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Research Article

**FORMULATION AND EVALUATION OF PH-DEPENDENT
EUDRAGIT S-100 COATED MATRIX TABLETS OF
TOFACITINIB CITRATE FOR COLON TARGETED DRUG
DELIVERY****Satyam Pahariya***, Akanksha Tiwari, Rekha Rani, Priyanka Keshri
School of Pharmacy, ITM University, Turari, Gwalior, (M. P.), India**Abstract:**

The goal of the current study was to create and assess pH-dependent Eudragit S-100 coated matrix tablets containing tofacitinib citrate for colon-targeted medication delivery. Using chitosan and Carbopol 940 P as release-retarding polymers and citric acid and sodium bicarbonate as gas-generating agents, matrix tablets were made by direct compression. Bulk density, tapped density, compressibility index, Hausner ratio, hardness, thickness, friability, weight variation, drug content, floating lag time, and total floating duration were among the pre-compression and post-compression parameters that were assessed for a total of nine formulations (F1–F9). Every formulation showed adequate buoyancy behavior and acceptable physicochemical properties. All formulations displayed sustained release characteristics in *in vitro* drug release experiments, with formulation F8 exhibiting optimal drug release with a floating lag time of 28 ± 2 seconds and a cumulative drug release of $98.95 \pm 1.40\%$ at 12 hours. The optimized formulation followed Higuchi diffusion kinetics with a non-Fickian diffusion mechanism, according to drug release kinetic experiments. The optimized formulation's good stability was confirmed by stability testing conducted under accelerated settings, which showed no appreciable changes in physical appearance, drug content, hardness, and drug release profile.

According to the study's findings, Eudragit S-100 coated matrix tablets of tofacitinib citrate may be a viable method for efficient colon-targeted medication delivery with extended drug release and enhanced therapeutic efficacy.

Keywords: Tofacitinib citrate, Colon targeted drug delivery, Eudragit S-100, Matrix tablets, Chitosan, Carbopol 940 P, Floating tablets, Sustained release, pH-dependent coating, Drug release kinetics.

Corresponding author:**Satyam Pahariya,**

School of Pharmacy, ITM University,

Turari, Gwalior, (M. P.), India

Mail Id: satyamgupta1575@gmail.com

QR CODE



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INTRODUCTION:

The ability of colon targeted drug delivery systems (CTDDS) to transport medications to the colon selectively for both local and systemic therapeutic effects has drawn a lot of attention in recent years (Muhammed *et al.*, 2024).

Reduced dose frequency, increased therapeutic efficacy, fewer systemic side effects, and protection of medications against upper gastrointestinal tract degradation are just a few benefits of colon targeting. These systems are particularly helpful in treating Crohn's disease, rheumatoid arthritis, ulcerative colitis, colorectal cancer, and inflammatory bowel disorders (IBD). Furthermore, colon-targeted devices are useful for delivering proteins and peptides that are vulnerable to enzymatic breakdown in the small intestine and unstable in the stomach's acidic environment (Banerjee *et al.*, 2017).

The colon is a desirable location for regulated and site-specific drug delivery because of its distinct physiological features, which include extended transit time, decreased enzyme activity, almost neutral pH, and an abundance of microorganisms (Muhammed *et al.*, 2024). Numerous strategies, such as pH-dependent systems, time-dependent systems, pressure-controlled systems, osmotic-controlled systems, and microbially triggered delivery systems, have been studied for colon targeting. Since the pH of the gastrointestinal tract progressively rises from the stomach to the colon, pH-dependent drug delivery devices are one of these strategies that is extensively investigated. Therefore, enteric polymers that breakdown at alkaline pH and stay intact at acidic pH are widely employed for colon-specific drug release (Mishra *et al.*, 2026).

One of the most popular pH-sensitive polymers for colon-targeted treatments is Eudragit®. Based on methacrylic acid and methyl methacrylate, Eudragit S-100 is an anionic copolymer that dissolves at pH values higher than 7.0. This characteristic makes Eudragit S-100 appropriate for colon targeting since it permits medication release in the terminal ileum and colon while preventing premature drug release in the stomach and small intestine (Kshirsagar *et al.*, 2009).

An oral Janus kinase (JAK) inhibitor called tofacitinib citrate is frequently used to treat ulcerative colitis and rheumatoid arthritis. It works by blocking JAK-mediated signaling pathways that produce inflammatory cytokines. Despite tofacitinib's outstanding therapeutic efficacy in treating ulcerative colitis, its nonspecific drug distribution and substantial absorption in the upper gastrointestinal tract may result in systemic side effects when taken orally. Thus, tofacitinib citrate delivered to the colon may increase local drug concentration at the site of inflammation while

lowering systemic exposure and related side effects (Palasik *et al.*, 2021).

Because of their simplicity, affordability, ease of manufacture, and capacity to maintain drug release, matrix tablets are frequently used in controlled and colon-targeted medication administration. Drug release can be controlled over an extended period of time by including hydrophilic or hydrophobic polymers into matrix tablets (Amidon *et al.*, 2015). Matrix tablets can successfully shield the medication throughout passage through the stomach and small intestine and then release it in the colon when paired with pH-dependent coating polymers like Eudragit S-100. Eudragit S-100 coated matrix tablets produce minimal drug release in acidic environments and increased drug release at colonic pH values, according to earlier research (Gvozdeva and Staynova; 2025).

Therefore, the present study aims to formulate and evaluate pH-dependent Eudragit S-100 coated matrix tablets of tofacitinib citrate for colon targeted drug delivery. The developed formulation is expected to provide site-specific drug release in the colon, improve therapeutic efficacy in ulcerative colitis, minimize systemic side effects, and enhance patient compliance through controlled drug delivery.

Material and Methods

Material

Tofacitinib citrate was used as the active pharmaceutical ingredient for the preparation of colon targeted matrix tablets. Eudragit S-100 was used as a pH-dependent polymer for colon specific coating, while Chitosan and Carbopol 940 P were employed as release-retarding polymers for sustaining drug release. Sodium bicarbonate and citric acid were incorporated as gas-generating agents to impart floating properties to the tablets. Lactose was used as a diluent, magnesium stearate as a lubricant, and talc as a glidant. All chemicals and excipients used in the study were of analytical or pharmaceutical grade.

Methods

Formulation of Eudragit S-100 coated matrix tablets of Tofacitinib citrate

Matrix tablets of Tofacitinib citrate were prepared by direct compression method using varying polymer compositions. A total of nine formulations (F1 to F9) were developed, each containing 5 mg of Tofacitinib citrate. The polymers used included Chitosan (30 mg in all batches) and Carbopol 940 P (used only in F7, F8, and F9 at 20 mg), with Citric acid (5 mg) and Sodium bicarbonate (20 mg) added to each formulation as gas-generating agents to enhance floating properties.

All ingredients including the drug, polymers, and excipients were sieved through mesh #40 prior to mixing to ensure uniform particle size. The required quantity of each ingredient was accurately weighed as per the formulation design. The

ingredients were then blended thoroughly in a mortar to obtain a uniform mixture (Mehta *et al.*, 2013).

Optimization of matrix tablets of Tofacitinib citrate

Optimization of formulation carried out on the basis of OVAT (One variable at time) using amount of excipient used like Excipients like Chitosan and Carbopol 940 P.

Table 1: Formulations of Tofacitinib citrate loaded matrix tablets

Excipients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Tofacitinib citrate	5	5	5	5	5	5	5	5	5
Carbopol 940 P	-	-	-	-	-	-	20	20	20
Chitosan	30	30	30	30	30	30	30	30	30
Citric acid	5	5	5	5	5	5	5	5	5
Sodium Bicarbonate	20	20	20	20	20	20	20	20	20
Magnesium stearate	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5
Lactose	75	75	75	75	75	75	55	55	55
Total Weight	150	150	150	150	150	150	150	150	150

Enteric coating of the matrix tablets

The Tofacitinib citrate matrix tablets were further coated with Eudragit S-100 solution. A concentration (1%) of coating solution of Eudragit S-100 was prepared in a mixture of Isopropyl alcohol: acetone (1:1). The coating of the matrix tablets was performed by immersion in the coating solution followed by dip coating technique (Rohit *et al.*, 2013).

Evaluation of Precompression Parameter

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated by using following formula:

$$\text{LBD (Loose Bulk Density)} = \frac{\text{Mass of powder}}{\text{Volume of Packing}}$$

$$\text{TBD (Tapped Bulk Density)} = \frac{\text{Mass of powder}}{\text{Tapped Volume of Packing}}$$

Carr's index: Percent compressibility of powder mix was determined by Carr's compressibility index, calculated by using following formula (Kuksal *et al.*, 2006):

$$\text{Carr's Index} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \times 100$$

Hausners ratio: It is determined by comparing tapped density to the bulk density by using following equation (Chandran *et al.*, 2008):-

$$\text{Housner's ratio} = \frac{\text{Tapped bulk density}}{\text{Loose Bulk density}}$$

Hausner's ratio value <1.25 shows better flow properties

Evaluation of matrix tablets

General appearance

Five tablets from various batches were randomly selected and organoleptic properties such as color, odor, shape, were evaluated. Appearance was judged visually. Very good (+++), good (++), fair (+) poor (-), very poor (- -) (Tugcu-Demiroz *et al.*, 2004).

Thickness and diameter

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated (Khan *et al.*, 1999).

Drug content

Twenty tablets were taken and amount of drug present in each tablet was determined (Amrutkar and Gattani, 2009). The tablets were crushed in a mortar and the powder equivalent to 10mg of drug was transferred to 10ml standard flask. The powder was dissolved in 5 ml of phosphate buffer pH 7.2 and made up to volume with of phosphate buffer pH 7.2. The sample was mixed thoroughly and filtered through a 0.45 μ membrane filter. The filtered solution was diluted suitably and for drug content by UV spectrophotometer at λ_{max} of 290 nm using of phosphate buffer pH 7.2 as blank.

Hardness

For each formulation, the hardness of five tablets was resolved utilizing the Monsanto hardness tester (Shah *et al.*, 2011).

Friability

The friability of a sample of 10 tablets was estimated utilizing a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated (Ahmadi *et al.*, 2011).

Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated (Lopes *et al.*, 2006).

In vitro

buoyancy

studies

In vitro buoyancy was determined by floating lag time (Mura *et al.*, 2003). The tablets were separately in a 100 ml glass beaker containing simulated gastric fluid, pH 1.2 as per USP. The time necessary for the tablet to increase to the outside and float was determined as floating lag time.

Dissolution rate studies

The *in-vitro* drug release study of Tofacitinib citrate tablets was carried out using a USP dissolution apparatus type II (Paddle type). The dissolution medium consisted of 900 ml of phosphate buffer pH 7.2, maintained at $37 \pm 0.5^\circ\text{C}$, and the paddle speed was set at 75 rpm. One tablet was placed in each dissolution vessel and the

apparatus was allowed to run for 12 hours. Samples of 5 ml were withdrawn at predetermined time intervals of 0.5, 1, 1.5, 2, 3, 4, 6, 8, and 12 hours. After each withdrawal, an equal volume of fresh dissolution medium maintained at 37°C was added to maintain a constant volume in the vessel. The withdrawn samples were filtered and analyzed for drug content by measuring the absorbance at 290 nm using a UV-visible spectrophotometer. The cumulative percentage of drug release was calculated for each sampling interval.

Stability study

The stability study of the optimized matrix tablets formulation of Tofacitinib citrate (F8) was carried out to evaluate the physical and chemical stability of the formulation during storage. The study was performed according to the guidelines of the International Council for Harmonisation (ICH). The tablets were packed in suitable containers and stored under accelerated stability conditions at $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ relative humidity for a period of three months. Samples were withdrawn at predetermined intervals such as 0, 1, 2, and 3 months and evaluated for various parameters including physical appearance, hardness, drug content, and *in-vitro* drug release. These parameters were analyzed to determine any significant changes in the formulation during storage.

Results and Discussion

The matrix tablets of Tofacitinib citrate were successfully prepared by the direct compression method using different concentrations of polymers and excipients. The prepared formulations (F1–F9) showed satisfactory pre-compression and post-compression characteristics suitable for colon targeted drug delivery Table 1. The optimization of formulations was carried out using the OVAT approach by varying the concentration of polymers such as Chitosan and Carbopol 940 P.

The pre-compression parameters including bulk density, tapped density, compressibility index, and Hausner ratio demonstrated acceptable flow properties of the powder blend for all formulations, as presented in Table 2. The compressibility index values ranged from 23.67% to 26.97%, while Hausner ratio values ranged from 1.310 to 1.369, indicating fair to passable flow behavior suitable for direct compression.

The post-compression evaluation results indicated that all formulations complied with pharmacopeial limits for tablet quality parameters (Table 3). The thickness of tablets ranged from 2.3 ± 0.01 to 2.4 ± 0.03 mm, indicating uniform die filling during compression. Hardness values between 5.6 ± 0.11 and 5.8 ± 0.10 kg/cm² confirmed adequate mechanical strength of tablets. Friability values for all formulations were found below 1%, indicating good resistance to abrasion and handling. Drug content values ranged from $96.65 \pm 0.45\%$ to $99.05 \pm 0.30\%$, demonstrating uniform distribution of

Tofacitinib citrate throughout the formulations. All formulations exhibited total floating duration greater than 12 h, confirming excellent buoyancy characteristics suitable for prolonged gastric residence.

The buoyancy study results showed that the floating lag time decreased with the incorporation of Carbopol 940 P in the formulations, as shown in Table 4. Formulation F8 exhibited the lowest floating lag time of 28 ± 2 sec, indicating rapid buoyancy due to efficient carbon dioxide generation by sodium bicarbonate and citric acid. The rapid floating behavior may help in improving gastric retention and controlled drug release.

The in-vitro drug release studies revealed significant differences among the formulations depending on polymer composition (Table 5). Formulations F1–F7 showed comparatively faster drug release, whereas formulations containing Carbopol 940 P (F7–F9) exhibited sustained release behavior. Among all formulations, F8 demonstrated the most desirable controlled drug release profile with $98.95 \pm 1.40\%$ cumulative drug release at 12 h. The sustained release behavior of F8 may be attributed to the combined effect of Chitosan and Carbopol 940 P, which formed a strong gel barrier controlling drug diffusion. Therefore, F8 was selected as the optimized formulation.

The kinetic analysis of optimized formulation F8 demonstrated that the drug release followed Higuchi kinetics with the highest regression coefficient ($R^2 = 0.9892$), as shown in Table 7,

indicating diffusion-controlled drug release from the matrix system. The Korsmeyer–Peppas model also showed a high regression coefficient ($R^2 = 0.9827$), suggesting anomalous non-Fickian diffusion involving both diffusion and polymer relaxation mechanisms.

The detailed release kinetics data for optimized formulation F8 are presented in Table 6. The gradual increase in cumulative drug release over 12 h confirmed the sustained release behavior of the matrix tablet. The controlled release pattern may enhance site-specific delivery of Tofacitinib citrate to the colon and improve therapeutic efficacy in inflammatory bowel diseases.

The accelerated stability studies performed on optimized formulation F8 at $40 \pm 2^\circ\text{C}/75 \pm 5\%$ RH for three months demonstrated no significant changes in physical appearance, hardness, drug content, or drug release profile (Table 8). Drug content remained above 98%, and cumulative drug release at 12 h showed minimal variation during the study period, indicating good stability of the formulation under accelerated storage conditions.

The study demonstrated that Eudragit S-100 coated matrix tablets containing Chitosan and Carbopol 940 P could effectively provide controlled and colon targeted delivery of Tofacitinib citrate. The optimized formulation F8 exhibited satisfactory physicochemical characteristics, prolonged buoyancy, sustained drug release, and good stability, making it a promising candidate for colon targeted drug delivery applications.

Table 2: Result of pre-compression properties

Formulation Code	Bulk density(gm/ml)	Tapped density(gm/ml)	Compressibility index	Hausner ratio
F1	0.325	0.445	26.97	1.369
F2	0.328	0.436	24.77	1.329
F3	0.335	0.448	25.22	1.337
F4	0.326	0.439	25.74	1.347
F5	0.329	0.431	23.67	1.310
F6	0.328	0.439	25.28	1.338
F7	0.329	0.438	24.89	1.331
F8	0.335	0.446	24.89	1.331
F9	0.328	0.439	25.28	1.338

Table 3: Results of post compression properties of Tofacitinib citrate loaded matrix tablets

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)	2.3 ± 0.02	2.4 ± 0.03	2.3 ± 0.02	2.3 ± 0.02	2.3 ± 0.01	2.3 ± 0.02	2.4 ± 0.03	2.3 ± 0.02	2.3 ± 0.02
Hardness (kg/cm ²)	5.8 ± 0.10	5.7 ± 0.12	5.6 ± 0.11	5.8 ± 0.09	5.7 ± 0.10	5.6 ± 0.12	5.7 ± 0.11	5.8 ± 0.10	5.7 ± 0.09
Weight variation (mg)	150 ± 1.5	152 ± 1.8	148 ± 1.6	149 ± 1.4	153 ± 1.7	155 ± 1.9	152 ± 1.6	148 ± 1.5	150 ± 1.4
Friability (%)	0.665 ± 0.02	0.745 ± 0.03	0.698 ± 0.02	0.685 ± 0.02	0.674 ± 0.01	0.689 ± 0.02	0.712 ± 0.03	0.698 ± 0.02	0.705 ± 0.02
Drug content (%)	96.65 ± 0.45	97.45 ± 0.40	98.85 ± 0.35	98.12 ± 0.38	98.12 ± 0.36	98.33 ± 0.34	96.65 ± 0.42	99.05 ± 0.30	98.74 ± 0.33
Total floating duration (h)	>12	>12	>12	>12	>12	>12	>12	>12	>12

Table 4: Results of *in-vitro* buoyancy study (Floating time) of matrix tablets

S. No.	Formulation Code	Floating Lag Time (sec)
1	F1	74 ± 5
2	F2	68 ± 6
3	F3	63 ± 5
4	F4	59 ± 4
5	F5	55 ± 4
6	F6	51 ± 4
7	F7	45 ± 3
8	F8	28 ± 2
9	F9	40 ± 3

Table 5: *In-vitro* drug release study of matrix tablets

Time (hr)	% Cumulative drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.5	38.25 ± 0.85	34.15 ± 0.78	30.25 ± 0.72	36.45 ± 0.81	32.85 ± 0.75	31.45 ± 0.70	33.25 ± 0.76	15.25 ± 0.65	22.15 ± 0.70
1	52.45 ± 0.92	45.25 ± 0.88	40.35 ± 0.82	50.25 ± 0.90	44.65 ± 0.85	43.25 ± 0.80	45.15 ± 0.86	22.45 ± 0.75	30.25 ± 0.80
1.5	68.25 ± 1.05	60.45 ± 0.95	55.65 ± 0.90	65.25 ± 1.00	58.25 ± 0.92	56.45 ± 0.88	57.85 ± 0.90	32.65 ± 0.85	40.35 ± 0.88
2	85.45 ± 1.20	75.25 ± 1.05	68.45 ± 0.98	78.25 ± 1.10	70.45 ± 1.00	68.25 ± 0.95	69.85 ± 0.98	42.35 ± 0.90	50.45 ± 0.95
3	96.85 ± 1.35	88.45 ± 1.20	80.25 ± 1.10	90.25 ± 1.25	78.65 ± 1.05	76.85 ± 1.00	77.95 ± 1.05	52.25 ± 0.95	60.65 ± 1.00
4	–	96.25 ± 1.30	86.45 ± 1.15	97.85 ± 1.35	88.25 ± 1.20	86.45 ± 1.10	88.25 ± 1.15	60.85 ± 1.00	68.45 ± 1.05
6	–	–	95.65 ± 1.25	–	96.85 ± 1.30	94.65 ± 1.20	95.25 ± 1.22	72.45 ± 1.05	76.25 ± 1.10
8	–	–	–	–	–	98.25 ± 1.35	97.85 ± 1.30	84.25 ± 1.10	82.65 ± 1.15
12	–	–	–	–	–	–	–	98.95 ± 1.40	90.25 ± 1.20

Table 6: In-vitro drug release data for optimized formulation F8

Time (h)	Square Root of Time(h) ^{1/2}	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	15.25 ± 0.65	1.183	84.75	1.928
1	1.000	0.000	22.45 ± 0.75	1.351	77.55	1.890
1.5	1.225	0.176	32.65 ± 0.85	1.514	67.35	1.828
2	1.414	0.301	42.35 ± 0.90	1.627	57.65	1.761
3	1.732	0.477	52.25 ± 0.95	1.718	47.75	1.679
4	2.000	0.602	60.85 ± 1.00	1.784	39.15	1.593
6	2.449	0.778	72.45 ± 1.05	1.860	27.55	1.440
8	2.828	0.903	84.25 ± 1.10	1.926	15.75	1.197
12	3.464	1.079	98.95 ± 1.40	1.995	1.05	0.021

Table 7: Regression analysis data of matrix tablets

Batch	Zero Order	First Order	Higuchi	Peppas
	R ²	R ²	R ²	R ²
F8	0.9195	0.9125	0.9892	0.9827

Table 8: Results of stability study of matrix tablets (F8)

S. No.	Storage Condition	Time (Month)	Physical Appearance	Hardness (kg/cm ²)	Drug Content (%)	% Drug Release (12 hr)
1	Initial	0	No change	6.4 ± 0.05	99.05 ± 0.66	98.95±0.45
2	40 ± 2°C / 75 ± 5% RH	1	No change	6.35 ± 0.05	98.82 ± 0.60	98.45±0.36
3	40 ± 2°C / 75 ± 5% RH	2	No change	6.30 ± 0.04	98.56 ± 0.58	98.25±0.74
4	40 ± 2°C / 75 ± 5% RH	3	No change	6.25 ± 0.05	98.20 ± 0.55	98.10±0.54

CONCLUSION:

The present study successfully developed and evaluated pH-dependent Eudragit S-100 coated matrix tablets of Tofacitinib citrate for colon targeted drug delivery. Among all formulations, formulation F8 showed the most desirable characteristics, including satisfactory floating behavior, controlled drug release up to 12 h, and good stability under accelerated conditions. The optimized formulation followed Higuchi release kinetics with non-Fickian diffusion mechanism, indicating effective sustained drug release. The developed matrix tablets demonstrated promising potential for colon-specific delivery of Tofacitinib citrate with improved therapeutic efficacy and reduced systemic side effects.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this research work.

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