

FORMULATION AND IN-VITRO EVALUATION OF SUSTAINED RELEASE TABLETS CONTAINING ETIFOXINE HYDROCHLORIDE

Ayush Suryawanshi*, Priyanka Rathore, Nilesh Jain, R.B. Goswami

Sagar Institute of Research Technology & Science – Pharmacy, Ayodhya Bypass Road,
Bhopal (M.P.)

Corresponding Author mail id: ayushsuryawanshi108@gmail.com

DOI: [https://doi.org/10.63001/tbs.2026.v21.i04.S.I\(4\).pp230-242](https://doi.org/10.63001/tbs.2026.v21.i04.S.I(4).pp230-242)

KEYWORDS

*Etifoxine hydrochloride,
Sustained release tablets,
Floating tablets, Chitosan,
Carbopol 940 P,
Direct compression,
In-vitro drug release,
Gastroretentive drug delivery
system,
Release kinetics,
Stability studies.*

Article Info

Received: 16/09 /2026

Accepted :02/10/2026

Published: 10/10/2026

Abstract

The present study was aimed at the formulation and in-vitro evaluation of sustained release floating tablets containing Etifoxine hydrochloride using Chitosan and Carbopol 940 P as release-retarding polymers. Sustained release tablets were prepared by direct compression method employing different polymer compositions to achieve prolonged drug release and enhanced gastric retention. The prepared formulations were evaluated for pre-compression parameters including bulk density, tapped density, compressibility index, and Hausner ratio, which indicated acceptable flow properties suitable for compression. Post-compression evaluation demonstrated satisfactory tablet characteristics such as hardness, friability, thickness, weight variation, and drug content uniformity within acceptable pharmacopoeial limits.

The buoyancy study revealed that all formulations exhibited floating duration greater than 12 h, while formulation F8 showed the shortest floating lag time of 28 ± 3 seconds. In-vitro drug release studies indicated that formulation F8 provided controlled and sustained drug release up to 12 h with 99.25% cumulative drug release. Drug release kinetic analysis showed that the optimized formulation followed Higuchi and Korsmeyer–Peppas release models, indicating diffusion-controlled non-Fickian drug release behavior. Stability studies performed under accelerated conditions for three months confirmed that the optimized formulation remained stable without significant changes in physical appearance, hardness, drug content, or drug release profile.

The results of the present investigation demonstrated that sustained release floating tablets of Etifoxine hydrochloride can be successfully developed using Chitosan and Carbopol 940 P to provide prolonged drug release, improved gastric retention, and enhanced therapeutic efficacy.

Introduction

Anxiety disorders are among the most prevalent psychiatric conditions worldwide and significantly affect the quality of life of affected individuals. These disorders are characterized by excessive fear, nervousness, tension, and emotional disturbances that may interfere with daily functioning^[1].

Conventional anxiolytic agents such as benzodiazepines are commonly used for the treatment of anxiety; however, their long-term use is often associated with adverse effects including sedation, dependence, tolerance, cognitive impairment, and withdrawal symptoms. Therefore, there is a continuous need for safer and more effective therapeutic alternatives with improved

patient compliance and reduced side effects [2].

Etifoxine hydrochloride is a non-benzodiazepine anxiolytic agent widely used for the management of anxiety disorders. It exerts its pharmacological action through modulation of γ -aminobutyric acid (GABA) neurotransmission and stimulation of neurosteroid synthesis, thereby producing anxiolytic effects without causing marked sedation or dependence. Compared to classical benzodiazepines, etifoxine demonstrates better tolerability and lower risk of abuse, making it a promising therapeutic option for chronic anxiety management [3].

Despite its therapeutic advantages, Etifoxine hydrochloride possesses a relatively short biological half-life, which necessitates frequent administration to maintain effective plasma drug concentration. Repeated dosing may reduce patient adherence and lead to fluctuations in plasma drug levels, resulting in inconsistent therapeutic response. Sustained release drug delivery systems are designed to overcome these limitations by releasing the drug gradually over an extended period, thereby maintaining uniform plasma concentration, reducing

dosing frequency, minimizing side effects, and improving patient compliance [4].

Among the various sustained release dosage forms, matrix tablets are widely preferred because of their simplicity, cost-effectiveness, ease of manufacturing, and ability to provide controlled drug release. Hydrophilic and hydrophobic polymers are commonly employed in sustained release formulations to regulate the rate of drug diffusion and matrix erosion. Selection of appropriate polymers and optimization of formulation variables play a crucial role in achieving the desired release profile and tablet characteristics [5].

The present study was therefore undertaken to formulate and evaluate sustained release tablets containing Etifoxine hydrochloride using suitable release-retarding polymers. The prepared formulations were evaluated for various pre-compression and post-compression parameters including angle of repose, bulk density, tapped density, Carr's index, Hausner ratio, hardness, friability, weight variation, thickness, drug content, and in-vitro drug release studies. The objective of the study was to develop a stable sustained release tablet formulation capable of providing prolonged drug release

with improved therapeutic efficacy and patient compliance.

Material and Methods

Material

Etifoxine hydrochloride, Chitosan, Carbopol 940 P, Citric acid, Sodium bicarbonate, Lactose, Magnesium stearate, and Talc were used for the preparation of sustained release floating tablets. Etifoxine hydrochloride was used as the active drug, while Chitosan and Carbopol 940 P served as release-retarding polymers. Citric acid and Sodium bicarbonate were incorporated as effervescent agents to impart floating characteristics to the tablets. Lactose was used as a diluent, whereas Magnesium stearate and Talc were employed as lubricant and glidant respectively. All chemicals and reagents used in the study were of analytical grade.

Methods

Preparation of Sustained Release Tablets of Etifoxine Hydrochloride

Sustained release tablets of Etifoxine hydrochloride were prepared by the direct compression method using different polymeric compositions. A total of nine formulations (F1–F9) were developed, each containing 50 mg of Etifoxine hydrochloride. Chitosan was used as the primary matrix-forming polymer in all

formulations at a fixed concentration of 30 mg, whereas Carbopol 940 P was incorporated additionally in formulations F7, F8, and F9 at a concentration of 20 mg to modify the drug release profile.

Citric acid (5 mg) and sodium bicarbonate (20 mg) were incorporated in all formulations as effervescent agents to impart floating characteristics to the tablets. Lactose was used as a diluent in varying quantities to maintain a constant tablet weight of 200 mg. Magnesium stearate and talc were added as lubricant and glidant, respectively.

All the ingredients including Etifoxine hydrochloride, polymers, and excipients were passed through sieve no. 40 separately to ensure uniform particle size distribution. The accurately weighed quantities of ingredients were mixed thoroughly in a mortar to obtain a homogeneous powder blend. Finally, magnesium stearate and talc were added and mixed gently before compression. The prepared powder blends were compressed into tablets using a suitable tablet compression machine ^[6]. The composition of all formulations is presented in Table 1.

Optimization of Sustained Release Tablets of Etifoxine Hydrochloride

Optimization of sustained release tablets was carried out using the OVAT (One Variable At a Time) approach by varying the concentration and combination of

release-retarding polymers such as Chitosan and Carbopol 940 P. The effect of polymer composition on tablet characteristics and drug release behavior was evaluated to obtain an optimized sustained release formulation.

Table 1: Formulations of Etifoxine hydrochloride sustain release tablets

Excipients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Etifoxine hydrochloride	50	50	50	50	50	50	50	50	50
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	80	80	80	80	80	80	60	60	60
Total Weight	200	200	200	200	200	200	200	200	200

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: ^[7]

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

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

Carr's index: Percent compressibility of powder mix was determined by Carr's compressibility index, calculated by using following formula ^[60]:

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

Hausners ratio: It is determined by comparing tapped density to the bulk density by using following equation:-

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

Hausner's ratio value <1.25 shows better flow properties

Evaluation of sustain release 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 (- -).

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 ^[8].

Drug content

Twenty tablets were taken and amount of drug present in each tablet was determined ^[9]. 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 0.1 N HCl

and made up to volume with of 0.1 N HCl. 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 273 nm using of 0.1 N HCl as blank.

Hardness

For each formulation, the hardness of five tablets was resolved utilizing the Monsanto hardness tester ^[10].

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 ^[11].

Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated ^[12].

***In vitro* buoyancy studies:**

In vitro buoyancy was determined by floating lag time as per the method described by Rosa *et al.* 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 ^[12].

Dissolution rate studies

The in-vitro drug release study of Etifoxine hydrochloride tablets was carried out using a USP Dissolution Apparatus Type II (Paddle type). The dissolution medium consisted of 900 ml of 0.1 N HCl, 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 273 nm using a UV-visible spectrophotometer. The cumulative percentage of drug release was calculated for each sampling interval ^[12].

Stability study

The stability study of the optimized sustained release tablet formulation of Etifoxine Hydrochloride (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 ^[12].

Results and Discussion

The present study was carried out to formulate and evaluate sustained release floating tablets of Etifoxine hydrochloride using Chitosan and Carbopol 940 P as release-retarding polymers. The prepared formulations were evaluated for pre-compression characteristics, post-compression parameters, buoyancy behavior, in-vitro drug release, release kinetics, and stability studies.

The pre-compression properties of all powder blends indicated satisfactory flow behavior and compressibility suitable for direct compression. As shown in Table 2, the bulk density values ranged from 0.342 to 0.356 g/ml, while tapped density ranged from 0.456 to 0.478 g/ml. The compressibility index values were found between 22.94% and 26.57%, and Hausner ratio values ranged from 1.298 to 1.362, indicating acceptable flow properties of the powder blends for tablet compression.

The post-compression evaluation results presented in Table 3 demonstrated that all formulations complied with pharmacopeial limits for tablet quality control parameters. The thickness of tablets ranged from 2.7 ± 0.04 mm to 2.9 ± 0.05 mm, indicating uniform die filling during compression. Hardness values were found between 6.2 ± 0.04 and 6.5 ± 0.04 kg/cm², suggesting

adequate mechanical strength of tablets. Friability values of all formulations were below 1%, confirming good resistance to abrasion and handling. Weight variation and drug content studies also showed uniform distribution of the drug within the formulations, with drug content ranging from $96.25 \pm 0.75\%$ to $99.05 \pm 0.66\%$. All formulations exhibited total floating duration greater than 12 h, demonstrating effective gastroretentive behavior.

The in-vitro buoyancy study results shown in Table 4 revealed that floating lag time decreased progressively from formulation F1 to F9. Formulation F8 exhibited the shortest floating lag time of 28 ± 3 seconds, indicating rapid buoyancy. The improved floating behavior may be attributed to the optimized concentration of gas-generating agents along with the swelling and gel-forming properties of Chitosan and Carbopol 940 P, which facilitated entrapment of carbon dioxide within the tablet matrix.

The in-vitro drug release study presented in Table 5 demonstrated significant variation in release profiles among different formulations depending upon polymer composition. Formulations F1–F7 showed comparatively rapid drug release, whereas formulation F8 exhibited a controlled and

sustained release pattern extending up to 12 h with 99.25% cumulative drug release. The incorporation of Carbopol 940 P in combination with Chitosan in F8 effectively controlled the drug diffusion and matrix erosion, thereby prolonging the release of Etifoxine hydrochloride. Formulation F9 also showed sustained release behavior but with comparatively lower cumulative drug release at 12 h (92.85%).

The release kinetic analysis of optimized formulation F8 was performed using different kinetic models as shown in Table 6 and Table 7. The regression coefficient (R^2) values for Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models were found to be 0.8795, 0.9406, 0.9723, and 0.9736 respectively. The highest R^2 value was observed for the Peppas model followed closely by the Higuchi model, suggesting that the drug release mechanism involved diffusion-controlled release with polymer matrix relaxation. The results indicated that the sustained release behavior of

formulation F8 followed anomalous non-Fickian diffusion.

Stability studies of the optimized formulation F8 were carried out for three months under accelerated storage conditions of $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ RH as presented in Table 8. No significant changes were observed in physical appearance, hardness, drug content, or percentage drug release during the study period. The formulation retained satisfactory stability with drug content remaining above 98% and cumulative drug release above 98% after three months, indicating good stability of the optimized sustained release tablets.

The study demonstrated that sustained release floating tablets of Etifoxine hydrochloride could be successfully formulated using Chitosan and Carbopol 940 P. Among all formulations, F8 was found to be the optimized formulation due to its excellent floating behavior, prolonged drug release profile, acceptable physicochemical properties, and good stability characteristics.

Table 2: Result of pre-compression properties

Formulation Code	Bulk density(gm/ml)	Tapped density(gm/ml)	Compressibility index	Hausner ratio
F1	0.342	0.456	25.00	1.333
F2	0.351	0.478	26.57	1.362

F3	0.348	0.463	24.84	1.330
F4	0.356	0.462	22.94	1.298
F5	0.348	0.469	25.80	1.348
F6	0.342	0.459	25.49	1.342
F7	0.346	0.462	25.11	1.335
F8	0.347	0.458	24.24	1.320
F9	0.356	0.469	24.09	1.317

Table 3: Results of post compression properties of Etifoxine hydrochloride tablets

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)	2.8 ± 0.05	2.9 ± 0.04	2.8 ± 0.05	2.8 ± 0.05	2.7 ± 0.04	2.9 ± 0.04	2.7 ± 0.05	2.8 ± 0.04	2.9 ± 0.05
Hardness (kg/cm²)	6.2 ± 0.06	6.3 ± 0.05	6.2 ± 0.05	6.2 ± 0.04	6.3 ± 0.06	6.3 ± 0.05	6.5 ± 0.04	6.4 ± 0.05	6.3 ± 0.05
Weight variation (mg)	202 ± 1.8	203 ± 2.0	205 ± 1.7	204 ± 1.9	202 ± 1.8	201 ± 1.6	203 ± 1.7	203 ± 1.8	198 ± 2.1
Friability (%)	0.698 ± 0.012	0.712 ± 0.015	0.695 ± 0.014	0.678 ± 0.013	0.712 ± 0.016	0.698 ± 0.014	0.663 ± 0.012	0.715 ± 0.017	0.698 ± 0.013
Drug content (%)	97.12 ± 0.72	96.65 ± 0.68	96.25 ± 0.75	97.45 ± 0.70	98.85 ± 0.65	96.32 ± 0.74	97.44 ± 0.71	99.05 ± 0.66	97.45 ± 0.69
Total floating duration (h)	>12	>12	>12	>12	>12	>12	>12	>12	>12

Table 4: Results of *in-vitro* buoyancy study of Etifoxine hydrochloride tablets floating time

S. No.	Formulation Code	Floating Lag Time (sec)
1	F1	72 ± 6
2	F2	66 ± 7
3	F3	61 ± 5
4	F4	58 ± 4

5	F5	54 ± 4
6	F6	50 ± 5
7	F7	46 ± 4
8	F8	28 ± 3
9	F9	42 ± 3

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

Time (hr)	% Cumulative Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.5	42.15	35.25	32.45	40.65	36.15	33.25	34.35	18.25	24.15
1	55.45	46.35	42.65	54.35	48.25	45.15	47.25	26.45	35.25
1.5	69.85	65.25	58.45	70.85	60.25	58.65	61.85	38.65	46.35
2	88.65	78.45	69.85	79.65	72.45	71.25	70.85	48.35	55.45
3	97.85	89.65	82.45	91.25	80.25	79.85	78.95	58.25	64.85
4	—	98.65	88.95	99.05	90.65	89.85	90.25	66.85	71.45
6	—	—	97.85	—	98.45	96.85	97.25	78.45	79.85
8	—	—	—	—	—	99.05	98.85	89.65	86.25
12	—	—	—	—	—	—	—	99.25	92.85

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	18.25	1.261	81.75	1.912
1	1	0	26.45	1.422	73.55	1.867
1.5	1.225	0.176	38.65	1.587	61.35	1.788
2	1.414	0.301	48.35	1.684	51.65	1.713
3	1.732	0.477	58.25	1.765	41.75	1.621

4	2	0.602	66.85	1.825	33.15	1.520
6	2.449	0.778	78.45	1.895	21.55	1.333
8	2.828	0.903	89.65	1.953	10.35	1.015
12	3.464	1.079	99.25	1.997	0.75	-0.125

Table 7: Regression analysis data of sustain release tablets

Batch	Zero Order	First Order	Higuchi	Peppas
	R ²	R ²	R ²	R ²
F8	0.8795	0.9406	0.9723	0.9736

Table 8: Results of stability study of Etifoxine hydrochloride sustained release 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	99.25
2	40 ± 2°C / 75 ± 5% RH	1	No change	6.3 ± 0.06	98.72 ± 0.70	98.85
3	40 ± 2°C / 75 ± 5% RH	2	No change	6.3 ± 0.05	98.45 ± 0.68	98.42
4	40 ± 2°C / 75 ± 5% RH	3	No change	6.2 ± 0.05	98.12 ± 0.72	98.05

Conclusion

The present study successfully formulated and evaluated sustained release floating tablets of Etifoxine hydrochloride using Chitosan and Carbopol 940 P as release-retarding polymers. All formulations exhibited satisfactory pre-compression and post-compression characteristics with

acceptable hardness, friability, drug content, and buoyancy properties. Among all formulations, batch F8 showed optimum floating lag time, sustained drug release up to 12 hours, and good kinetic release behavior following Higuchi and Peppas models. Stability studies confirmed that the optimized formulation remained stable under accelerated storage conditions. Thus,

the developed sustained release floating tablet of Etifoxine hydrochloride may provide prolonged drug release, improved gastric retention, and enhanced therapeutic efficacy.

References

1. Javaid SF, Hashim IJ, Hashim MJ, Stip E, Samad MA, Ahbabi AA. Epidemiology of anxiety disorders: global burden and sociodemographic associations. Middle East Current Psychiatry. 2023 May 26;30(1):44.
2. Nardi AE, Quagliato LA. Benzodiazepines are efficacious and safe for long-term use: Clinical research data and more than sixty years in the market. Psychotherapy and Psychosomatics. 2022 Aug 17;91(5):300-3.
3. Nuss P, Ferreri F, Bourin M. An update on the anxiolytic and neuroprotective properties of etifoxine: from brain GABA modulation to a whole-body mode of action. Neuropsychiatric Disease and Treatment. 2019 Jul 3:1781-95.
4. Poisbeau P, Gazzo G, Calvel L. Anxiolytics targeting GABAA receptors: Insights on etifoxine. The World Journal of Biological Psychiatry. 2018 Jun 22;19(sup1):S36-45.
5. Nagendrakumar D, Keshavshetti GG, Shardor AG. An overview: Matrix tablets as sustained release. Recent Research in Science and Technology. 2014 Jan 14;5(4).
6. Vijay D. Gulkari, Suparna S. Bakhle, Leena S. Yelane. Development and evaluation of ofloxacin floating tablets using natural polymer: *Sterculia foetida* Linn. gum. International Journal of Pharmacy and Pharmaceutical Sciences. 2016; 8(5): 356-360.
7. Wasnik S, Parmar P, Singh D, Ram A. Preparation and characterization of floating drug delivery system of azithromycin. Acta Pol Pharm 2012; 69:515-22.
8. Kadivar A, Kamalidehghan B, Javar HA, Davoudi ET, Zaharuddin ND, Sabeti B, et al. Formulation and in vitro, in vivo evaluation of effervescent floating sustained release imatinib mesylate tablet. PLOS One 2015; 10: 1-23.
9. Rahim SA, Carter PA, Elkordy AA. Design and evaluation of effervescent floating tablets based on

hydroxyethyl cellulose and sodium alginate using pentoxifylline as a model drug. Drug Des Dev Ther 2015; 9:1843-57.

10. Taghizadeh DE, Ibrahim NM, Kadivar A, Kamalidehghan B, Farjam AS, Akbari Javar H. Preparation and characterization of a gastric floating dosage form of capecitabine. Biomed Res Int 2013; 1-8.
11. Pawar HA, Gharat PR, Dhavale RV, Joshi PR, Rakshit PP. Development and evaluation of gastroretentive are floating tablet of an antihypertensive drug using hydrogenated cottonseed oil. ISRN Pharm 2013; 1-9.
12. Meka VS, Nali SR, Songa AS, Kolapalli VR. Characterization and in vitro drug release studies of natural polysaccharide *Terminalia Catappa* Gum (Badam Gum). AAPS PharmSciTech 2012; 13: 1451-64.