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RESEARCH ARTICLE

New Derivative Spectrophotometric Methods for the Determination of Fluoxetine - An Antidepressant Drug

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Abstract: Fluoxetine is an antidepressant of the selective serotonin reuptake inhibitor class. Two simple, rapid and sensitive first and second derivative spectrophotometric methods are developed for the determination of fluoxetine (FLX) in pharmaceutical dosage forms (capsules). The absorption minima was chosen (at 235 nm) in first order (Method A) and amplitude (229-238.5 nm) was selected in second order derivative spectral calculations. Fluoxetine follows Beer's law in the concentration range of 1-60 µg mL^{-1} (r^2= 0.999) in first order as well as in second order (r^2 = 0.9994) derivative spectroscopy respectively. The proposed methods can be successfully applied for the determination of Fluoxetine in commercial brands of pharmaceutical formulations. No interferences were observed from the common excipients in the formulations. The methods were validated according to ICH guidelines.

Keywords: Fluoxetine HCl, Derivative spectrophotometry, Antidepressant drug

Introduction

Fluoxetine[1] HCl (FLX) chemically, *N*-methly-3-phenyl-3-[4-(trifluoromethyl) phenoxy] propan-1-amine. It is available as white crystals with molecular weight 309.33 g/mol with molecular formula, $C_{17}H_{18}F_3NO$ (Figure 1). It is an antidepressant of the selective serotonin reuptake inhibitor class; it is approved for the treatment of major depression, obsessive compulsive disorder, anorexia nervosa, panic disorder, bulimia nervosa and premenstrual dysphonic behavior. The literature survey reveals that spectrophotometric and fluorimetric methods[2-4] and liquid chromatographic[5-6] methods were developed. Mandrioli[7] *et al* developed spectrofluorimetric and capillary zone electrophoretic methods for the determination if FLX. Further Souverain[8] *et al.,* analysed fluoxetine and its metabolites in plasma by LC/MS with column-switching approach and in the present work two new spectrophotometric methods were developed for the estimation of Fluoxetine in capsules and validated as per the ICH guidelines[9].

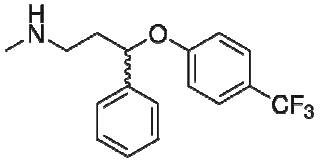

Figure 1. Chemical structure of fluoxetine

Experimental

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe was employed with spectral bandwidth of 1 nm and wavelength accuracy of ±0.3 nm with a pair of 10 mm matched quartz cells. All weights were taken on electronic balance (Denver, Germany).

Chemicals and reagents

Analytical grade Methanol (Merck) was purchased. Fluoxetine (FLX) was obtained from Sun Pharma Ltd. (India) and was used as such without further purification.

Recommended procedure and calibration curve

Preparation of stock solution

The standard solution of fluoxetine was prepared by dissolving accurately weighed 25 mg of the drug was dissolved in methanol in a 25 mL volumetric flask and diluted with methanol to obtain a working standard solution (100 µg mL^{-1}).

First-order derivative spectrometry (Method A)

The drug solution was scanned (200-400 nm) against reagent blank and the absorption spectrum was recorded. This spectrum was derivatised to get first order derivative spectra (Figure 2) and the zero crossing point was found to be at 227 nm.

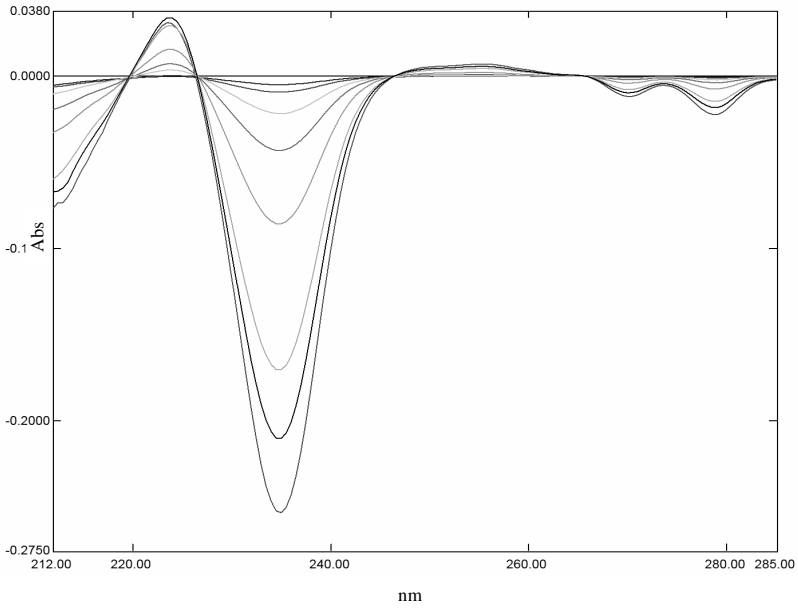

Figure 2. First derivative overlay spectrum (D_1) of Fluoxetine

A series of solutions (1-60 µg mL^{-1}) were prepared, scanned against reagent blank and their of the corresponding troughs (or minima) were measured at 235.0 nm and plotted against the concentration (Figure 3).

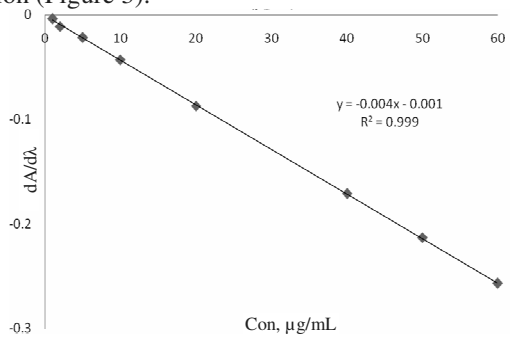

Figure 3. Calibration curve of Fluoxetine (Method A)

Second-order derivative spectrometry (Method B)

The drug solution was scanned (200-400 nm) against reagent blank and the absorption spectrum was recorded and was derivatised to get second order derivative spectra (Figure 4). This spectrum shows minima (229 nm) as well as maxima (238.5 nm) and therefore the amplitude was chosen for the analytical determinations.

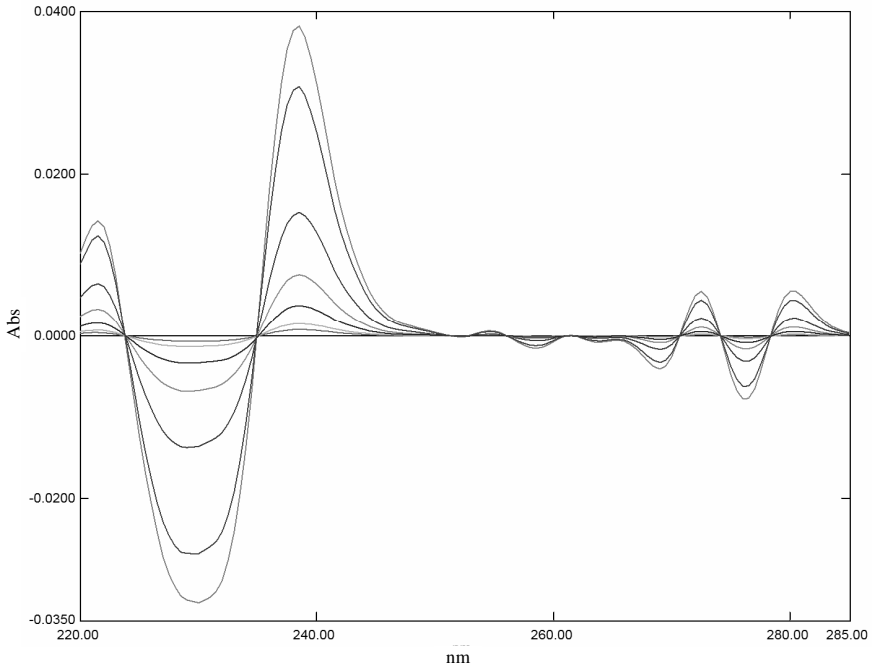

Figure 4. Second derivative overlay spectrum (D_2) of Fluoxetine

A series of solutions (1-60 µg mL^{-1}) were prepared, scanned against reagent blank and their amplitude was measured. A graph was plotted by taking the concentration on the *x*-axis and the corresponding amplitude values on *y*-axis (Figure 5).

Assay procedure for the commercial formulations (Capsules)

Fluoxetine is available as capsules in local market with brand names DAWNEX (20 mg, Micro labs), FLUDAC (10, 20 and 60 mg, Cadila Pharma), FLUNIL ((10, 20 and 60 mg, Intas) and PRODEP ((10, 20 and 60 mg, Sun Pharma) and are procured from the medical store.

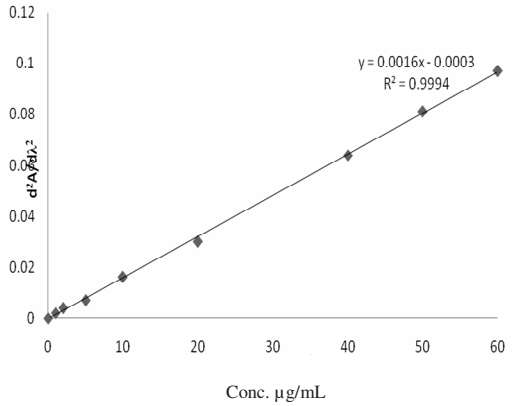

Figure 5. Calibration curve of Fluoxetine (Method B)

20 Capsules were taken from three different brands and the FLX equivalent to 25 mg was weighed from each brand and extracted with methanol, sonicated and make up to volume with methanol in three separate 25 mL volumetric flasks (1 mg/mL) and filtered. The dilutions were made from this stock with methanol as per the requirement. A series of solutions (1.0–60.0 µg/mL) were prepared, scanned and the corresponding values were recorded and calibration curves were drawn. A straight line was obtained and the results obtained were shown in Table 1.

Table 1. Assay of commercial formulations

Brand	Labelled Amount, mg	Amount Obtained, mg Method		% Recovery Method		% RSD Method	
		A	B	A	B	A	B
I	20	19.967	19.786	99.835	98.931	0.8673	0.6578
II	20	19.865	19.564	99.325	97.822	0.9876	0.8741
III	20	19.891	19.831	99.455	99.155	1.3421	0.8321

[*]*Each value is average of three determinations*

Precision and accuracy

The precision study was done by recording the response of six replicates in Method A (20 µg/mL) and Method B (40 µg/mL) and the %RSD was calculated. Accuracy was evaluated by the percent recovery studies by the addition of 80%, 100% and 120% of pure sample solution to the pre-analysed formulation solution. For the present study 20 µg/mL of FLX solution extracted from the formulation was taken and 80%, 100% and 120% of pure sample solution (*i.e.* 16, 20 and 24 µg/mL) and the %RSD was calculated.

Results and Discussion

Beer's law was obeyed in the concentration range of 1.0–60.0 µg/mL for both the methods A

and B. The linear regression equations are found to be y = -0.004x - 0.001, y = 0.0016x-0.0003 (where x is the concentration (µg/mL) and y is the absorbance derivative) with correlation coefficient 0.999. The %RSD values in precision studies were found to be 0.3054 (Method A) and 0.8321 (Method B) which are less than 2% indicating that the method is more precise. The %RSD values in accuracy studies were found to be 0.8192 (Method A) and 1.0253 (Method B) which are less than 2% indicating that the method is more precise.

Conclusion

The present methods can be employed for the estimation of Fluoxetine in pharmaceutical formulations successfully.

Acknowledgement

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