissolution fluid of 500 cc of pH 6.8 phosphate buffer was used in each experiment, with the conditions being 37°C, 50 rpm, and speed of rotation. Taking 5 ml samples of the dissolving liquid at 2 min intervals allowed us to monitor its concentration of GTF using absorbance measurements at 286 nm. A 5 ml volume of test media was removed at predetermined times and replenished with a 6.8 pH phosphate buffer throughout all experiments.

Release Kinetics[18]

The findings from the in-vitro diffusion investigation were used to investigate the drug release kinetics of GTF dispersible tablets, including their order and mechanism. The zero order, first order, and Higuchi equations were among the kinetic models that were plotted; the Korsmeyer-Peppas equations were used to determine the release.

Stability Studies [19, 20, 21]

If a drug wants to be registered in the US, EU, or Japan, it must pass certain stability tests that are laid out in the ICH Guidelines, particularly the "Stability testing of new drug substance and products" (QIA). Stability studies for the present research conducted at 40º C ± 2ºC/75% ± 5% RH for the made a selection and used it for three months.

RESULTS AND DISCUSSION

Calibration of GTF in phosphate buffer pH 6.8

A phosphate buffer solution with a pH of 6.8 was used to generate the GTF calibration curves. At 286 nm, the wavelength of maximum absorption, the absorbance was measured. A correlation coefficient of 0.9864 has been computed. It was found that the standard curve correlation coefficient was getting close and presented in Figure 1.

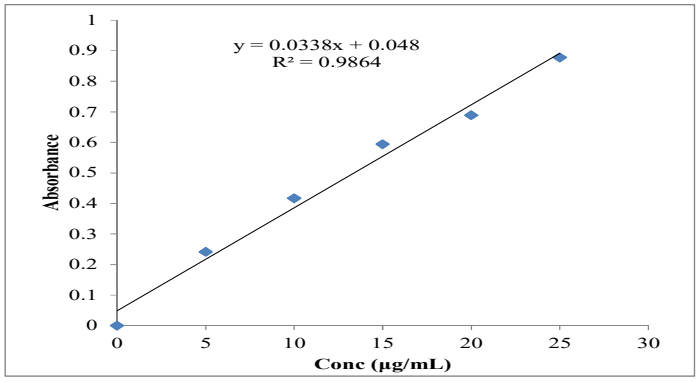

Fig 1: Standard graph of GTF 6.8 pH phosphate buffer

Drug and Excipient Compatibility Studies Using Fourier Transform Infrared Spectroscopy (FT-IR):

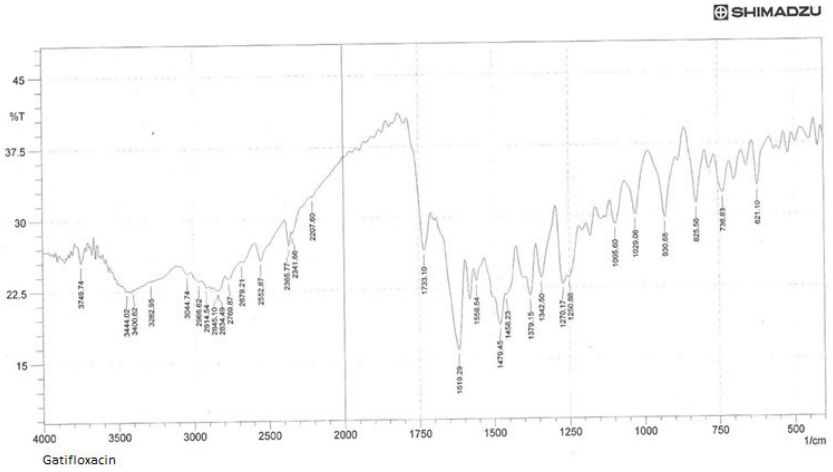

Fig 2: FTIR spectra pure drug of GTF

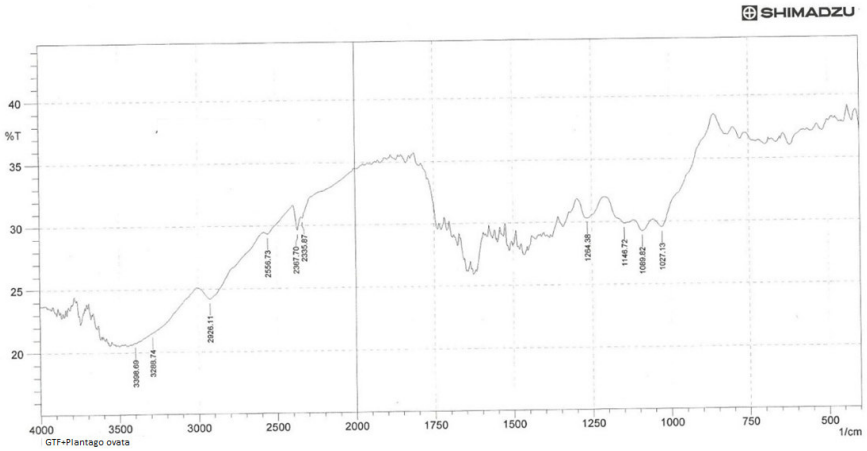

Fig 3: FTIR spectra of GTF with plantago ovata

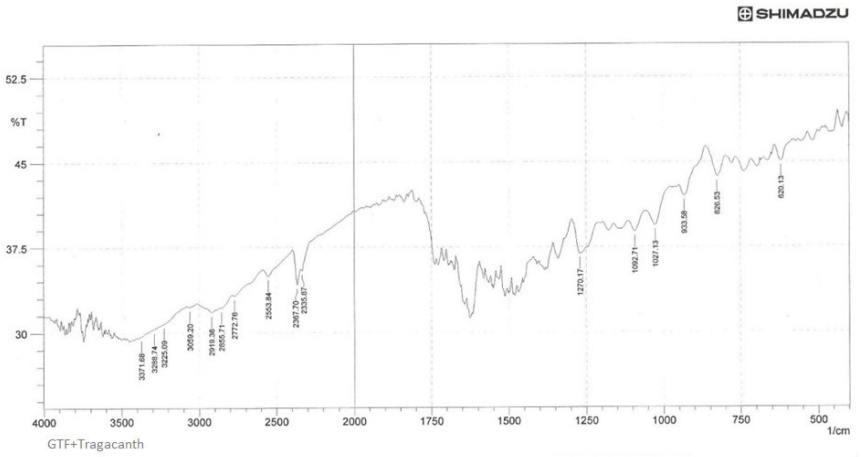

Fig 4: FTIR spectra of GTF with tragacanth

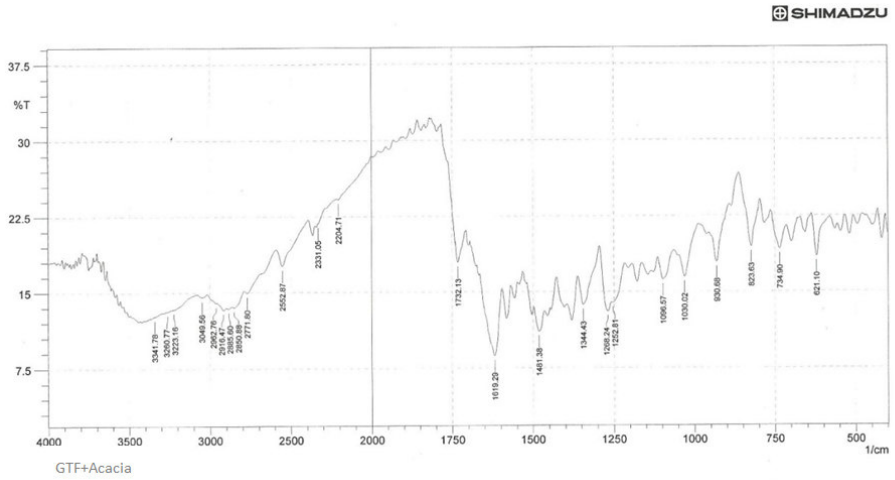

Fig 5: FTIR spectra of GTF with acacia

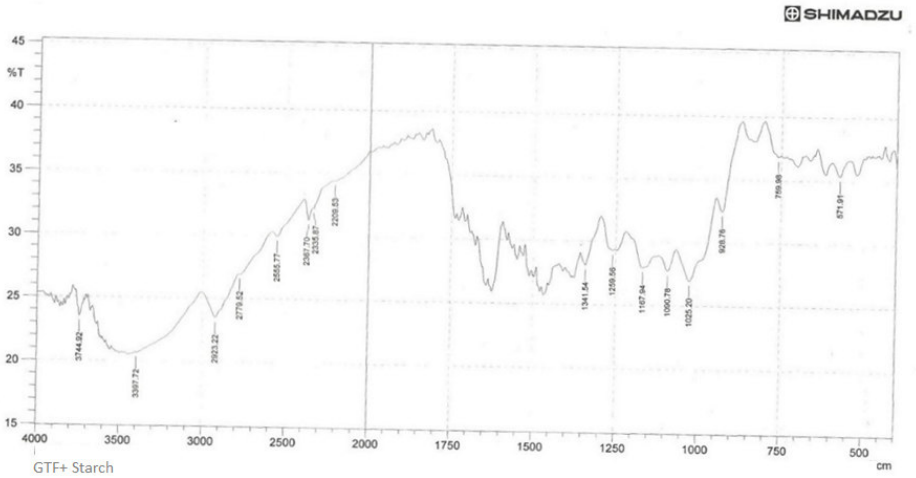

Fig 6: FTIR spectra of GTF with starch

Table 5: FTIR spectral interpretation

Sample	O-H Stretching	C–H Stretching	C=O Stretching	C=C Stretching
Pure GTF	3400	2914	1619	1458
GTF+Plantago ovata	3398	2926		
GTF+Tragacanth	3371	2919		
GTF+Acacia	3341	2916	1619	1481
GTF+Starch	3397	2923		

Studies of drug-excipient interactions

First Spectrum: The IR spectra of pure drug GTF showed the existence of a O-H group at 3400 cm-1and C-H group at 2914 cm-1. Shoulders between 1458 cm-1 have emerged as the peak caused by the C=C. The peak of C=O was observed at 1619 cm-1. The medication molecule's intricate structure is to blame for this. Figure 2 displays the infrared spectrum of the pure medication GTF.

Second Spectrum: Plantago ovata and medication are employed for this formulation. The final output showed an extremely well-resolved infrared spectrum with distinct absorption peaks. The well-defined depression has been detected at 3398 cm-1. Speculating that the O-H group overlap in the superdisintegrant could be the cause. These

findings suggested that there hasn't been any chemical reaction with the medicine. It is merely a blend of materials. Figure 3 displays this formulation's infrared spectrum.

Third Spectrum: Tragacanth and medication are employed in this formulation. The final output showed an extremely well-resolved infrared spectrum with distinct absorption peaks. The noticeable hump is located at 3371 cm-1. Speculating that the O-H group overlapping in the disintegrant could be the cause. These findings suggested that there hasn't been any chemical reaction with the medicine. It is merely a blend of materials. Figure 4 displays this formulation's infrared spectrum.

Fourth Spectrum: Acacia and medication are utilised in this formulation. The final output showed an extremely well-resolved infrared spectrum with distinct absorption peaks. The noticeable hump is located at 3341 cm-1. Speculating that the disintegrant's C-Cl group overlap could be the cause. These findings suggested that there hasn't been any chemical reaction with the medicine. It is merely a blend of materials. Figure 5 displays this formulation's infrared spectrum.

Fifth Spectrum: Starch and medication are employed in this formulation. The final output showed an extremely well-resolved infrared spectrum with distinct absorption peaks. The noticeable hump is located at 3397 cm-1. Speculating that the O-H group overlapping in the disintegrant could be the cause. These findings suggested that there hasn't been any chemical reaction with the medicine. It is merely a blend of materials. Figure 6 displays this formulation's infrared spectrum.

EVALUATION OF DISPERSIBLE TABLETS FORMULATIONS:

The precompression parameters are as follows

Based on tabulation in Table 7, it was determined that the results were within the 17.2±0.36-22.4±0.35 range. This shows that the powder blend has good flow properties. The bulk density values obtained for each of the twelve formulations (F1-F12) a range of 0.47±0.07-0.55±0.03 g/cm^3. All of the formulations (F1-F12) have the 0.56±0.06 to 0.61±0.02 g/cm^3 tapped density range. Compressibility index **v**alues, fall within the range of 13.2±0.57-17.9±0.68%, suggesting that the powder blends possess the necessary flow characteristics for direct compression. Hausner's ratio values, were determined to be between 1.08±0.13-1.22±0.04.

Table 6: Pre-compression parameters of all formulations

Formulations	Bulk Density (g/cm^2)	Tap Density (g/cm^2)	Carr's Index (%)	Hausner's ratio	Angle Of Repose(Θ)
F1	0.53±0.02	0.60±0.02	13.2±0.57	1.08±0.13	21.6±0.21
F2	0.49±0.01	0.61±0.01	15.3±0.63	1.12±0.04	22.4±0.35
F3	0.50±0.02	0.60±0.03	16.4±0.61	1.19±0.06	18.5±0.14
F4	0.49±0.03	0.58±0.05	14.1±0.52	1.20±0.08	19.9±0.42
F5	0.52±0.05	0.59±0.02	13.4±0.54	1.22±0.04	18.4±0.33
F6	0.49±0.04	0.57±0.04	15.6±0.66	1.18±0.09	20.3±0.18
F7	0.47±0.07	0.58±0.01	14.3±0.59	1.21±0.12	18.9±0.27
F8	0.52±0.06	0.59±0.04	16.8±0.64	1.19±0.11	19.5±0.32
F9	0.50±0.08	0.58±0.03	17.6±0.69	1.18±0.07	18.7±0.41
F10	0.55±0.03	0.61±0.02	15.9±0.53	1.11±0.05	19.8±0.38
F11	0.52±0.02	0.56±0.06	16.4±0.61	1.13±0.07	18.2±0.29
F12	0.54±0.06	0.58±0.03	17.9±0.68	1.21±0.13	17.2±0.36

After compression parameters

Table 8 presents the measured hardness of tablets in each batch, which varied from 4.24±0.37-5.05±0.25 kg/cm^2. The tablets were mechanically stable since the percentage of friability was less than 1% in every formulation which is in between 0.45±0.04% to 0.71±0.03%. Weight variation for each formulation, which ranged from 397.5±4.1 to 403.4±3.9. The results showed that the disintegration duration of the formulated tablets ranged from 19.34±1.43 to 26.78±2.28 seconds. Analytical tests were conducted on the prepared mixtures. The laboratory investigations determined the drug content values of all the formulations ranged from 97.15±2.27% to 99.43±3.27%.

Table 7: Evaluation of tablets-1

F code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time (sec)	Friability (%)	Assay (%)
F1	399.8±3.4	4.52±0.22	4.34±0.24	19.34±1.43	0.48±0.04	9.43±3.27
F2	398.4±5.5	4.49±0.12	4.29±0.27	20.56±1.56	0.59±0.05	8.89±4.22

F3	397.5±4.1	4.47±0.31	4.51±0.35	22.27±2.11	0.67±0.06	7.75±3.24
F4	401.7±5.6	5.05±0.25	4.39±0.42	25.32±2.23	0.45±0.04	8.34±2.29
F5	399.3±4.2	4.86±0.13	4.47±0.34	23.37±1.64	0.68±0.06	7.45±4.27
F6	402.2±5.5	4.59±0.23	4.28±0.33	22.11±2.26	0.71±0.03	6.24±5.28
F7	401.2±3.8	4.24±0.37	4.36±0.21	22.67±1.87	0.59±0.04	6.95±3.24
F8	398.5±4.9	4.37±0.22	4.57±0.23	24.21±2.35	0.63±0.07	7.15±2.27
F9	403.4±3.9	4.71±0.34	4.28±0.22	26.78±2.28	0.69±0.06	98.82±4.12
F10	399.3±4.3	4.85±0.31	4.49±0.35	25.34±1.57	.58±0.04	7.51±5.25
F11	402.6±3.7	4.47±0.21	4.53±0.29	23.28±2.36	.62±0.06	8.34±3.27
F12	401.7±4.8	4.69±0.13	4.32±0.41	24.42±1.51	.68±0.05	7.81±4.36

Table 8 displays the wetting timings for each formulation. The wetting times of the tablets made using various superdisintegrants and disintegrants, such as plantago ovata, tragacanth, acacia, and starch, were found to be 145-165, 190-223, 170-215, and 220-264 seconds, in that order. It was discovered that the control formulation's wetting time was 145 seconds. The wetting time rose in tandem with the superdisintegrant concentration. The water absorption ratios of the tablets made with various superdisintegrants and disintegrants, such as plantago ovata, tragacanth, acacia, and starch, were 49.42, 59.46, 53.04, and 61.9, respectively. The absorption of water increased linearly as the concentration of superdisintegrants decreased.

Table 8: Evaluation of tablets-2

F code	Percentage of water absorbed	Wetting time (sec)
F1	49.42± 0.34	145±0.34
F2	44.17± 0.35	152±0.13
F3	38.16±0.21	165±0.21
F4	59.46±0.51	190±0.37
F5	55.16±0.29	200±0.31
F6	49.14±0.37	223±0.11
F7	53.04±0.35	170±0.51
F8	48.32±0.35	183±0.11
F9	44.27±0.37	215±0.73
F10	61.9±0.26	220±0.25
F11	59.62±0.44	246±0.23
F12	56.04±0.13	264±0.73

In vitro Dissolution Study

Phosphate buffer 6.8 (simulated fluid) is used to assess the GTF tablet's in vitro dissolution. As seen in Figs.7-10, the plot of the percentage cumulative drug release V/s time (min) was plotted and illustrated. The drug release research from formulations including plantago ovata (F1-F3) was determined to be 98.75%, 95.35%, and 88.24% drug release, respectively, based on the in vitro dissolving data. Tragacanth containing formulations (F4–F6) yielded results of 87.46%, 84.65%, and 80.29, in that order. Acacia-containing formulations (F7–F9) displayed 89.21%, 85.96%, and 81.96%, in that order. Starch-containing formulations (F10–F12) displayed 86.30%, 83.96%, and 79.96%, in that order. The findings showed that the plantago ovata formulations exhibited the highest dissolution rate, releasing over 98.75% of the drug in 20 minutes; the tragacanth formulations released over 87.46% of the drug in 20 minutes; the acacia formulations released over 89.21% of the drug in 20 minutes; and the starch formulation released over 86.30% of the drug in 20 minutes. The dissolving rate decreased linearly in all formulations up to 15% concentration. The dissolving rate decreased in all formulations at greater concentrations. Thus, for all the superdisintegrants, 5% is the ideal value. Reduction in the rate of disintegration as superdisintegrants are added.

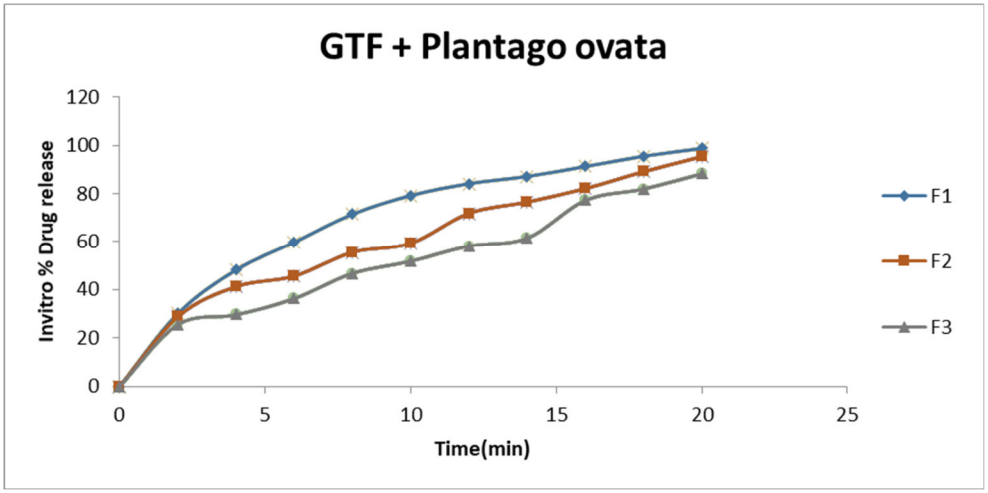

Fig 7: *in-vitro* drug dissolution graph of GTF with Plantago ovata

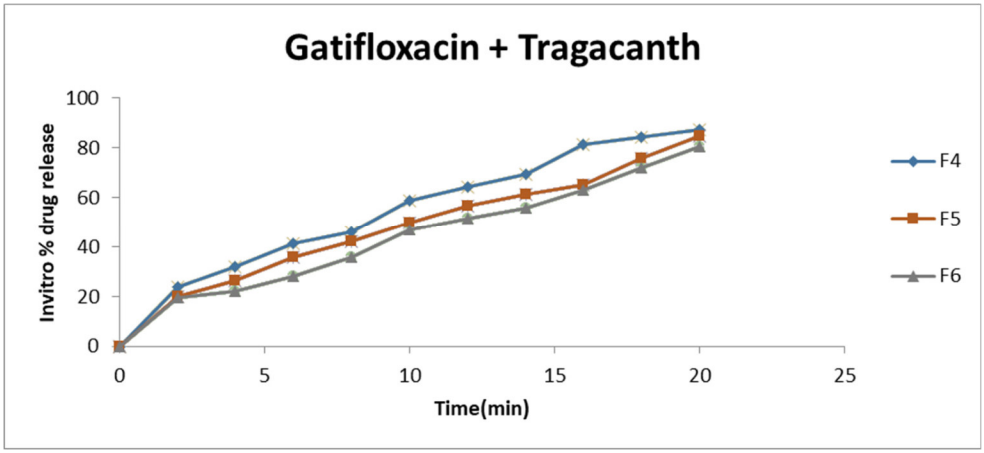

Fig 8: *in-vitro* drug dissolution of Gatifloxacin with Tragacanth

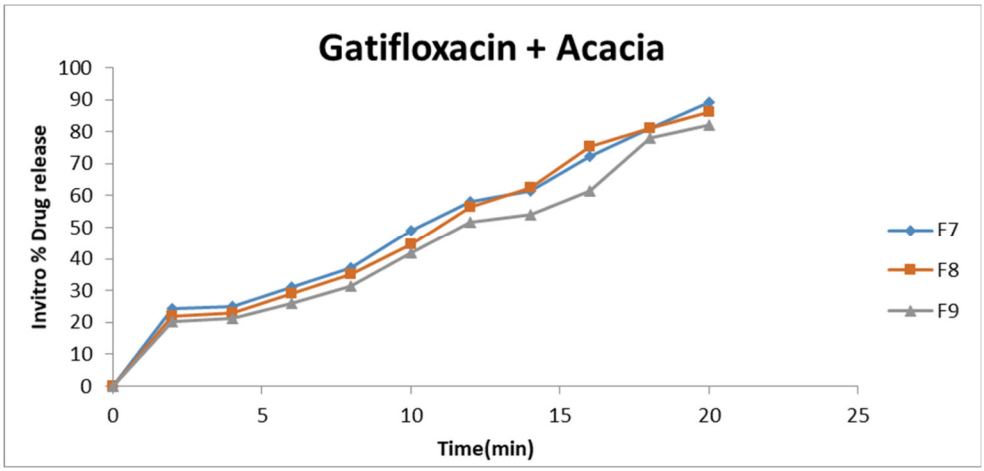

Fig 9: *in-vitro* drug dissolution of Gatifloxacin with Acacia

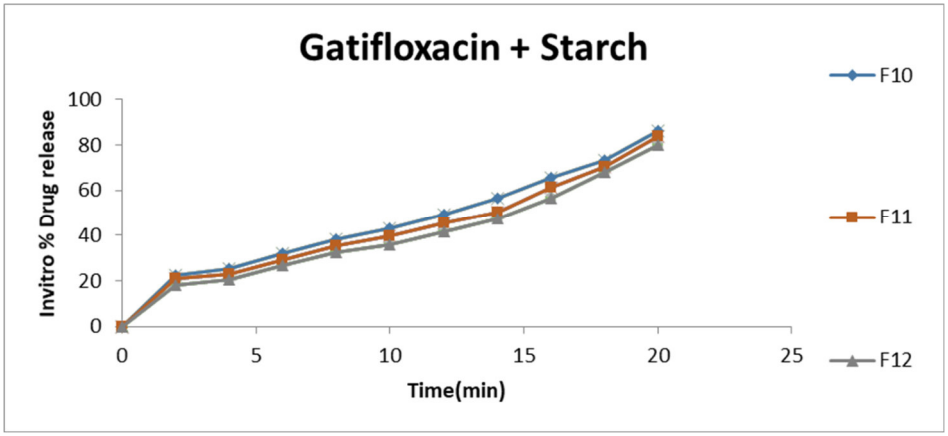

Fig 10: in-vitro drug dissolution of Gatifloxacin with Starch

Curve Fitting Analysis

The results of dissolution data were compared to different drug release kinetic equations to ascertain the sequence of release by processing the data in line with Zero and First order, Higuchi and Korsmeyer Peppas equation. The kinetic values that were established for the different formulations are listed in Table 10. The linearity suggests that the medication is released from the tablets in accordance with first order principles.

Table 9: Model fitting for optimized formulation

Time	% drug release	Log % unreleased	Log t	SQRT	Log % drug release
2	30.06	1.844726	0.30103	1.414214	1.477989
4	48.13	1.714916	0.60206	2	1.682416
6	59.75	1.604766	0.778151	2.44949	1.776338
8	71.45	1.455606	0.90309	2.828427	1.854002
10	79.21	1.317854	1	3.162278	1.89878
12	85.16	1.171434	1.079181	3.464102	1.930236
14	89.14	1.03583	1.146128	3.741657	1.950073
16	93.25	0.829304	1.20412	4	1.969649
18	96.52	0.541579	1.255273	4.242641	1.984617
20	98.75	0.09691	1.30103	4.472136	1.994537

Table 10: R^2 values for optimized formulation

Formulation code	Zero order R^2	First order R^2	Higuchi R^2	Korsmeyar peppas R^2
F1	**0.8678**	**0.9508**	**0.9882**	**0.9791**

Stability analyses

By conducting stability tests on an optimized formulation (F1) for three months at accelerated circumstances of 40°C + 75% RH, stability of this combination (Table 12) was determined. The degree of hardness, disintegration time, drug content, and in-vitro drug release pattern of the formulation were all reported to be stable. All of the metrics were within the predetermined range, and there was no discernible change from the original data. Measurements were taken every 30 days throughout the three-month in-vitro dissolving research. Exposure to elevated temperatures and controlled humidity levels had no effect on the release patterns.

Table 11: Stability studies of optimized (F1) formulation

Parameters	Time in months			
	0 (Initial)	**1st month**	**2nd month**	**3rd month**
Hardness (kg/cm^2)	3.14± 0.02	3.14± 0.05	3.14± 0.02	3.14± 0.03
Friability (%)	0.39±0.03	0.39±0.04	0.39±0.04	0.39±0.02
Disintegration time(sec)	31±0.31	31±0.23	31±0.21	31±0.27
Drug content (%)	98.75±0.027	98.75±0.027	98.75±0.015	98.80±0.011
In-vitro drug release (%)	98.75±0.61	98.75±0.035	98.75±0.025	98.72±0.018

CONCLUSION

In this investigation Dispersible tablets were effectively created as a fast-dissolving drug delivery strategy for GTF, providing a realistic and appropriate means of achieving the intended goal of increased bioavailability and faster disintegration and dissolving properties. Plantago ovate, tragacanth, acacia, and starch were used as superdisintegrants and disintegrants to create dispersible GTF tablets.

The results of this investigation indicate that: GTF dispersible tablets made with superdisintegrants and disintegrants performed well in terms of not chipping, capping, or adhering; all tablet formulations had the same amount of medicine. The medication and disintegrants are compatible, according to FT-IR research. It was discovered that the ratio of the medication to the superdisintegrants affected the drug's release from the formulations. It was discovered that drug release rates increased when the amount of superdisintegrating agent decreased. Compared to the other formulations, Formulations F1, F2, and F3 exhibit better release, hardness, low friability, and the shortest wetting and disintegration times. Out of all the formulations, the one that uses plantago ovata as a superdisintegrant satisfies all the requirements. In comparison to other formulations, it has demonstrated exceptional in vitro disintegration and dissolution. The prepared tablets break down quickly and don't require water, which improves absorption and raises the product's bioavailability. The study came to the conclusion that GTF may be successfully made into dispersible tablets since it meets all the requirements for a dispersible tablet and can serve as a substitute for the traditional tablets that are currently on the market. The prepared formulations held up well over a 90-day storage period at a regulated temperature of 40°C and relative humidity of 75%.

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