CODEN: WJAPAC Impact Factor: 3.87 ISSN: 3049-3013

World Journal of Advance Pharmaceutical Sciences

Volume 2, Issue 3. Page: 161-167 Research Article www.wjaps.com

A NEW ANALYTICALAL METHOD DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR ESTIMATION OF FLUVOXAMINE IN BULK AND TABLET DOSAGE FORM

Umme Kulsum[1]* and Naveen Kumar G. S.[2]

[1]2nd Year M Pharma, Student of Department of Pharmaceutical Analysis, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka, India -571422.

[2]Professor and HOD of Department of Pharmaceutical Analysis, Bharathi College of Pharmacy, Bharathinagara, Mandya District, Karnataka, India -571422.

How to cite this Article Umme Kulsum and Naveen Kumar G. S. (2025). A NEW ANALYTICALAL METHOD DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR ESTIMATION OF FLUVOXAMINE IN BULK AND TABLET DOSAGE FORM, 2(3), 161-167. https://doi.org/10.5281/zenodo.17235445

Article Info

Article Received: 17 August 2025,

Article Revised: 07 September 2025,

Article Accepted: 27 September 2025.

DOI: https://doi.org/10.5281/zenodo.17235445

***Corresponding author:**

***Umme Kulsum**

2nd Year M Pharma, Student of Department of Pharmaceutical Analysis, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka, India -571422.

ABSTRACT

A simple, rapid, precise, sensitive and reproducible reverse phase high performance liquid chromatography (RP-HPLC) method has been developed for the quantitative analysis of Fluvoxamine in pharmaceutical dosage form. Chromatographic separation of Fluvoxamine was achieved on Prominence LC-20A Quaternary Gradient HPLC system, by using Shimpack C-18 (5µm, 4.6 x 250mm) column and the mobile phase containing Acetonitrile and Phosphate Buffer with pH of 4.5 in a 54:45 v/v ratio. The flow rate was 1.0ml/min; detection was carried out by absorption at 254 nm using a UV detector at ambient temperature. LOD and LOQ were found to be 6.39µg/ml and 19.36µg/ml respectively and retention time was found to be 3.66mins. The % Recovery was found to be 99.42-100.71%. The number of theoretical plates and tailing factor for Fluvoxamine were not less than 2000 and not more than 2 respectively. % Relative standard deviation of peak areas of all measurements always less than 2.0. The proposed method was validated according to ICH guidelines. The method was found to be simple, economical, suitable, precise, accurate and robust method for quantitative analysis of Fluvoxamine.

KEYWORDS: Fluvoxamine, High performance liquid chromatography, Method development, Validation.

INTRODUCTION

Fluvoxamine is an anti-depressant; it selectively inhibits the reuptake of serotonin but has relatively little effect on noradrenaline reuptake. The drug is structurally unrelated to the tricyclic group of antidepressants. In the treatment of depression, fluvoxamine is given orally as the maleate salt, in doses of 100 to 200 mg daily.[1] Fluvoxamine may be particularly beneficial in potentially suicidal patients with severe depression, in those with an underlying compulsive personality or cardiovascular disorder, in patients with coexistent anxiety or agitation, and in the elderly. Gastrointestinal adverse effects, especially nausea, are commonly reported with fluvoxamine but are generally mild to moderate in severity. The tolerability profile of fluvoxamine appears to be more favourable than that of tricyclic antidepressants in terms of cardio toxic and anticholinergic adverse effects, sedation, weight gain and death from over dosage. Peak plasma concentrations are achieved within approximately 2 to 8 hours. Food does not significantly affect the rate or extent of absorption. Mean elimination half-life (t ½] is approximately 19 and 22 hours after single and multiple

doses.[2] Fluvoxamine is effective in inhibiting 5-HT uptake by blood platelets and brain synaptosomes. Due to inhibition of the membrane pump the compound prevents 5-HT depletion by the tyramine derivatives H 75/12 and H 77/77. As a result of the interference with the neuronal re-uptake mechanism for 5-HT, fluvoxamine produces a decreased 5-HT turnover in the brain.[3] Fluvoxamine is chemically identified as 2-[(*E*)-[5-methoxy-1-[4-(trifluoromethyl)phenyl] pentylidene] amino]oxyethanamine. Presenting as White to off white in color, it is sparingly soluble in water, freely soluble in ethanol and chloroform and practically insoluble in diethyl ether. With a molecular formula of $C_{15}H_{21}F_3N_2O_2$, a molecular weight of 523.32 $gmol^{-1}$. Fluvoxamine is characterized by these chemical and physical attributes.

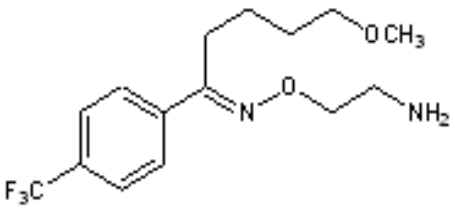

Figure 1: Chemical Structure of Fluvoxamine.

According to a literature review, few analytical techniques have been published for determining Fluvoxamine in pure medication and pharmaceutical dosage forms employing UV[4-7], RP-HPLC[8-13] and Spectro fluorimetry[14], The current effort aims to develop and verify a new Reverse phase-High performance liquid chromatography for estimating Fluvoxamine in tablet and bulk dose form that is quick, easy, accurate, and specific.

MATERIALS AND METHODS

Apparatus and Software

Chromatographic separation was performed on a Prominence LC-20A Quaternary Gradient HPLC system as the instrument model and column used is Shimpack C-18 5µm, 4.6 x 250mm.

Chemicals and Reagents

Fluvoxamine pure form was obtained as gifted sample from gift sample by Nuwill Research and Innovations Pvt. Ltd, Bengaluru and pharmaceutical dosage form Fluvoxamine 20 tablets (Luvox) labelled claim 20mg from Bayer zydus pharma private limited. Ethanol and water obtained from Bharathi college of pharmacy Bharathinagara, K.M. Doddi, Maddur TQ & Mandya dist. India. All the Chemicals used in this investigation were HPLC grade.

Selection of mobile phase

Based on sample solubility, stability and suitability various mobile phase compositions were tried to get a good resolution and sharp peaks. The standard solution was run in different mobile phases. From the various mobile phases Acetonitrile and Phosphate Buffer in a 55:45 v/v ratio with detection wavelength of 254 nm, since it gave sharp peak with good symmetry within limits.

Preparation of mobile phase

Mobile phase was prepared by mixing Acetonitrile and water with Potassium Dihydrogen Phosphate at pH of 4.5 taken in ratio 55:45 v/v. It was filtered through FCP-305µ membrane filter to remove the impurities which may interfere in the final chromatogram.

Preparation of standard stock solution

Accurately weigh and transfer 100mg of Fluvoxamine working standard into a 100ml clean dry volumetric flask add Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution) Further pipette 1ml of the above stock solutions into a 10ml volumetric flask and dilute up to the mark with diluent. (100ppm of Fluvoxamine).

Preparation of sample solution

Accurately weighed and transfer 100mg of Fluvoxamine sample into a 100ml clean dry volumetric flask add diluent and sonicate it up to 30min to dissolve, and centrifuge for 30min to dissolve it completely and make volume up to the mark with the same solvent. Then it is filtered through 0.2µ Whatman Uniflo Nylon filter (Stock solution). Further pipette 1ml of the above stock solutions into a 10ml volumetric flask and dilute up to the mark with diluent (100ppm of Fluvoxamine).

Flow rate selection

Different flow rates were studied. A flow rate of 1.0ml/min gave an optimal signal to noise ratio with a reasonable separation time.

Validation of Analytical Method

The method is validated according to the ICH guidelines; Validation of an analytical method is the process to establish by laboratory studies that the performance characteristic of the method meets the requirements for the intended analytical application. Performance characteristics are expressed in terms of Analytical parameters.

System suitability

20µl of the standard solution was injected under optimized chromatographic conditions to evaluate the suitability of system. Parameters such as number of theoretical plates (N), tailing factor (T), retention time (tr), asymmetry and area were determined. The obtained values indicate good performance of system.

Solution stability

In order to demonstrate the stability of both standard and sample solutions during analysis, both solutions were analyzed over a period of 24hr at room temperature. The results show that for solutions, the retention time and peak area of Fluvoxamine remained almost

unchanged (% RSD less than 2.0).

Specificity

Specificity of the HPLC method was checked for interference of impurities, degradants or excipients in the analysis of sample solution and was determined by injecting a volume of 20µl of sample solution and the chromatogram was recorded. There is no interference of impurities, excipient peak on the peak of Fluvoxamine, indicating the high specificity of method.

Linearity and Range

The linearity of the method was demonstrated over the concentration range of 80- 180µg/ml of the target concentration. Aliquots of 80,100,120,140,160 and 180µg/ml were prepared from above prepared stock solution. Different concentrations of the pure drug were injected into the chromatographic system. Calibration curve of Fluvoxamine was constructed by plotting peak area v/s applied concentration of Fluvoxamine. The obtained results shown an excellent correlation between peak area and concentration of pure drug within the concentration range & it has shown in Fig: 6.0. The correlation coefficient for the average area at each level versus concentration of analyte was calculated and is presented in Table and their calibration parameters were shown in Table.

Precision

The precision of the analytical method was determined by intra-day and inter- day precision Table respectively. The sample solution was prepared as per the test method. In intra-day precision, the same concentration of sample solution was injected 6 times in the same day and in inter-day precision, injecting six solutions of same concentration for six different days in a week. The average and standard deviation of mean area were taken and %RSD was calculated and reported. %RSD values were within the limits and the method was found to be precise.

Accuracy

The accuracy of the method was determined by recovery studies by the determination of % mean recovery of the drug at three different levels (80%, 100% and 120%). At each level, three determinations were performed. A known amount of standard pure drug was added to pre analyzed tablet powder and the sample was then analyzed by developed method. Results of recovery studies were reported, the observed data were within the range, which indicates good recovery values.

Robustness

Robustness is a measure of capacity of a method to remain unaffected by small but deliberate variations in the method conditions, and is indications of the reliability of the method. A method is robust, if it is unaffected by small changes in operating conditions. To determine the robustness of this method, the experimental conditions were deliberately altered at by changing parameters like change in Flow rate of the Mobile phase and change in organic phase, and the results were shown in Table. The method has no effect on the retention time and chromatographic response of the 6 solutions indicating that the method was robust.

Limit of detection

Limit of detection is determined by the analysis of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be reliably detected. The results of LOD were shown in Table.

Limit of quantitation

Limit of quantitation is determined by the analysis of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be reliably Quantitate. The LOQ can also be calculating based on the LOD strength, the LOD values were multiplied by three times to get LOQ. The results of LOQ were shown in Table.

RESULTS AND DISCUSSION

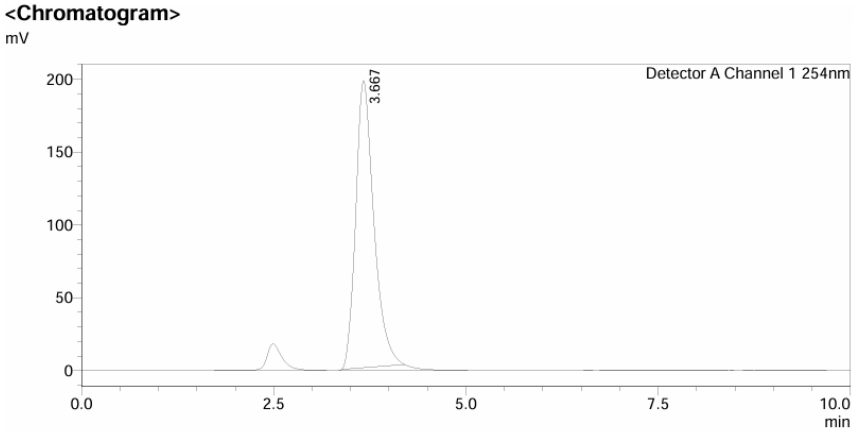

Fig. 1: Chromatogram of Fluvoxamine.

Table 1: Optimized chromatographic conditions.

Optimized conditions	Values
Column	Shimpack C-18 (5µm, 4.6 x 250mm)
Mobile phase	Acetonitrile and phosphate buffer with pH of 4.5 in a 50:50 v/v ratio
Flow rate	l.0 ml/min
Injection volume	20µl
Wavelength	235nm
Temperature	40ºC
Retention time	4.848min
Run time	10min
Elution	Isocratic

Table 1.1: System suitability studies of Fluvoxamine by RP-HPLC method.

System suitability Parameters	Acceptance criteria	Results
Tailing factor	T ≤ 2	1.41
Theoretical plates	N ≥ 2000	2744
Retention time	-	3.66
Area	-	3632800

Specificity

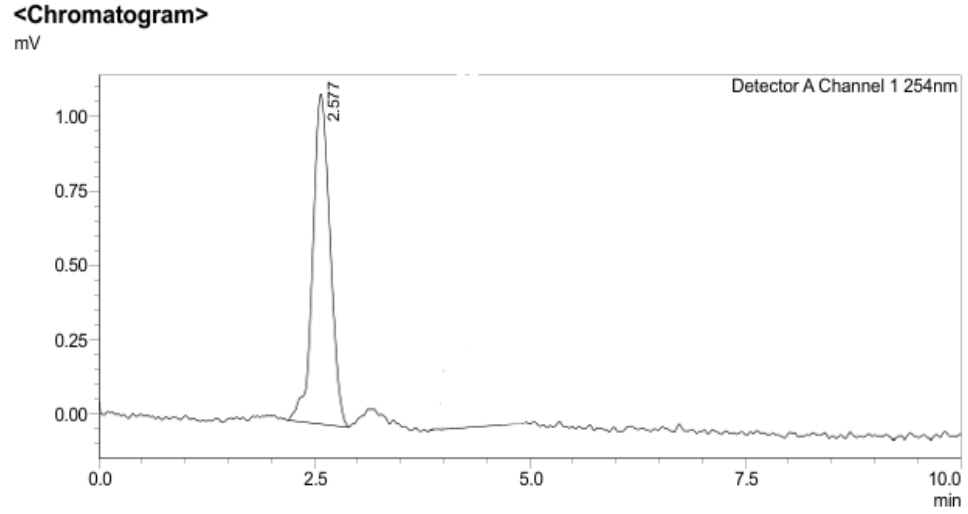

Fig. 2: Chromatogram of Blank.

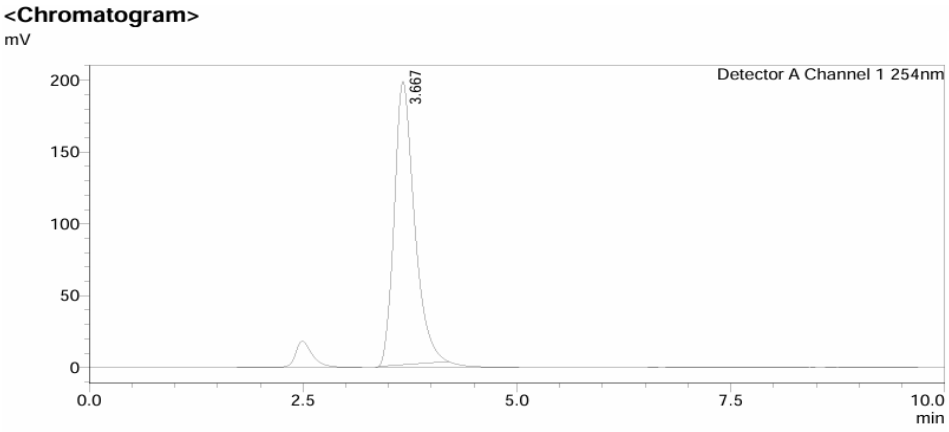

Fig. 3: Chromatogram of sample.

Table 1.2: Calibration data of Fluvoxamine by RP-HPLC method.

Concentration (µg/ml)	Peak area* (mv)
0	0
80	2211989
100	2845784
120	3265527
140	3834211
160	4344652
180	4853457

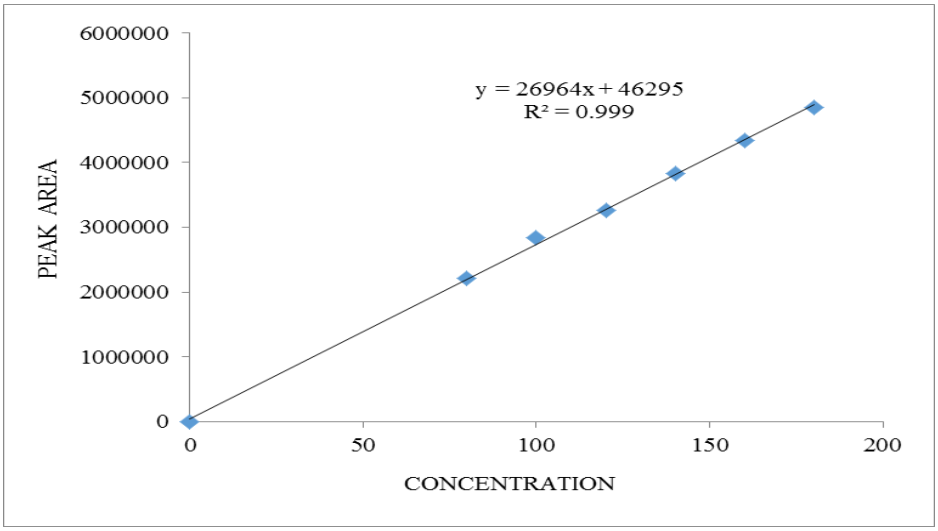

Fig. 4: Calibration curve of Fluvoxamine by RP-HPLC.

Table 1.3: Regression parameters table of Fluvoxamine by RP- HPLC Method.

Optimized conditions	Values
Linearity range(µg/ml)	80-180µg/ml
Regression equation(Y*)	y = 26964x + 46295
Correlation Coefficient (r^2)	0.999
Slope(a)	46295
Intercept(b)	26964

*Y= bX+a, where X is the concentration of compound in mcg/ml and Y is the peak area.

Table 1.4: Intra-day Precision results for Fluvoxamine by RP-HPLC.

SL NO	Concentration (µg/ml)	Area (mv)	Concentration Found (µg/ml)	Mean* (µg/ml)	±SD	%RSD
1	100	2845775	100.71	99.93	0.681	0.681
	100	2745765	100.03			
	100	2843567	99.05			
2	180	4851676	179.36	179.90	0.453	0.251
	180	4892431	179.88			
	180	4881419	180.47			

*Average of three determination.

Table 1.5: Inter-day precision results for Fluvoxamine by RP-HPLC.

SL NO	Concentration (µg/ml)	Area (mv)	Concentration Found (µg/ml)	Mean* (µg/ml)	±SD	%RSD
1	100	2845675	100.26	100.2	0.393	0.392
	100	2745573	100.66			
	100	2843350	99.70			
2	180	4850539	179.87	180.2	0.466	0.258
	180	4891456	180.86			
	180	4881327	179.87			

*Average of three determination

Table 1.6: Accuracy results for Fluvoxamine by RP-HPLC.

SL NO	Spiked level	Amount of Standard (µg/ml)	Amount of sample (µg/ml)	Total amount of drug	Total amount of drug Found	% Recovery	Mean*	±SD	%RSD
1	80%	0.5	0.4	0.9ml (90µg/ml)	89.49	99.44	99.5	0.12	0.122
					89.68	99.64			
					89.48	99.42			
2	100%	0.5	0.5	1ml (100µg/ml)	100.71	100.71	100.47	0.31	0.317
					100.11	100.11			
					100.60	100.60			
3	120%	0.5	0.6	1.1ml (110µg/ml)	110.57	100.52	100.44	0.13	0.129
					110.32	100.29			
					110.56	100.51			

*Average of three determination

Table 1.7: Robustness results for Fluvoxamine by RP-HPLC.

Parameters	Level	Factor	Mean area ± SD	%RSD
Flow rate(1ml/min±1)	-1	0.9ml/min	326225.6 ± 1921.5	0.58
	+1	1.1ml/min	231456.7± 268.4	0.11
Wavelength (254nm±2)	-2	252nm	332444 ± 1088.2	0.32
	+2	256nm	306734±2314.2	0.72
Column oven temperature (30˚C±1)	-1	29˚C	352316±1213.8	0.34
	+1	31˚C	323453±1027.9	0.31

Table 1.8: Determination of LOD and LOQ results of Fluvoxamine by RP-HPLC.

Sl. No	Parameters	Values
1	**LOD (3.3×SD of Intercepts/average of slopes)**	6.39 µg/ml
2	**LOQ (10×SD of Intercepts/ average of slopes)**	19.36µg/ml

**Mean value obtained from six calibration curves.

CONCLUSION

The current analytical method satisfies the acceptance requirements and has been validated in accordance with ICH recommendations. The new analytical approach was shown to be simple, sensitive, accurate, and cost-effective. It may be applied to the regular analysis of Fluvoxamine in pharmaceutical dosage forms and bulk drug.

REFERENCES

1. Foda NH, Radwan MA, Al Deeb OA. Fluvoxamine maleate. In Analytical Profiles of Drug Substances and Excipients. Academic Press, 1996 Jan 1; 24: 165-208.
2. Wilde MI, Plosker GL, Benfield P. Fluvoxamine: an updated review of its pharmacology, and therapeutic use in depressive illness. Drugs, 1993 Nov; 46: 895-924.
3. Claassen V, Davies JE, Hertting G, Placheta P.Fluvoxamine, a specific 5-hydroxytryptamine uptake inhibitor. British J of pharmacol, 1977 Aug; 60(4): 505-16.
4. Revathi S, Rahaman S, Prathyusha V, Maheswari G, Neeharika M. Development and validation of UV spectrophotometric method for the estimation of fluvoxamine maleate in bulk and pharmaceutical dosage form. Indo Am. J. Pharm. Res., 2013; 3(8): 6373-80.
5. Misztal GE, Skibinski RO. Application of UV spectra derivatives for the determination of paroxetine hydrochloride and fluvoxamine maleate in tablets. Acta Pol. Pharm., 1999; 56(2): 95-100.
6. Dikkar JS, Ahmed SA. Development and Validation of UV Spectrophotometric Rp-Hplc Method For Simultaneous Estimation of Fluvoxamine in Tablet and Bulk, 2024 June; 2(6): 401-13.
7. Devarajan S, Manavalan G, Balasubramanian K, Annamalai J, Madduri N. A new spectrophotometric method for the determination of fluvoxamine maleate in pure form and in pharmaceutical formulation. J. Appl. Pharm. Sci., 2015 Feb 27; 5(2): 081-6.
8. Foda NH. Quantitative analysis of fluvoxamine maleate in tablet formulations by HPLC. J of Liq Chromatogr Relat Technol, 1995 Apr 1; 18(8): 1591-601.
9. Ulu ST. HPLC method for the determination of fluvoxamine in human plasma and urine for application to pharmacokinetic studies. JPBA., 2007 Mar 12; 43(4): 1444-51.
10. Pullen RH, Fatmi AA. Determination of fluvoxamine in human plasma by high-performance liquid chromatography with fluorescence detection. J. Chromatogr. B Biomed. Sci. Appl., 1992 Feb 7; 574(1): 101-7.
11. Hemke AT, Gupta KR. Force degradation study and rp-hplc method development for estimation of fluvoxamine maleate in tablet. Int J Pharm Pharm Sci., 2015; 7(6): 196-202.

12. Souri E, Donyayi H, Tehrani MB. A stability indicating HPLC method for the determination of fluvoxamine in pharmaceutical dosage forms. Iranian J of Pharm Res: IJPR., 2015; 14(4): 1059-65.
13. Berzas JJ, Guiberteau C, Contento AM, Rodriguez V. Sensitive and rapid high-performance liquid chromatographic method for simultaneous determination of antidepressants in pharmaceutical formulations. Chromatographia, 2002 Nov; 56: 545-51.
14. El-Enany N. Spectrofluorometric determination of fluvoxamine in dosage forms, spiked plasma, and real human plasma by derivatization with fluorescamine. J of AOAC Int., 2007 Mar 1; 90(2): 376-83.
15. ICH, Q2A text on validation of analytical procedures, 1994.
16. ICH, Q2B validation of analytical methodology, 1996.
17. ICH, Q2 (R1) validation of analytical procedures: text and methodology, 2005.