WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 13, 1418-1426. Research Article ISSN 2277–7105

VALIDATED SPECTROPHOTOMETRIC METHOD FOR THE QUANTITATION OF FLUVOXAMINE IN BULK AND PHARMACEUTICAL DOSAGE FORM

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Article Received on
16 May 2025,

Revised on 05 June 2025,
Accepted on 25 June 2025

DOI: 10.20959/wjpr202513-37449

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ABSTRACT

Simple, precise and accurate zero-order derivative UV spectroscopic method has been developed and validated for the estimation of Fluvoxamine in bulk and pharmaceutical dosage form. Fluvoxamine exhibits maximum absorbance at 256 nm in Ethanol, and its concentration follows Beer's Law within the range of 5–30 µg/ml. The linearity study was carried out and regression coefficient (R^2) was found to be 0.999 and it has showed good linearity, precision during this concentration range. The percentage recovery was found to be 98.8% and 101.39%, while the limits of detection (LOD) and quantification (LOQ) were found to be 0.049 µg/ml and 0.150 µg/ml, respectively. The method also demonstrated excellent precision, with relative standard deviation (%RSD) values below 2%. All validation parameters—linearity, accuracy, precision, robustness, ruggedness, LOD, and LOQ—were assessed according to ICH guidelines. The developed and validated method can be successfully applied for routine estimation of Fluvoxamine in bulk and pharmaceutical dosage form.

KEYWORDS: Fluvoxamine, Zero order derivative spectroscopy, Validation, Pharmaceutical formulation.

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 C15H21F3N2O2, a molecular weight of 523.32 $gmol^{-1}$ Fluvoxamine is characterized by these chemical and physical attributes.

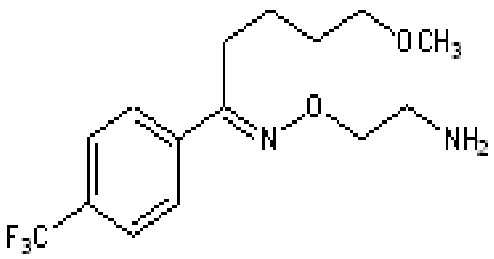

Fig. 1: Chemical Structure of Fluvoxamine.

Extensive literature survey reveals that few spectrophotometric methods[4-7], RP-HPLC[8-13] and Spectrofluorimetry[14] methods for the determination of the Fluvoxamine alone or in combination various pharmaceutical formulations and biological fluids including stability studies, this information related to the analyte is surveyed for synthesis, physical and chemical properties, solubility and relevant analytical methods. Hence there is a need for the development of newer, simple, sensitive, rapid, accurate, and chromatographic methods for the routine estimation of Fluvoxamine in bulk drug and pharmaceutical dosage form.

MATERIALS AND METHODS

Instrument: UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with UV probe software. All weights were taken in analytical balance.

Chemicals: Fluvoxamine pure drug was obtained as a gift sample from Nuwill Research and Innovations Pvt. Ltd, Bengaluru and its pharmaceutical dosage Fluvoxamine 20 tablets (fluvoxin) labelled claim 100mg from Bayer zydus pharma private limited.

Solvent: Ethanol is used as a solvent.

Selection of analytical wavelength: Appropriate dilutions of Fluvoxamine were prepared from standard stock solution and using spectrophotometer solution was scanned in the wavelength range 200-400 nm. The absorption spectra obtained and show maximum absorbance at 256 nm, as the wavelength for detection.

Preparation of standard stock solution: 100mg of Fluvoxamine was weighed accurately transferred into 100 ml of volumetric flask and diluted in ethanol upto the mark. From this, the solution was further diluted into 100µg/ml and pipetted out 0.5, 1.0, 1.5, 2.0, 2.5 and 3.0ml into 10 ml individual volumetric flask and diluted in ethanol upto the mark, this gives 5, 10, 15, 20, 25 and 30µg/ml concentration.

Preparation of sample solution: 20 tablets of Fluvoxamine marketed formulations was weighed and powdered. A quantity of tablet powder equivalent to 100mg of Fluvoxamine was transferred into 100ml volumetric flask then it was diluted with ethanol and makes upto the mark.

METHOD AND VALIDATION

The method was validated according to the ICH guidelines.[15-17]

RESULT AND DISCUSSION

METHOD: ZERO ORDER DERIVATIVE SPECTROSCOPY

Linearity: The linearity of an analytical method is its capacity to show the test results that are directly proportional to the concentration to the analyte in the sample within the range. The linearity was established in the range of 5-30µg/ml was measured at 256nm and absorbance values are shown in table 1. The calibration curve was prepared by plotting graph against the concentration and absorbance and therefore the graph shown in Fig-3 statistical variables like slope, intercept, regression equation, correlation coefficient and Sandell's sensitivity were determined and shown in table-2.

Precision: The precision of an analytical method express the closeness of series of individual analytical measurement obtained from the multiple sampling of equivalent sample. Precision was established by intra-day and inter-day was determined by analysing the same concentration for six times in a same day. Inter-day precision was analysing the same concentration daily for six days shown in table-3.

Accuracy: The accuracy of an analytical method says that closeness of test results obtained by that method of the true value. To assess the accuracy of the developed method, recovery studies were carried out at three different levels at 50%, 100% and 150%. In which the formulation concentration kept constant and varied pure drug concentration. Shown in table-4.

Ruggedness: The ruggedness is defined as the reliability of results when the method is performed under the variation in condition. This includes distinct analyst, laboratories, instruments, temperature etc. Ruggedness was determined between different analyst, the value of %RSD was found to be less than 2. (Table-5).

LOD and LOQ: The limit of detection is an individual analytical method is the smallest amount of analyte in the sample which can be reliably detected by the analytical method. The limit of quantification is an individual analytical procedure is the smallest amount of analyte in the sample which can be quantitatively determined. LOD and LOQ were calculated by using following formula.

LOD = 3.3(SD)/S and LOQ = 3(LOD)

LOD and LOQ value of Fluvoxamine were found be 0.0497 µg/mL and 0.150 µg/ml.

Table 1: Results of calibration curve at 256nm by zero order derivative spectroscopy.

Sl No.	Concentration in µg/ml	Absorbance ± Standard deviation
1	0	0
2	5	0.125±0.00082
3	10	0.255±0.0009
4	15	0.392±0.00082
5	20	0.527±0.00069
6	25	0.676±0.00075
7	30	0.811±0.00075

**Average of six determinations*

Table 2: Regression parameters of Fluvoxamine by Zero order spectroscopy.

Regression Parameter	Results
Range	5-30 µg/ml
λ_{max}	256nm
Regression equation	Y=0.0272x-0.0099
Slope(b)	0.027
Intercept (a)	-0.0099
Correlation coefficient (r^2)	0.999
Sandell's sensitivity	0.0382
Limit of detection (µg/ml)	0.049
Limit of quantification (µg/ml)	0.150

Y=bx+a**

Table 3: Determination of Precision results for Fluvoxamine at 256 nm by Zero order spectroscopy.

Concentration (µg/ml)	Intra-day Absorbance ±Standard deviation*	%RSD**	Inter-day Absorbance ±Standard deviation*	%RSD**
5	0.125±0.00082	0.656	0.124±0.00094	0.758
10	0.255±0.0009	0.352	0.255±0.00082	0.321
15	0.392±0.00082	0.209	0.391±0.00115	0.294
20	0.527±0.00069	0.130	0.528±0.00134	0.254
25	0.676±0.00075	0.110	0.677±0.00094	0.139
30	0.811±0.00075	0.092	0.814±0.0010	0.131

Average of six determinations, Percentage relative standard deviation.*

Table 4: Determination of accuracy results for Fluvoxamine at 256nm by Zero order spectroscopy.

Spiked levels	Amount of sample (µg/ml)	Amount of standard (µg/ml)	Amount recovered	%Recovery± Standard deviation*	%RSD**
50	15	7.5	22.76	101.28%±0.35	0.34
100	15	15	29.6	98.80%±0.330	0.33
150	15	22.5	38.00	101.39%±0.374	0.368

Average of six determinations, Percentage relative standard deviation.*

Table 5: Determination of ruggedness results of Fluvoxamine at 256nm by Zero order spectroscopy.

Analysts	Analyst 1	Analyst 2
Mean absorbance	0.392	0.393
± Standard deviation*	0.00082	0.00096
%RSD**	0.209	0.244

Average of six determinations, Percentage relative standard deviation.*

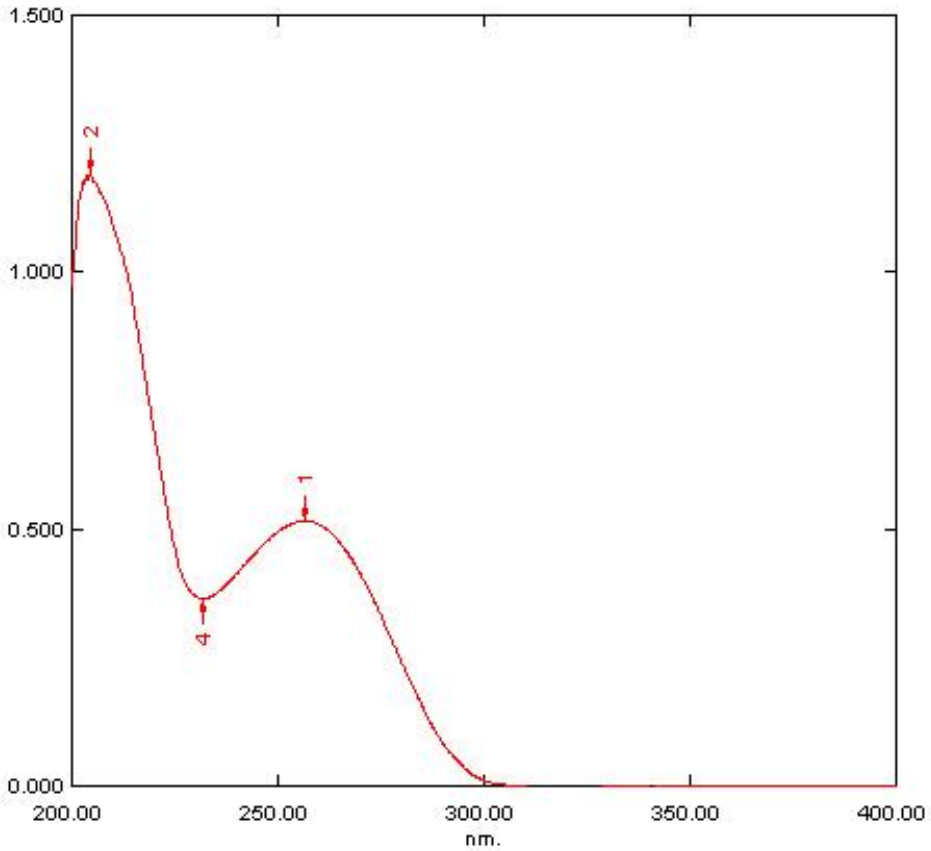

Fig. 2: Zero order spectrum of Fluvoxamine at 256nm.

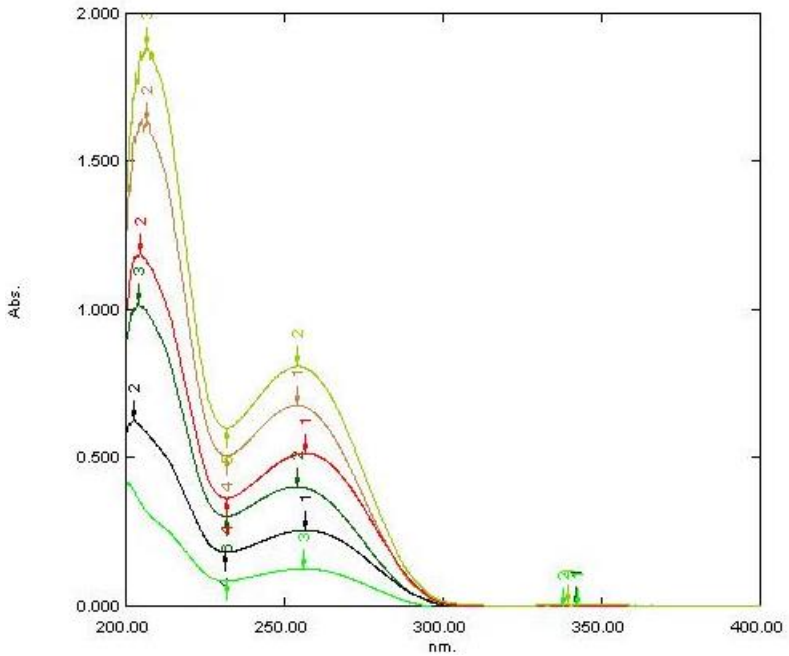

Fig. 3: Zero order overlain spectra of Fluvoxamine showing absorbance at 256nm.

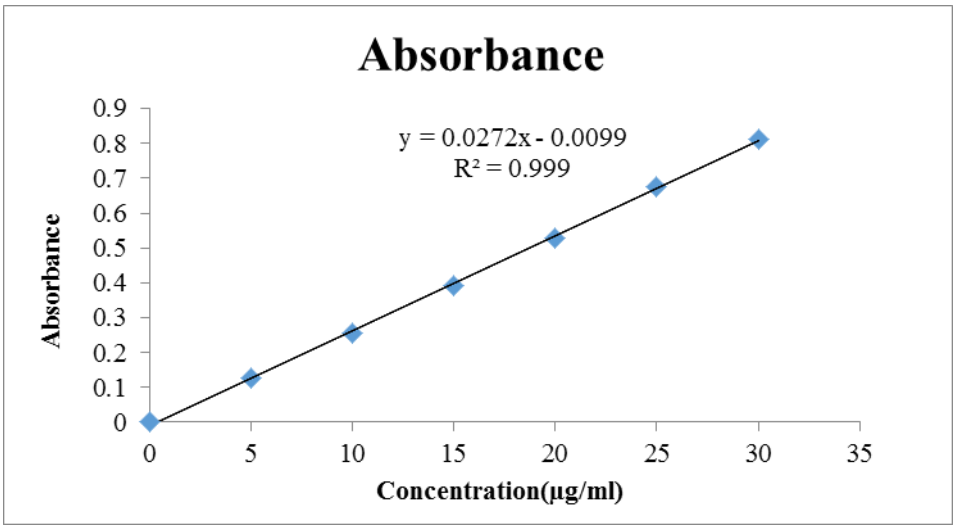

Fig. 4: Calibration curve of Fluvoxamine by Zero order derivative spectroscopy.

CONCLUSION

The analytical method developed for Fluvoxamine was validated as per ICH guidelines demonstrating simplicity, specificity, accuracy, economy, and sensitivity. This method is suitable for regular analysis of Fluvoxamine in both bulk form and pharmaceutical preparations.

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