ORIGINAL ARTICLE

Derivative spectrophotometric methods for the determination of escitalopram oxalate (an antidepressant)

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Abstract

Introduction: Escitalopram oxalate is an antidepressant drug. FDA has given approval for the treatment of major depressive disorder in adolescents and adults. New spectrophotometric techniques have been proposed for the determination of Escitalopram oxalate in sodium acetate buffer, borate buffer, and phosphate buffer (pH 6.8). **Materials and Methods:** Double beam UV-VIS spectrophotometer (SHIMADZU Model UV-1800) was used for the present study. Zero-order and first-order derivative spectrophotometric techniques have been developed for the determination of Escitalopram oxalate in sodium acetate buffer, borate buffer, and phosphate buffer. **Results and Discussion:** Escitalopram oxalate has shown absorption maxima at 238 nm in all the methods and linearity was observed 1.0–60 µg/ml in all the reagents such as sodium acetate buffer, borate buffer, and phosphate buffer and the methods were validated as per the ICH guidelines. **Conclusions:** These methods are simple, economical and can be successfully applied for the estimation of Escitalopram oxalate in pharmaceutical dosage forms.

Key words: Escitalopram oxalate, first-order derivative spectroscopy (D_1), ICH guidelines, validation, zero-order (D_0)

INTRODUCTION

Escitalopram oxalate [Figure 1] is a newer antidepressant used for the treatment of depression.[1] Escitalopram oxalate is the pure S. Enantiomer of the racemic bicyclic naphthalene derivative of citalopram. Escitalopram oxalate is the s (+)-1-[3(dimethylamino) propyl]-1-p-flurophenyl-5-phthalene carbonitrile. It acts by potentiating serotonergic activity in the CNS neuronal reuptake of serotonin.[2] It is chemically known as (1S)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-2-benzofuran-5-carbonitrile. Escitalopram oxalate was given FDA approval for the treatment of major depressive disorder in adolescents and adults, and generalized anxiety disorder in adults.[3] Escitalopram oxalate was determined by different analytical methods such as spectrophotometry[4-9] and high-performance liquid chromatography.[10,11] In the present study, the authors have proposed three new spectrophotometric techniques for the assay of Escitalopram oxalate in tablets and validated as per the ICH guidelines.[12]

MATERIALS AND METHODS

Model No. UV-1800 double beam UV-VIS spectrophotometer (Shimadzu) with quartz cells is used for the entire study, and all the solutions were scanned 200–400 nm.

Preparation of Solutions

Buffer solutions such as sodium acetate buffer, borate buffer, and phosphate buffer (pH 6.8) were prepared as per the IP 2010. Stock solution of Escitalopram oxalate was prepared by dissolving 25 mg of Escitalopram oxalate in 25 ml volumetric flask with methanol (1000 µg/ml) and further

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working standard solutions were prepared by diluting the stock solution with respective buffers as per the requirement for the proposed methods. Escitalopram oxalate is available as tablets with brand name Articalm (Cadila Healthcare Ltd: Label claim: 10 mg, 20 mg) C-Pram-S (Unichem Laboratories; Label claim: 5 mg, 10 mg, 20 mg), etc., in India.

Method Validation

Linearity

Zero-order spectroscopy (D_0)

A series of Escitalopram oxalate solutions 1–60 µg/ml were prepared from the stock solution on dilution with sodium acetate buffer (Method I), borate buffer (Method II), and phosphate buffer (pH 6.8) (Method III) and scanned (200–400 nm) against their reagent blanks. The zero-order spectrum so obtained has shown maximum absorbance (λ_{max}) at 238 nm in all the three methods. The absorbance of all the solutions was noted at λ_{max}, and a calibration curve was drawn by taking the concentration on the X-axis and the corresponding absorbance on the Y-axis for Method I, II, and III, respectively.

First-order derivative spectroscopy (D_1)

The individual zero-order absorption spectra of Escitalopram oxalate so obtained in Method I, II, and III were converted into their first-order derivative spectra with the help of inbuilt software of the instrument in all the three reagents. The resultant derivative spectra have shown both minima and maxima in all the three buffers, and therefore the amplitude was selected for the construction of calibration curves for Method I, II, and III.

Precision and accuracy studies

Precision studies were performed by calculating the percentage relative standard deviation (RSD) values of nine independent assays at three different concentration levels whereas the accuracy studies were carried out by standard addition method.

Assay of Escitalopram oxalate tablets

Twenty Escitalopram oxalate tablets were procured, and powder equivalent to 25 mg of Escitalopram oxalate was extracted with methanol in a 25 ml volumetric flask and dilutions were made with sodium acetate buffer, borate buffer, and phosphate buffer for Method I, II, and III, respectively, and the assay was carried out as per the procedure explained.

RESULTS AND DISCUSSION

Two different techniques – zero-order (D_0) and first-order derivative spectroscopy (D_1) have been developed for the determination of Escitalopram oxalate tablets in three different reagents such as sodium acetate buffer, borate buffer, and phosphate buffer. The present proposed method was compared with the previously reported methods in Table 1.

Zero-order Spectroscopy (D_0)

The overlay absorption spectrum obtained in zero-order spectrophotometric technique (D_0) in sodium acetate buffer, borate buffer, and phosphate buffer for Method I, II, and III was shown in Figure 2. Escitalopram oxalate has shown absorption maxima at 238 nm and obeys Beer-Lambert's law over the concentration range 1.0–60 µg/ml in sodium acetate buffer, borate buffer, and phosphate buffer [Table 2]. The linear regression equations [Figure 3] were found to be $y = 0.0436x - 0.0153$ ($R^2 = 0.9972$), $y = 0.0389x + 0.0082$ ($R^2 = 0.9996$), and $y = 0.0414x + 0.0003$ ($R^2 = 0.9982$) for Method I, II, and III respectively. The optical characteristics were given in Table 3. The percentage RSD in precision and accuracy studies were found to be <2 in all the three methods indicating that the methods are precise and accurate.

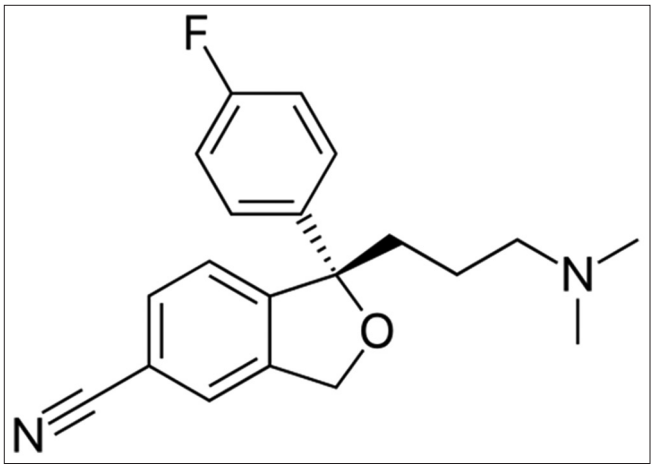

Figure 1: Chemical structure of Escitalopram

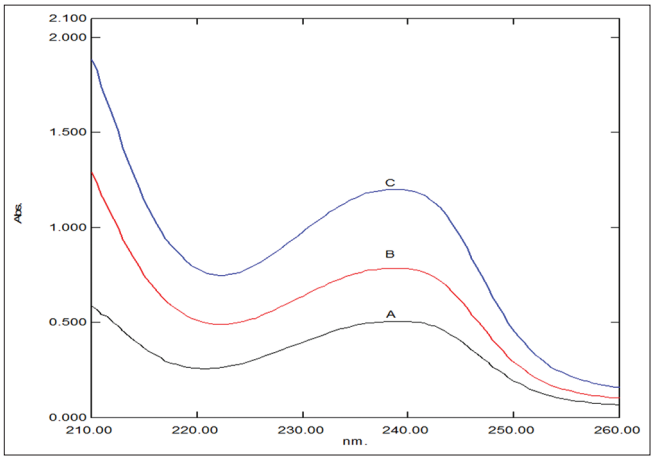

Figure 2: Absorption spectrum of Escitalopram oxalate in (a) sodium acetate buffer (pH 4.0) (10 µg/ml), (b) borate buffer (pH 9.0) (20 µg/ml), and (c) phosphate buffer (pH 6.8) (30 µg/ml)

First-order Derivative Spectroscopy (D_1)

The overlay first-order derivative spectra of Escitalopram oxalate in sodium acetate buffer, borate buffer, and phosphate buffer for Method I, II, and III, respectively, were shown in Figure 5 and the spectral characteristics observed were shown in Table 4. Escitalopram oxalate obeys Beer-Lambert's law over the concentration range 1.0–60 µg/ml in all the three methods and the linear regression equations were found to be $y = 0.0043x + 0.0082$ ($R^2 = 0.9951$) and $y = 0.0044x-0.0009$ ($R^2 = 0.9994$).

Table 1: Comparison of reported spectrophotometric methods with the present method

Reagents	Linearity (µg/mL)	References
Ethanol	0.5–8.0	[1]
Bromocresol green	2–10	[2]
HCl	4–12	[3]
WFB dye	5–40	[4]
Methanol: water (80:20)	2–20	[5]
7,7,8,8-Tetra Cyanoquinodimethane	4–20	[6]
Sodium acetate buffer borate buffer Phosphate buffer	1–60 1–60 1–60	Present method

WFB: Wool fast blue

Table 2: Linearity of Escitalopram oxalate – zero-order spectroscopy

Conc. (µg/ml)	*Absorbance		
	Method I	Method II	Method II
1	0.041	0.04	0.10
5	0.21	0.19	0.20
10	0.42	0.43	0.40
20	0.85	0.78	0.80
30	1.30	1.17	1.20
40	1.58	1.58	1.63
60	2.67	2.33	2.53

*Mean of three replicates

CONCLUSION

The two spectrophotometric techniques were validated and found to be very simple, precise, accurate, and economical and can be conveniently used for the routine analysis of Escitalopram tablets.

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Table 3: Optical characteristics of Escitalopram oxalate – zero-order spectroscopy

Parameters	Method		
	I	II	III
Linearity range (µg/ml)	1-60	1-60	1-60
λ_{max} (nm)	238	238	238
Molar extinction coefficient (liter/mole/cm)	1.64×10^4	1.29×10^4	1.39×10^4
Sandell's sensitivity (µg/cm²/0.001 absorbance unit)	0.0196	0.025	0.0232
Slope	0.0436	0.0389	0.0414
Intercept	0.0153	0.0082	0.0003
Correlation coefficient	0.9972	0.9996	0.9982
Precision (%RSD)	0.32–0.49	0.74–0.91	0.53–0.71
Accuracy (%RSD)	0.27–1.025	0.63–1.038	0.45–1.293
Assay (%)	99.83	99.32	99.82

RSD: Relative standard deviation

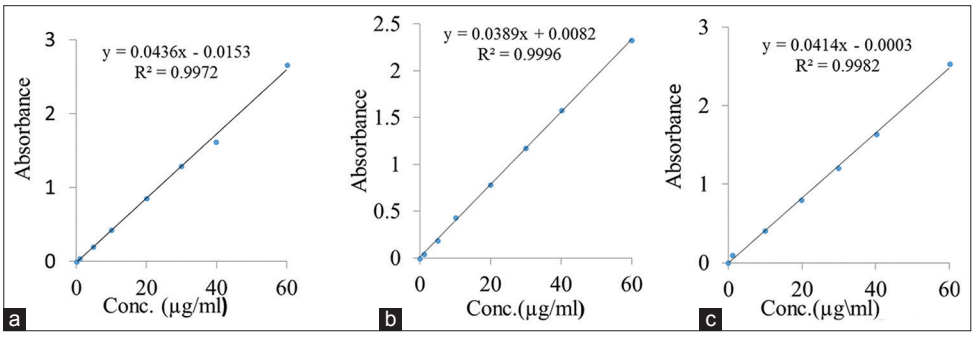

Figure 3: Calibration curves of Escitalopram oxalate (D_1) in (a) sodium acetate buffer, (b) borate buffer, and (c) phosphate buffer

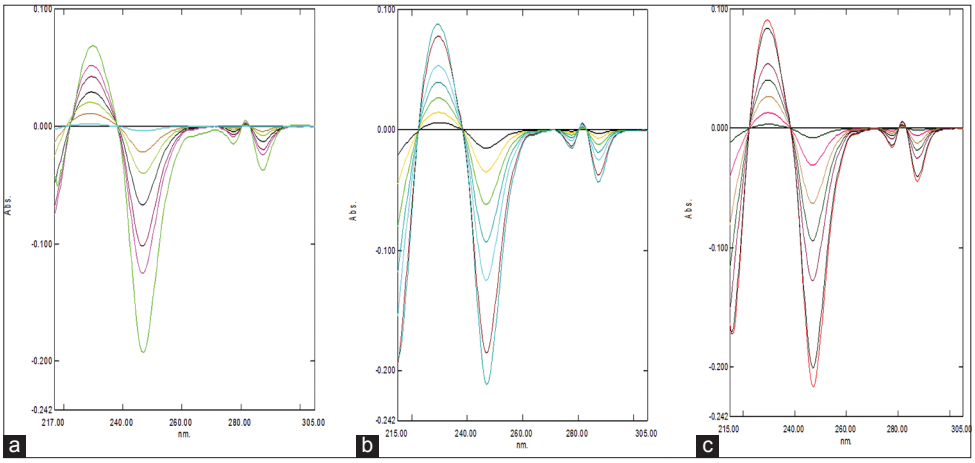

Figure 4: Calibration curves of Escitalopram oxalate (D_0) in (a) sodium acetate buffer, (b) borate buffer, and (c) phosphate buffer

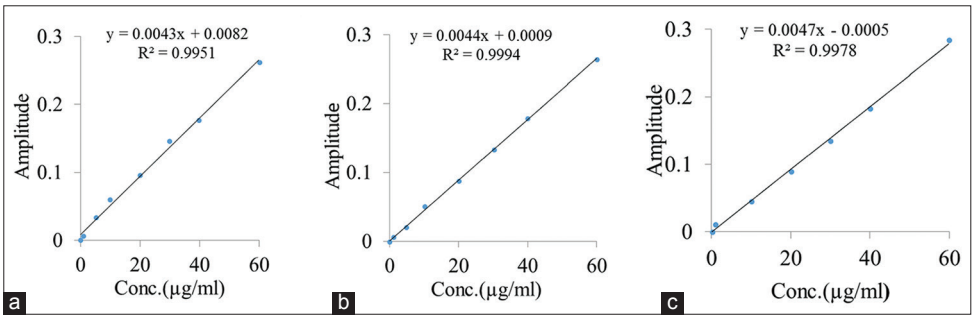

Figure 5: Overlay first-order derivative spectrum (D_1) of Escitalopram oxalate in (a) sodium acetate buffer pH 4, (b) borate buffer pH 9, and (c) phosphate buffer pH 6.8

Table 4: Linearity of Escitalopram oxalate - first-order derivative spectroscopy

Conc. (µg/ml)	Method I Sodium acetate buffer			Method II Borate buffer			Method III Phosphate buffer		
	Maxima	Minima	Amplitude	Minima	Maxima	Amplitude	Maxima	Minima	Amplitude
1	0.002	0.004	0.006	0.002	0.003	0.005	0.001	0.003	0.004
5	0.011	0.022	0.033	0.015	0.006	0.021	0.007	0.016	0.023
10	0.020	0.040	0.060	0.035	0.015	0.05	0.013	0.031	0.044
20	0.029	0.067	0.096	0.062	0.026	0.088	0.027	0.063	0.090
30	0.043	0.102	0.145	0.093	0.040	0.133	0.040	0.094	0.134
40	0.052	0.125	0.177	0.125	0.053	0.178	0.054	0.128	0.182
60	0.069	0.193	0.262	0.186	0.078	0.264	0.084	0.201	0.285

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