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Spectrophotometric Estimation of Citalopram and Nortriptyline in Pharmaceutical Dosage Form

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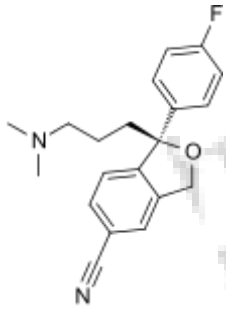
ABSTRACT

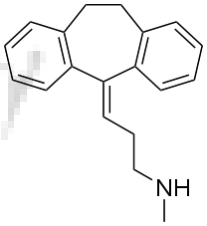
Medicinal plants in Cameroon, as is the case worldwide, has The precise and economical UV method has been developed for the estimation of citalopram and nortriptyline in pharmaceutical dosage form. Citalopram has the absorbance maxima at 227 nm, and nortriptyline has the absorbance maxima at 273 nm. Linearity for the detector response was observed in the concentration range of 1-70 µg mL and 1-80 µg mL for this method. The proposed methods were successfully applied for the simultaneous determination of citalopram and nortriptyline in commercial pharmaceutical preparation. The results of the analysis were validated statistically and by recovery studies it was found to be satisfactory.

INTRODUCTION

Citalopram hydrobromide belongs to a class of antidepressant agents known as selective serotonin-reuptake inhibitors. Citalopram and its N-demethylated metabolites exist as a racemic mixture. Nortriptyline hydrochloride, the *N*-demethylated active metabolite of amitriptyline, is a Dibenzocycloheptene-derivative tricyclic antidepressant. They contain a tricyclic ring system with an alkyl amine substituent on the central ring. In depressed individuals, nortriptyline exerts a positive effect on mood. Nortriptyline may be used to treat depression, chronic pain, irritable bowel syndromes and diabetic neuropathy. Literature survey reveals UV-Visible Spectroscopic determination of citalopram and nortriptyline in Pharmaceutical dosage forms is not reported earlier hence we have developed a UV method [1-5] for the estimation of Citalopram and nortriptyline in bulk and pharmaceutical formulation.



Citalopram



Nortriptyline

MATERIALS AND METHODS

Citalopram and nortriptyline analytically pure samples were gifted by Gen Pharmaceuticals Ltd., (Pune, India). All chemicals and reagents used were of HPLC grade for HPLC analysis and analytical grade for spectroscopic study is purchased from Merck Chemicals (Mumbai, India).

Apparatus:

A double-beam Shimadzu UV- Visible spectrophotometer, Shimadzu 1800, with spectral bandwidth of 2 nm, wavelength accuracy ± 0.5 nm and a pair of 10 mm matched quartz cells was used to measure the absorbance of the resulting solution.

Solvents:

Methanol was used as Solvent.

Stock solution:

The stock solutions (100 µg/ml) of nortriptyline and Citalopram were prepared by dissolving accurately 10 mg of drug in 25 ml methanol and then the volume was adjusted to 100 ml with distilled water separately.

Procedure:

For the selection of analytical wavelength, 1-70 ug/ml solution was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. From the spectra of drug (Fig. 1.1), λ_{max} of nortriptyline, 273.5 nm and for citalopram 227.5 nm (Fig. 1.2) respectively was selected for the analysis. The calibration curve was prepared in the concentration range of 1-70 ug/ml. By using the absorptivity value, the concentration of the sample solution can be determined.

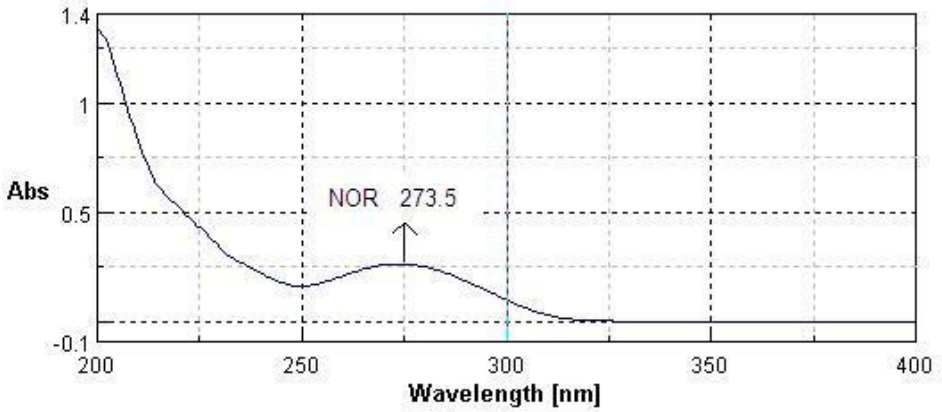


Fig. No. 1.1: UV spectrum of NOR (λ_{max} 273.5 nm)

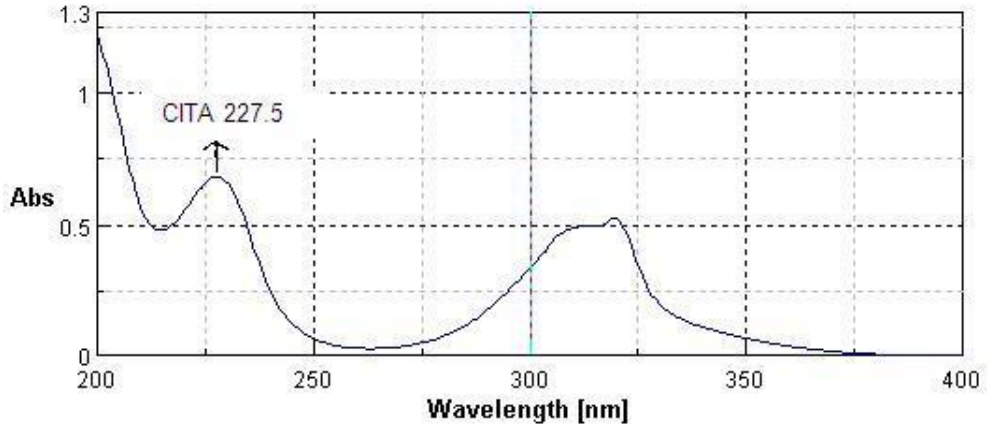


Fig. 1.2: UV spectrum of CITA (λ_{max} 227.5 nm)

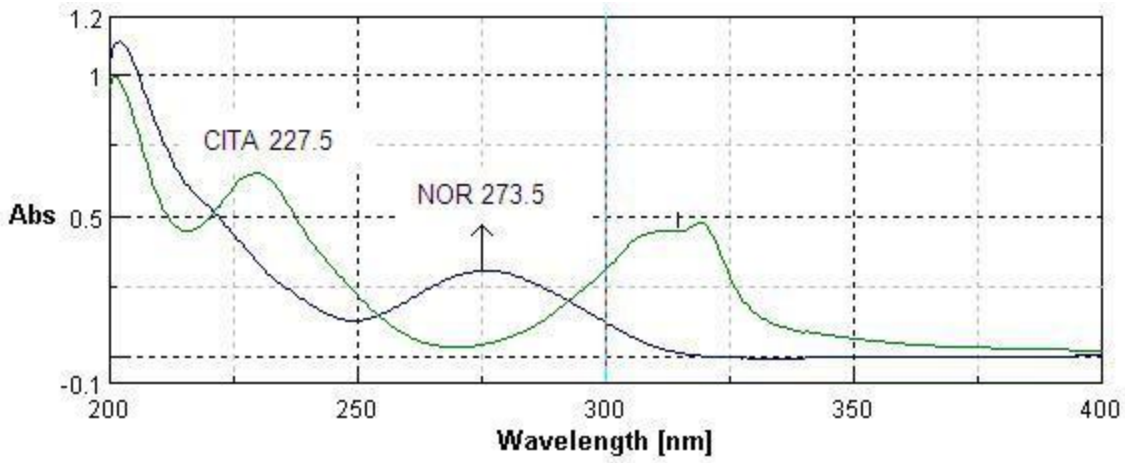


Fig. 1.3: UV spectrum of NOR and CITA Mixture

Validation[6-7]:

The proposed method was optimized and validated as per the International Conference on Harmonization (ICH) guidelines. The methods were validated with respect to linearity, accuracy, precision and selectivity.

Accuracy[8-12]:

Recovery studies were carried out by applying the method to drug contents present in tablet dosage form to which known amount of standard nortriptyline and standard citalopram was added at 80%, 100%, and 120% levels. The technique includes addition of standard drug solution to pre-analyzed sample solution. The recovery study was performed three times at each level. The results of the recovery studies along with its statistical validation are given in Table No. 1.4 and 20 respectively.

Linearity:

The linearity of measurement was evaluated by analyzing the different concentration of the standard solution of CITA & NOR. Beer-Lambert's concentration range was found to be 1-70 ug/ml for the above method.

Precision:

Precision of the method was demonstrated by intraday and interday variation studies. In intraday variation study, three different solutions of three different concentrations were analyzed in a day

i.e. from morning, afternoon and evening. In the interday variation studies, solution of three different concentration were analyzed three times for the three consecutive days and the absorbance result mean, standard deviation (S) and % RSD was calculated.

Table 1.1: Validation and system suitability studies[13]

Parameters	**CITA**	**NOR**
Linearity range (µg/ml)	1-70	1-80
Correlation coefficient	0.9998	0.9994
LOD (µg/ml)	3.22	0.0013
LOQ (µg/ml)	9.78	0.0041
Precision: Inter-day (% RSD) Intra-day (% RSD)	 0.33 0.17	 0.25 0.16

Table 1.2. Standard absorptivity values of NOR and CITA[14]

Drugs	**Absorptivity coefficient**	
	227.5 nm	273.5 nm
NOR	41.53	27.41
CITA	65.85	2.066

Table 1.3. Analysis data of Mixed Standards[15]

Concentrations of drugs taken (µg/ml)		**Concentrations of drugs found (µg/ml)**		*** % Drug found**	
NOR	**CITA**	**NOR**	**CITA**	**NOR**	**CITA**
10	10	9.99	9.90	99.95	99.01

Table 1.4. Repeatability Data (Statistical evaluation)[16-17]

Drugs	*** % Mean**	***S.D**	***% R.S.D.**
NOR	99.98	0.044	0.044
CITA	99.95	0.083	0.083

Table 1.5. Inter-Day and Intra-Day Precision[18]

Drugs	Inter-day			Intra-day		
	Mean	*S.D.	*% R.S.D	Mean	*S.D.	*% R.S.D
NOR	99.93	1.1454	1.1462	100.17	0.9457	0.9440
CITA	100.37	1.4012	1.3960	98.80	0.6646	0.6726

Table 1.6. Recovery Studies[19]

Level of Recovery (%)	Amount present (mg)		Amt of Std added (mg)		% Recovery	
	NOR	CITA	NOR	CITA	NOR	CITA
80	10	10	80	80	98.41	99.45
	10	10	80	80	97.07	98.14
	10	10	80	80	96.72	97.80
100	10	10	100	100	99.05	99.23
	10	10	100	100	99.94	99.53
	10	10	100	100	101.05	98.32
120	10	10	120	120	100.61	101.80
	10	10	120	120	100.26	99.45
	10	10	120	120	102.12	100.38

Table 1.7: Statistical Validation of Recovery Studies[20-21]

Level of % recovery	%Mean recovery*		Standard Deviation		% R.S.D	
	NOR	CITA	NOR	CITA	NOR	CITA
80	97.40	98.45	0.8940	0.8429	0.9178	0.8562
100	100.01	99.03	1.0002	0.6301	0.9999	0.6363
120	100.99	100.38	0.9904	1.2402	0.9807	1.2300.

Table 1.8: LOD and LOQ values[20-21]

Parameter	NOR	CITA
* L.O.D. (µg / ml)	0.1704	0.3415
* L.O.Q. (µg / ml)	0.5165	1.0350

RESULTS AND DISCUSSION

The precise and economical UV method has been developed for the estimation of citalopram and nortriptyline in pharmaceutical dosage form. Citalopram has the absorbance maxima at 227 nm, and nortriptyline has the absorbance maxima at 273 nm. Linearity for the detector response was observed in the concentration range of 1-70 µg mL and 1-80 µg mL for this method. The UV method was validated as per ICH guidelines. The standard deviation and % relative standard deviations calculated for the proposed methods are low, indicating high degree of precision of the methods. The results of the recovery studies showed the high degree of accuracy of the proposed methods. Hence, it can be concluded that the developed methods are accurate, precise and selective and it can be employed successfully for the estimation of NOR and CITA in bulk and pharmaceutical dosage form.

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