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Development and Validation of Area under Curve and First Derivative Spectrophotometric Methods for Ropinirole in Tablet Dosage Form

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Abstract

Two simple, precise and economical UV spectrophotometric methods have been developed for the estimation of Ropinirole in pharmaceutical dosage form. Method A applied was area under curve (AUC) in which area under curve was integrated in the wavelength range of 234.36 - 241 nm. Method B involves getting first order derivative spectrum of drug solution and measurement of derivative amplitude at 262.58 nm. Calibration curves were plotted for both methods by using instrumental response at selected wavelength and concentrations of analyte in the solution. Linearity for the detector response was observed in the concentration range of 4-20 µg/ml for both the methods. Two tablet formulations were analyzed and % assay determined was 99.79% – 100.68%. Acuuracy and precision studies were carried out and results were satisfactory. The proposed methods were validated as per ICH analytical method development guidelines. The results of the analysis were validated statistically. Limit of detection and limit of quantitation were determined for both methods.

Keywords: Ropinirole, UV spectrophotometry, derivative spectroscopy, area under curve, tablet formulation.

INTRODUCTION

Chemically, Ropinirole (ROPI) is 4-[2-(dipropylamino)ethyl]-1,3-dihydro-2*H*-indol-2-one. Ropinirole acts as a non-ergoline D_2, D_3, and D_4 dopamine receptor agonist with highest affinity for D_3. It has moderate in vitro affinity for the opioid receptors. Ropinirole is weakly active at the 5-HT_2, and α_2 receptors and is said to have virtually no affinity for the 5-HT_1, benzodiazepine, GABA, muscarinic, α_1, and β-adrenoreceptors.

Ropinirole is metabolized primarily by cytochrome P450 CYP1A2, and at doses higher than clinical, is also metabolized by CYP3A4. At doses greater than 24 mg, CYP2D6 may be inhibited, although this has only been tested in vitro. [1]

Literature survey revealed that Ropinirole is estimated by HPLC and simple absorbance UV Spectrophotometric method. To our knowledge AUC and First order Derivative UV Spectrophotometric methods are not available for estimation of ROPI in single component formulation. Hence, an attempt has been made to develop new UV methods for its estimation in pharmaceutical formulations with good accuracy, simplicity, precision and economy.

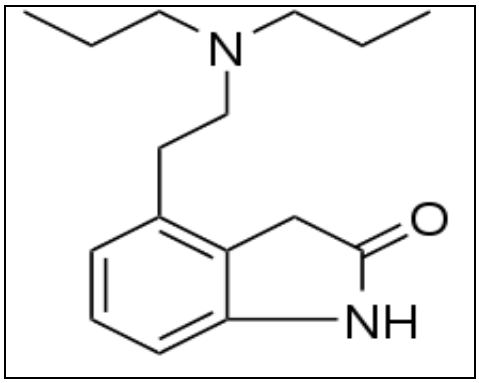

Fig I:- Chemical Structure of Ropinirole

MATERIAL AND METHOD

Spectroscopic grade HCL purchased from LOBA Chemie Pvt. Ltd., Mumbai and double distilled water was used through the study. Tablets used for analysis was Ropark of two different batches manufactured by Sun Pharmaceutical Industries, Bandra, India containing Ropinirole hydrochloride 0.5 mg per tablet. Pure drug sample of ROPI, % purity 98.5% was kindly supplied as a gift sample by Ranbaxy Laboratories Ltd., Dewas and was used without further purification.

Instruments:
An UV-Visible double beam spectrophotometer (Varian Cary 100) with 10 mm matched quartz cells were used for Spectrophotometric measurement. All weighing were done on electronic balance (Model Shimadzu AUW-220D).

Preparation of Standard Solution and Calibration Curve
Stock solution of drug having concentration 100 µg/ml was prepared by dissolving ROPI in 0.01N Hydrochloric acid. Aliquots of stock solutions were further diluted in distilled water to get the solutions in the range of 4-20 µg/ml of Ropinirole and were scanned in the wavelength range of 200–300 nm. For method A area was integrated at wavelength range of 234.36 - 241 nm and for method B derivative amplitude of first derivative was measured at 268.52 nm. Instrumental response and conc. obtained and was used for construction of calibration curve. The Beer's law was obeyed over the concentration range 4-20 µg/ml by ROPI. [2]

Preparation of Sample Solution and Formulation Analysis
Twenty tablets were weighed accurately and a quantity of tablet powder equivalent to 10 mg of ROPI was transferred to 100 ml volumetric flask, 80 ml of 0.01 N Hydrochloric acid was added to the same flask, sonicated for 5 min and filtered then diluted to 80 ml with 0.01 N Hydrochloric acid and filtered through What man filter paper No. 41, then filter paper was washed with 0.01 N

HCl. Resulting solution was further diluted with distilled water to obtain solution having concentration 12 µg/ml and proposed methods were followed to determine concentration of analyte and % assay was calculated.

Method A: Area under Curve Method

For the selection of analytical wavelength, 12µg/ml solution of ROPI was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 200 nm to 300 nm. From the spectra of drug, area under the curve in the range of 234.36-241.0 nm was selected for the analysis. The calibration curve was prepared in the concentration range of 4-20 µg/ml at their respective AUC range. By using the calibration curve, the concentration of the sample solution can be determined. [3, 4]

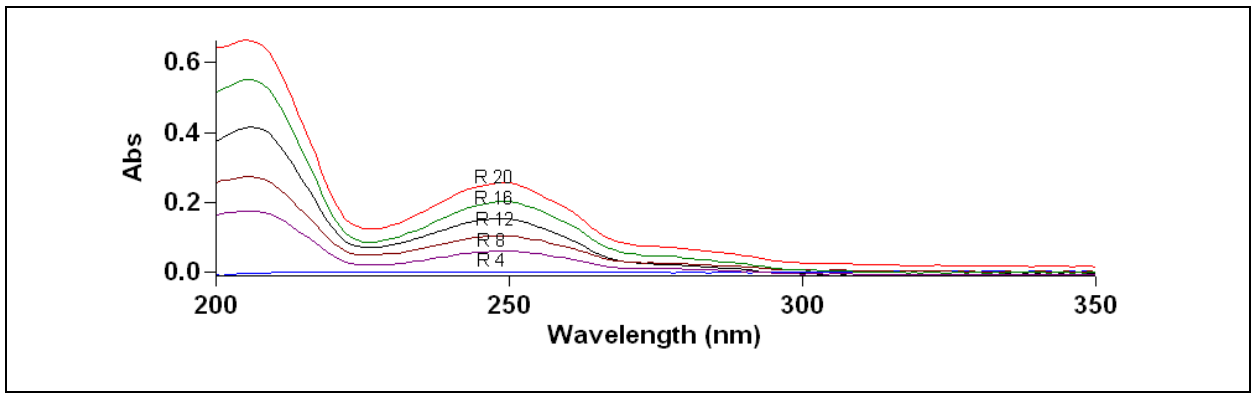

Fig.-II: Zero order spectra of Ropinirole in 0.01N HCl (Conc. Range 4-20 µg/ml)

Method B: First Derivative Spectroscopy

In this method, 12 µg/ml solution of ROPI was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 200 nm to 300 nm. The absorption spectra thus obtained were derivatized from first to fourth order. First order derivative spectra were selected for analysis of the drug. First order derivative spectra of drug (Fig. III), showed a sharp peak at 262.58 nm, which was selected for its quantitation. The calibration curve for ROPI was plotted in the concentration range of 4-20 µg/ml at wavelength 234.0 nm. The concentration of the drug present in the solution was determined against the calibration curve in quantitation mode. [5]

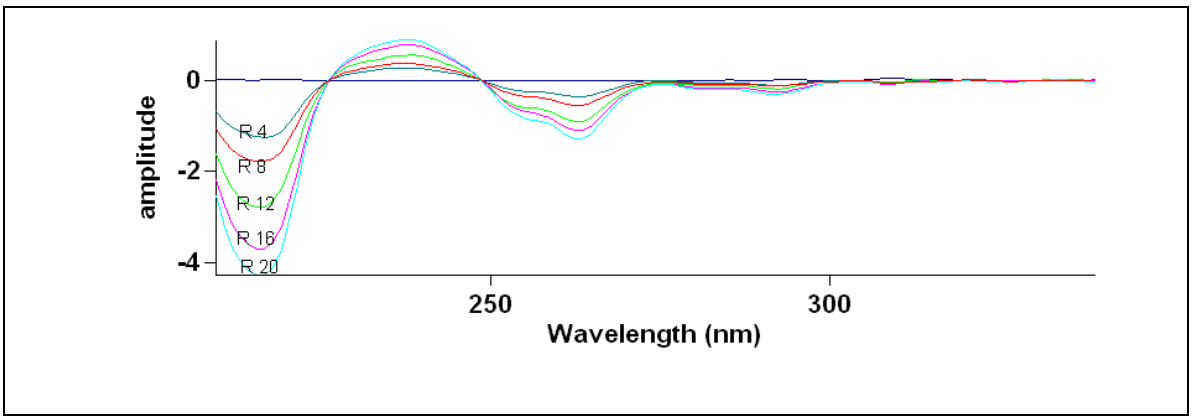

Fig.-III: First order derivative Spectra of Ropinirole in 0.01 N HCl (Conc. Range 4-20 µg/ml)

Recovery Studies

The accuracy of the proposed method was checked by recovery studies, by addition of standard drug solution to preanalysed sample solution at three different concentration levels (50 %, 100 % and 150 %) within the range of linearity for both the drugs. The basic concentration level of sample solution selected for spiking of the drugs standard solution was 12 µg/ml of ROPI.

RESULTS AND DISCUSSION

Under experimental conditions described, calibration curve, assay of tablets, recovery studies and precision studies were performed. Using appropriate dilutions of standard stock solution, the solutions were scanned. The zero order overlain spectra are shown in Fig II. A critical evaluation of proposed method was performed by statistical analysis of data where slope, intercept, correlation coefficient is shown in Table I. As per the ICH guidelines, the method validation parameters checked were linearity, accuracy and precision. Beer's law obeyed in the concentration range 4-20µg/ml and with correlation coefficient of 0.999 and 0.994 for METHOD A and METHOD B respectively. The proposed method was also evaluated by the assay of commercially available tablets containing Ropinirole. The % assay was found to be 99.84 % for ROPI in Table I. Results of recovery studies are shown in Table II. For ROPI, the recovery study results ranged from 99.79% to 100.68% with % RSD values ranging from 0.394 % to 0.777 %. The accuracy and reproducibility is evident from the data as results are close to 100 % and standard deviation is low.

Table I. Optical Characteristics and Validation Data of Ropinirole

PARAMETERS		METHOD A	METHOD B
λ nm		262.58	234.36-241
Beer's law limit (µg /ml)		4-20	4-20
Regression Equation (y = mx + c)	Slope	0.0246	0.066
	Intercept	0.0002	0.02306
Regression coefficient(r^2)		0.994	0.997
Precision	**Repeatability**	0.58	1.66
	Inter-day (%RSD)	0.67	1.23
	Intra-day (%RSD)	0.85	0.97
	Analyst	0.71	0.68
Formulation analysis	From I	99.72	99.96
	From II	99.14	99.31

Table II: Recovery Study of Ropinirole For both methods

Level of % Recovery	Amount Spiked(µg /ml)	% Mean recovery, R.S.D.(n= 6)	
		Method A	Method B
50	6.06	100.33,0.33	99.60,0.48
100	12.12	98.76,0.53	99.75,0.63
150	18.18	99.55,0.66	99.55,0.71

CONCLUSION

The validated Spectrophotometric method employed here proved to be simple, fast, accurate, and precise and sensitive thus can be used for routine analysis of Ropinirole Hydrochloride in combined tablet dosage form without prior separation. The methods can be further extended to determine analyte in biological samples.

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