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DEVELOPMENT AND VALIDATION OF A SPECTROPHOTOMETRIC METHOD FOR DETERMINATION OF FLUVOXAMINE MALEATE IN BULK DRUG AND PHARMACEUTICAL FORMULATION

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ABSTRACT

A simple, sensitive and accurate spectrophotometric method has been developed for the determination of Fluvoxamine maleate in raw material and tablets. The λ max of the Fluvoxamine was found to be 251.5nm.The method shows high sensitivity with linearity 10 to 60µg/ml. All the calibration curves show a linear relationship between the absorbance and concentration and coefficient correlation was found to be 0.999. The regression of the curve was Y =0.024X +0.006. %RSD value is below 2.0 for intraday and interday precision indicated that method is highly precised. The percentage recovery value was higher than 100 %, indicates the accuracy of the method and absence of interference of the excipients present in the formulation. The proposed method will be suitable for the analysis of Fluvoxamine in bulk and pharmaceutical formulation.

KEYWORDS : *Fluvoxamine maleate, spectroscopy, estimation, validation.*

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INTRODUCTION

Fluvoxamine chemically is1-pentanone, E-5-methoxy-1-[4-(trifluoromethyl)phenyl] o-(2-aminoethyl)oxime[1] an antidepressant which functions pharmacologically as a selective serotonin reuptake inhibitor[2]. Though it is in the same class as other SSRI drugs .it is most often used to treat obsessive-compulsive disorder [3] . Literature survey reveled that various analytical methods such as Polarographic[4], Spectrophotometric[5,6], fluorimetry[7,8], LC-MS[9], methods have been reported for estimation of fluvoxamine maleate from its formulations and biological fluids. However very few methods were reported for quantitation of Fluvoxamine in tablet dosage forms in the literature.

OBJECTIVE

The objective of the present investigations was to develop simple, accurate and economical spectrophotometric methods for estimation of fluvoxamine tablet formulation.

MATERIALS & METHODS CHEMICALS & REAGENTS

Standard fluvoxamine maleate was receieved as a gift sample from captab biotec baddi(H.P)and fluvoxamine maleate tablets (50 mg) manufactured by psycogen captab were purchased from local market. Analytical grade methanol used as solvent.

INSTRUMENT

UV-Visible double beam spectrophotometer Jasco UV 630.

SELECTION OF WAVELENGTH

In order to ascertain the wavelength of maximum absorption (λmax) of the drug, different solutions of the drugs (10 µg/ml and 20 µg/ml) in methanol were scanned using spectrophotometer within the wavelength region of 200 – 400 nm against methanol as blank.The resulting spectra were shown in Fig and the absorption curve showed characteristic absorption maxima at 251.5 nm for fluvoxamine.

PREPARATION OF STANDARD SOLUTION FOR CALIBRATION CURVE

10 mg Standard was accurately weighed fluvoxamine and transferred to 100 ml volumetric flask and was dissolved properly and diluted up to the mark with methanol to produce a stock solution of 100 µg/ml. Then 1ml of this solution was diluted to 10ml with methanol gives 10ug/ml. similarly prepared 20,30,40,50 and 60ug/ml of solution.

PREPARATION OF SAMPLE SOLUTION

Twenty tablets were weighed accurately and powdered. Tablet powder equivalent to 10mg of fluvoxamine was weighed and transferred to a 100ml volumetric flask. About 40ml of methanol was added and sonicated for 5 min for complete dissolution of drugs, the volume was made up to the mark with the same solvent and then the above solution was filtered through Whatmann filter paper. Now 1ml of the filtrate is transferred to a 100 ml volumetric flask and then the volume was made up to the mark with the same solvent. After suitable dilution, the absorbance of final sample was recorded against the blank at 251.5 nm. All determinations were conducted in triplicate.

THE PROPOSED METHOD WAS VALIDATED ACCORDING TO ICH GUIDELINES FOR LINEARITY, ACCURACY, PRECISION, LOD AND LOQ. [10]

LINEARITY

The linearity of this method was determined at six concentration levels ranging from 10 to 60µg/ml The plot of absorbance Vs respective concentration of fluvoxamine was found to be linear in the range of 10 to 60 µg/ml. Beer's law was obeyed over this concentration range. The regression equation was found to be Y =0.024X +0.006 and the correlation coefficient (r) of the standard curve was found to be 0.999.

PRECISION

The precision of the assay was determined by repeatability (intraday) and intermediate precision (inter-day) and reported as RSD %. For this, 50 µg/ml concentration solution was measured three times in day and same was measured in next three days. The RSD% was calculated.

RECOVERY STUDIES (ACCURACY)

Recovery studies were performed to judge the accuracy of the method. Recovery studies were carried out by adding a known quantity of pure drug to the preanalyzed formulation and the proposed method was followed. From the amount of drug found, percentage recovery was calculated. Recovery study was carried out at three levels 80%, 100% and 120% for the formulation concentration of 50 µg/ml.

LOD & LOQ

LOD (k = 3.3) and LOQ (k = 10) of the method were established according to ICH definitions.LOD and LOQ of method are reported in table. In this study, LOD and LOQ were based on the standard deviation of the response and the slope of the corresponding curve using the following equations

LOD = 3.3 S/M; LOQ = 10 S/M
Where S is the standard deviation of the absorbance of the sample and
M is the slope of the calibrations curve.

RESULT & DISCUSSION

The λ max of the fluvoxamine was found to be 251.5 nm from the optical characteristics (Table 2) of the proposed method, it was found that fluvoxamine obeys linearity within the concentration range of 10 to 60µg/ml and coefficient correlation was found to
be 0.999. The regression of the curve was Y =0.024X +0.006.The detection and quantization limits as LOD (k=3.3) and LOQ (k=10) were calculated and these were found to be 0.825 µg/ml and 2.5 µg/ml respectively. The precision (measurements of intraday andinterday) results showed (Table 2) good reproducibility with percent relative standard deviation (% RSD) is below 2.0. This indicated that method is highly precised. The percentage recovery value (Table 3), which was higher than 100 %, indicates the accuracy of the method and absence of interference of the excipients present in the formulation. The proposed method was also applied for the assay of fluvoxamine maleate in tablet formulation (in triplicate) and the results as tabulated in Table 4. The results obtained were good agreement with the label claims.

The chemical structure of fluvoxamine maleate is shown in Figure 1.

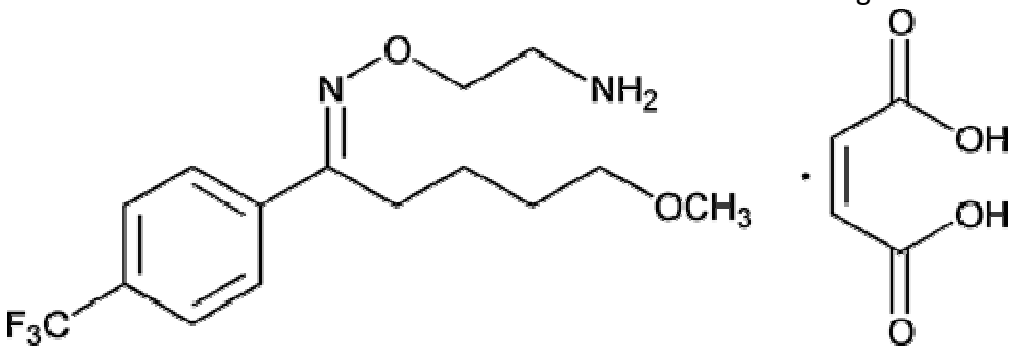


Figure 1: structure of Fluvoxamine maleate

Figure 2: UV Spectrum of Fluvoxamine maleate in methanol

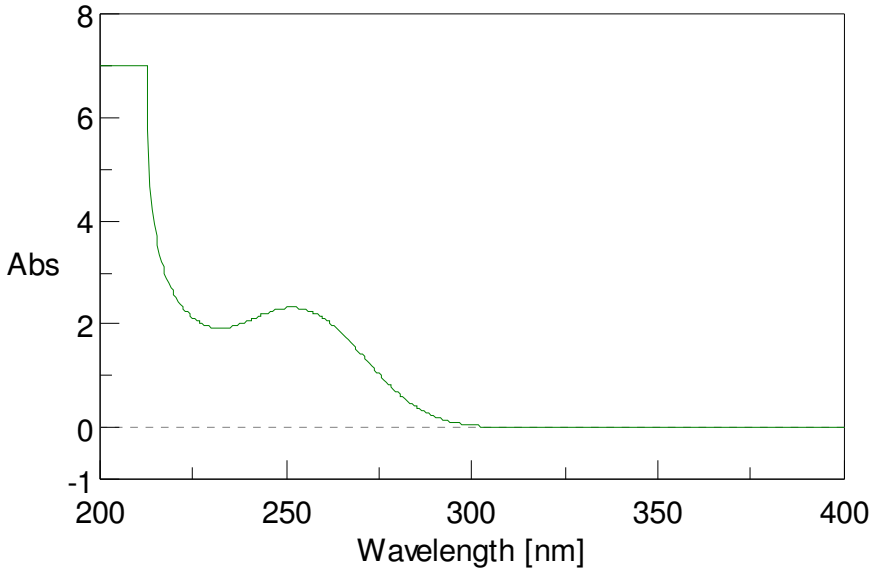
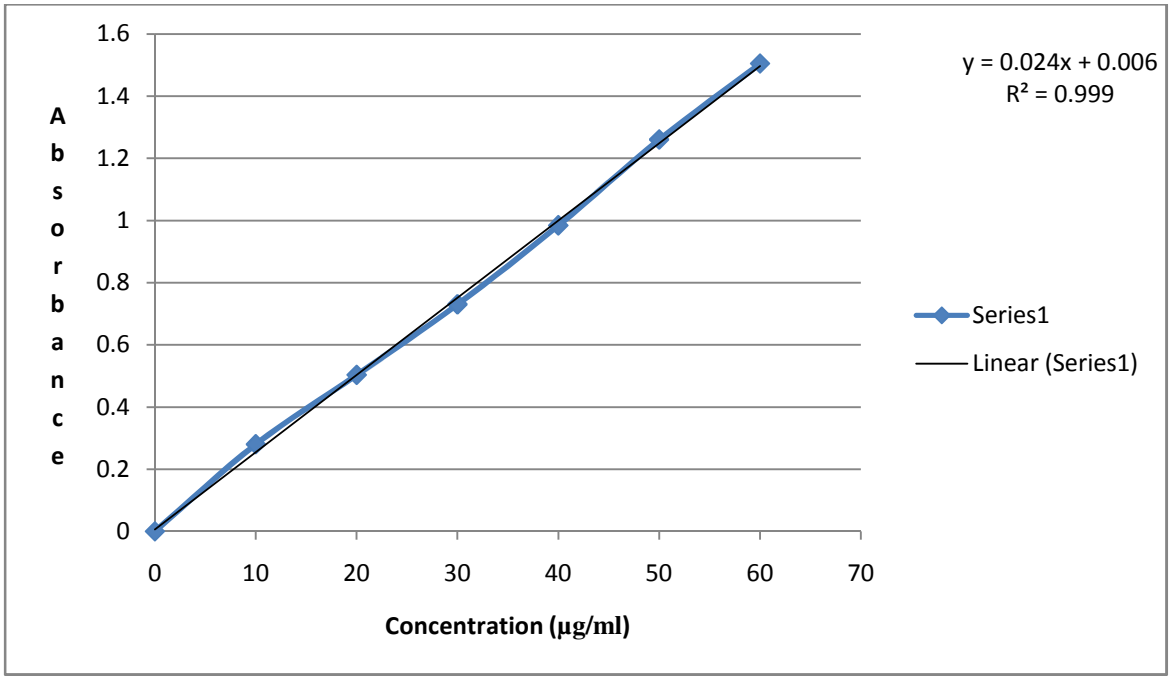


Table 1: Data for the standard curve of Fluvoxamine maleate

Concentration(µg/ml)	absorbance
0	0.000
10	0.280
20	0.503
30	0.730
40	0.984
50	1.26
60	1.50

Figure 3: standard curve for Fluvoxamine



S.D= 0.014

LOD = $\frac{3.3\times0.006}{0.024}$ = 0.825

LOQ = $\frac{10\times S.D}{SLOPE} = \frac{10\times0.006}{0.024}$ = 2.5

Table 2: Validation Parameters

Parameters	**Results**
Absorption maxima(nm)	251.5
Linearity range (µg/ml)	10 to 60ug/ml
Standard Regression equation	Y =0.024X +0.006
Correlation coefficient	0.999
LOD (µg/ml)	0.825
LOQ (µg/ml)	2.5

Precision

Concntration	Intraday (%RSD)	Interday (%RSD)
50(ug/ml)	0.018	0.360

Table 3: Recovery Study

Level of Addition (%)	Formulation (µg/ml)	Addition of pure drug (µg/ml)	% Recovery of pure drug
80	50	40	100.4%
100	50	50	100.44%
120	50	60	100.2%

Table 4: Determinations of Active Ingredients In Tablets

Sample	Label claimed	Amount found	% Labeled Claim*
Fluvoxamine maleate	50mg/tab	50.18	100.36

(*Average of three determinations)

CONCLUSION

The proposed method was simple, sensitive and reliable with good precision and accuracy. The proposed method is specific while estimating the commercial formulations without interference of excipients and other additives. Hence, this method can be used for the routine determination of fluvoxamine in pure samples and pharmaceutical formulations.

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