April 2007 Volume 5 Issue 1-6

Trade Science Inc.

Analytical CHEMISTRY
An Indian Journal

Full Paper

ACAIJ, 5(1-6), 2007 [79-82]

Simultaneous Estimation Of Escitalopram Oxalate And Clonazepam In Tablet Formulation By Ratio Spectra Derivative Spectroscopy

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Received: 7th February, 2007
Accepted: 12th February, 2007

Web Publication Date : 15th April, 2007

ABSTRACT

A new sensitive, simple, rapid and precise method for simultaneous estimation of escitalopram oxalate and clonazepam in combined tablet dosage form has been developed. The method is based on ratio derivative spectrophotometry. The amplitude in first derivative of the ratio spectra at 246.8nm and 214.4nm (minima) were selected to determine escitalopram oxalate and clonazepam in combined formulation respectively. The method showed good linearity, accuracy and reproducibility. Results of analysis validated statistically and by recovery studies.

KEYWORDS

Escitalopram oxalate;
Clonazepam;
Ratio derivative;
Spectrophotometry.

INTRODUCTION

Escitalopram oxalate(ESC) is chemically known as S-(+)-1-[3-(dimethyl-amino) propyl]-1-(p-fluro-phenyl)-5-phthalancarbonitrile oxalate, which belongs to the class of compounds known as antidepressant and is the S-enantiomer of racemic citalopram[1]. It is yet not official in any pharmacopoeia. It is highly selective serotonin reuptake inhibitor, developed for the treatment of depression and anxiety disorders. Several analytical methods that have been reported for the estimation of escitalopram oxalate in biological fluids and/or pharmaceutical formulations include liquid chromatography coupled with mass spectrometry[2], HPLC[3], chiral liquid chromatography[4] and capillary electrophoresis[5].

Clonazepam(CLO) chemically known as 5-(o-chlorophenyl)-1,3-dihydro-7-nitro-2H-1,4-benzodiazepin-2-one is benzodiazepine with prominent anticonvulsant properties and has been most effective for the treatment of typical and atypical absence, myoclonic and akinetic seizures and infantile spasms[6]. It is official in the U.S.P., which describes HPLC method for estimation of clonazepam from tablet formulation[7]. Several analytical methods that have been reported for the estimation of clonazepam in biological fluids and/or pharmaceutical formulations include HPLC[8-15], spectrophotometry[16-17], fluorim-

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etry[17], potentiometry[18], and GC-MS[19].

Extensive literature survey revealed that no method available for simultaneous estimation of escitalopram oxalate and clonazepam in combined dosage form by ratio spectra derivative spectroscopy[20-21]. Aim of present work was to develop simple, economical, reproducible and rapid method for simultaneous estimation of binary drug formulation.

MATERIALS AND METHODS

Equipment

The instrument used in the present study was JASCO double beam UV/Visible spectrophotometer (Model UV-530) with fixed slit width 2nm connected to a computer with spectra manager software. All weighing were done on electronic balance(Shimadzu AY 120).

Chemicals and reagents

Pure drug samples of clonazepam and escitalopram oxalate were obtained from Torrent Pharmaceuticals Ltd. (Gujarat, India) and Cipla Ltd. (Pune, India) respectively, which were used as such without further purification. All chemicals used in spectrophotometric analysis were of analytical grade.

Pharmaceutical formulation

Commercial tablets of escitalopram oxalate (10mg) and clonazepam USP(0.5mg) (C-prams plus, Atoz life sciences) were procured from the local market.

Procedure

Preparation of standard stock solution

Standard stock solution of escitalopram oxalate was prepared by dissolving 25mg of drug in 25ml of methanol to get concentration of 1mg/ml. 10ml of stock solution was further diluted to 100ml with distilled water to get a working standard solution of concentration 100µg/ml. Similarly standard stock solution of clonazepam was prepared by dissolving 10mg of drug in 10ml of methanol to get concentration of 1mg/ml. 1ml of stock solution was further diluted to 100ml with distilled water to get a working solution of concentration 10g/ml.

Preparation of sample stock solution

Twenty tablets were weighed accurately and powdered. Powder equivalent to 25mg of escitalopram oxalate(1.25mg of CLO) was weighed accurately and transferred to 25ml volumetric flask. The solution was filtered through Whatmaan filter paper no. 41 and first few ml were rejected. 10ml of this filtrate was further diluted to 100ml with distilled water. 2ml of this solution was further diluted to 10ml with distilled water to get required concentration.

RESULTS AND DISCUSSION

The method involves dividing the spectrum of mixture into the standardized spectra for each of the analyte and deriving the ratio to obtain spectra that is independent of analyte concentration used as a divisor.

Using appropriate dilutions of standard stock solution the two solutions were scanned separately. The ratio spectrums of different ESC standards at increasing concentrations are obtained by dividing each

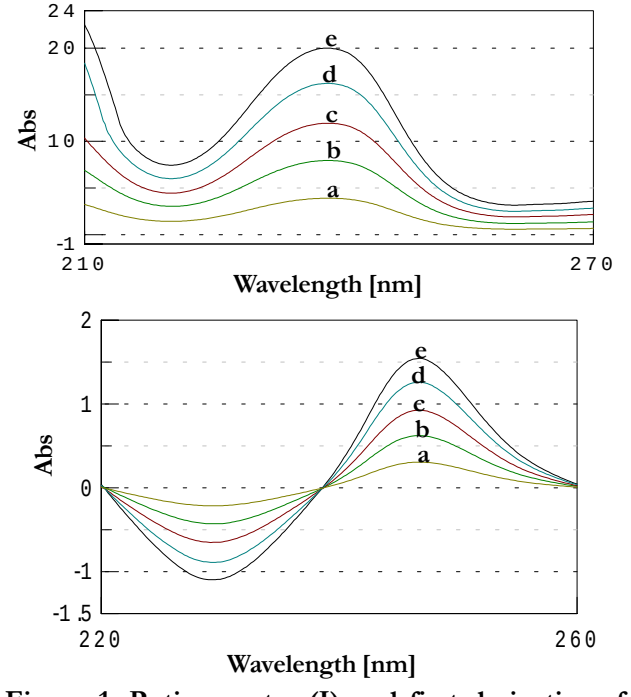

Figure 1: Ratio spectra (I) and first derivative of the ratio spectra (II) of (a) 10g/ml, (b) 20.0µg/ml, (c) 30.0µg/ml, (d) 40.0µg/ml, (e) 50µg/ml solution of ESC when 2µg/ml solution of CLO is used as divisor (Δλ=21nm)

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with the stored spectrum of the standard solution of CLO(2μg/ml, Scaling factor 1) by computer aid are shown in figure 1 (I) and the first derivative of these spectra traced with the interval of Δλ=21nm (the influence of Δλ for the first derivative of the ratio spectra was tested to obtain the optimum wavelength interval, Δλ=21nm was considered to be suitable) are illustrated in figure 1 (II). Wavelength 246.8nm was selected for the quantification of ESC in ESC+CLO mixture. The ratio and ratio derivative spectra of the solutions of CLO at different concentrations traced with the interval of Δλ=21nm by using the standard spectrum of ESC(10μg/ml, Scaling factor 0.1) as divisor by computer aid are demonstrated in figure 2 (I) and (II), respectively. Wavelength 214.4nm(minima) was selected for the quantification of CLO in ESC+ CLO mixture. Measured analytical signals at these wavelengths are proportional to the concentrations of the drugs. The coincident first derivative ratio spectra of pure and sample solution for estimation of ESC and CLO are shown in the figure 3.

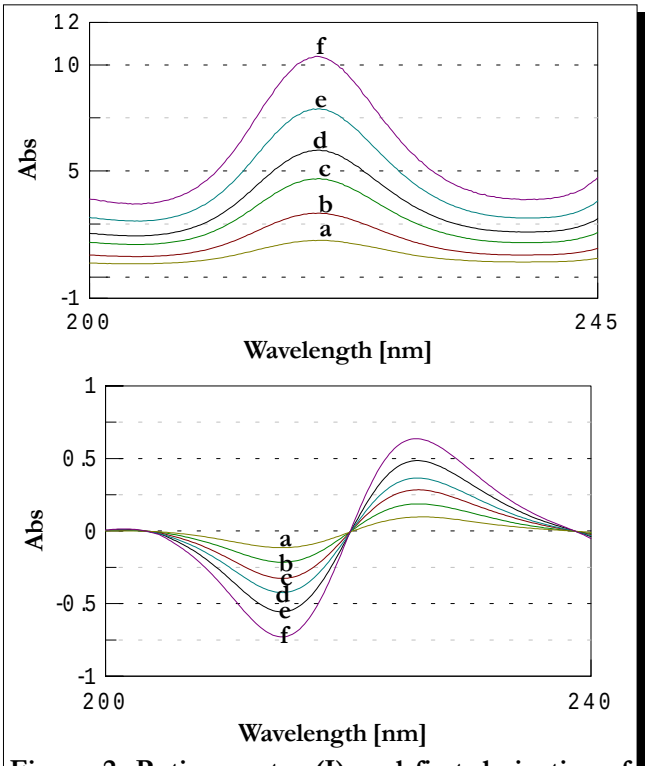

Figure 2: Ratio spectra (I) and first derivative of the ratio spectra (II) of (a) 0.5g/ml, (b) 1.0μg/ml, (c) 1.5μg/ml, (d) 2.0μg/ml, (e) 2.5μg/ml, (f) 3.0μg/ml solution of CLO when 10μg/ml solution of ESC is used as divisor (Δλ=21 nm)

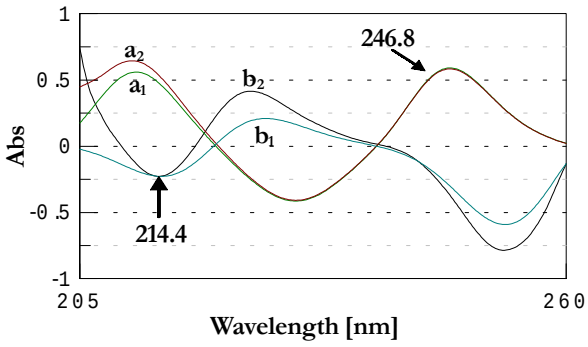

Figure 3: The coincident first derivative ratio spectra of (a_1) 20μg/ml of pure ESC and (a_2) sample solution (20μg/ml of ESC and 1μg/ml of CLO); 2μg/ml CLO as a divisor and (b_1) 1μg/ml of pure CLO and (a_2) sample solution (20μg/ml of ESC and 1μg/ml of CLO); 10μg/ml of ESC as a divisor

Under experimental conditions described, calibration curve, assay of tablets and recovery studies were performed. A critical evaluation of proposed method was performed by statistical analysis of data where slopes, intercept, correlation coefficient are shown in TABLE 1. Results of analysis of commercial formulation are reported in TABLE 2. Low standard deviation values of determination indicate reproducibility of the method. Recovery studies were

TABLE 1: Optical characteristics of the proposed method

Parameters	Escitalopram oxalate	Clonazepam
λmax	246.8	214.4(minima)
Beer's law limit (μg/ml)	10-50	0.5-3.0
Molar absorptivity*	1.379×10^4	8.208×10^4
Regression equation (y = mx + c)		
Slope (m)	0.0332	-0.2638
Intercept (c)	0.0019	0.0046
Correlation coefficient	0.9997	0.9987

*obtained from the first derivative ratio spectra

TABLE 2: Results of analysis of commercial formulation

Drug	Label claim (mg/tablet)	% of Label claim estimated*	Standard deviation	Standard error
ESC	10	99.10	0.2905	0.1186
CLO	0.5	100.72	0.5465	0.2231

*average of six determinations

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TABLE 3: Recovery studies of escitalopram oxalate and clonazepam

Level of % recovery	% Mean recovery*		Standard deviation		% R.S.D.		Standard error	
	ESC	CLO	ESC	CLO	ESC	CLO	ESC	CLO
80	99.81	99.10	0.3179	0.6166	0.31850	0.6222	0.1835	0.3559
100	98.54	98.75	0.3602	0.3114	0.3655	0.3153	0.208	0.1798
120	101.18	100.20	0.3709	0.6701	0.3666	0.6689	0.2141	0.3869

*avg. of three determinations, R.S.D. is relative standard deviation

carried out by the addition of standard drug solution to preanalyzed tablet sample solution at three different concentration levels within the range of linearity for both the drugs. Results of recovery studies are shown in TABLE 3.

ACKNOWLEDGMENTS

The authors thank to Torrent Pharmaceutical Ltd., Gujarat, India and Cipla Ltd., Pune, India for providing gift sample of escitalopram oxalate and clonazepam respectively. Authors would also like to thank to the Principal, Dr. K.G.Bothara, for providing infrastructure facilities and encouragement.

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