

Novel Method for the Quantification of Ropinirole Hydrochloride in Pure API and its Marketed Formulations Using 3-Methyl-2-benzothiazolinone Hydrazone Hydrochloride and *p*-Dimethylamino-cinnamaldehyde as Chromogenic Reagents by Spectrophotometry

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Abstract: Two novel simple and sensitive spectrophotometric methods in visible region were developed for the estimation of ropinirole hydrochloride (RPH) in pure and its pharmaceutical dosage forms. Method-A based on the oxidative coupling product with 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) in presence of ferric chloride to give intense blue colored azodye complex having λ_{\max} at 680 nm and method-B based on the reaction of *p*-dimethylamino-cinnamaldehyde (PDAC) under acidic media to give yellow colored Schiff base having λ_{\max} at 420 nm. Both these methods obey Beer's law in the concentration range of 5-50 $\mu\text{g/mL}$. All variables in these methods are optimized and the reaction mechanisms are presented. No interference was observed from tablet additives and the applicability of these methods was examined by analyzing tablets containing RPH. The proposed methods are precise, accurate and reproducible. It can be extended to the analysis of ropinirole hydrochloride in marketed formulations.

Keywords: Chromogen, MBTH, PDAC, Ropinirole hydrochloride, Spectrophotometry

Introduction

Ropinirole hydrochloride (RPH) (Figure 1) is chemically named as 4-[2-(dipropylamino)ethyl]-1,3-dihydro-2*H*-indol-2-one, it is an anti parkinsonian agent (Dopamine agonist) and also used to treat restless legs syndrome. It is a white to yellow solid with a melting range of 243 to 250 °C and a solubility of 133 mg/mL in water. From extensive literature survey reveals that the drug can be estimated by various spectrophotometric methods like visible¹, ultra-violet^{2,3},

spectrofluorimetry², chromatographic methods like RP-HPLC^{4,6}, LC-UV⁵, HPTLC³, UPLC⁷ and also combination of chromatographic and spectrophotometric method, LC-MS/MS⁸ were developed in biological fluids and pharmaceutical formulations. The drug isolated from impurities by capillary liquid chromatography, capillary electrophoresis^{9,10}, chemometric evaluation method¹¹.

Spectrophotometry is the most common and convenient analytical tool due to its inherent simplicity and low costing. It is used in most of the quality control and clinical laboratories. A very few visible spectrophotometric methods were developed with different chromogens. The main aim of this study was to develop two simple, sensitive spectrophotometric methods for quantification of RPH by using MBTH and PDAC in pure and its marketed formulations. The proposed methods for the quantification of RPH were successfully validated as per ICH guidelines^{12,13}.

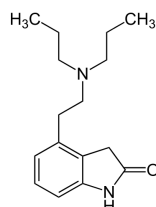


Figure 1. Structure of ropinirole hydrochloride

Experimental

A Systronics UV-Visible spectrophotometer model AU-2701 with 10 mm matched quartz cells were used for all spectral measurements and for pH measurements using ELICO digital pH meter model-LI 127. The API, ropinirole hydrochloride procured from micro labs, Bangalore. All the chemicals used were of analytical grade and so used without further purification. Distilled water was used for diluting the standard, reagents and samples. All the prepared reagents were stored in the amber colored bottles and protected from direct sunlight. ROPARK, REQUIP and ROPITOR tablets were purchased from local market commercially.

Preparation of standard stock solution

The standard stock solution (1 mg/mL) of RPH was prepared by dissolving 100 mg of RPH initially in 10 mL of 0.1 M sodium hydroxide, followed by dilution to 100 mL with distilled water. The working standard solution of RPH (100 µg/mL) was obtained by appropriately diluting the standard stock solution with the same solvent. The prepared stock solution was stored at 4 °C protected from light. From this stock solution, a series of standards were freshly prepared during the analysis day.

Preparation of sample solution

20 Tablets were weighed accurately to get the average tablet weight and pulverized into fine form. The tablet powder equivalent to 10 mg of RPH was weighed, dispersed in 25 mL of methanol, sonicated for 10 min and filtered through Whatman filter paper no. 41. The filtrate was evaporated to dryness and the residue was dissolved as under standard solution preparation.

Recommended methods

Method A

Aliquots of the working standard RPH solution (0.5 mL, 5.0 mL and 100 µg/mL) were placed in a series of 10 mL separating funnels. A volume of 0.5 mL of 1 M hydrochloric acid,

2 mL of 1% ferric chloride reagent and 0.5 mL of 0.5% MBTH reagent were added. The contents were shaken well and diluted up to 10 mL with distilled water and the intensity of color was measured at 680 nm (Figure 2) against blank reagent. The calibration curve was plotted by taking concentration ($\mu\text{g/mL}$) on x-axis and absorbance on y-axis. The amount of drug was computed from its calibration graph.

Method B

Aliquots of the working standard RPH (0.5 mL, 5.0 mL and 100 $\mu\text{g/mL}$) were placed in a series of 10 mL separating funnels. A volume of 1 mL of freshly prepared 1% PDAC, 1 mL of 0.5 M HCl and then final volume was made up to 10 mL with distilled water and the intensity of color was measured at 420 nm (Figure 3) against blank reagent. The calibration curve was plotted by taking concentration ($\mu\text{g/mL}$) on x-axis and absorbance on y-axis. The amount of drug was computed from its calibration graph.

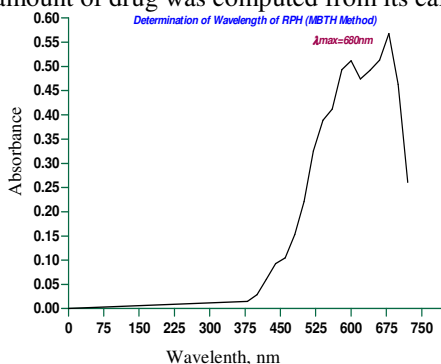


Figure 2. Determination of λ_{max} of RPH (MBTH method)

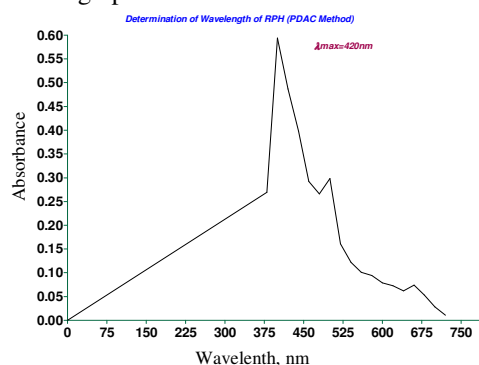


Figure 3. Determination of λ_{max} of RPH (PDAC method)

Results and Discussion

The optical characteristics such as Beer's law limit, molar absorptivity, Sandell's sensitivity, slope and intercept are summarized in Table 1.

Table 1. Optical parameters of proposed methods

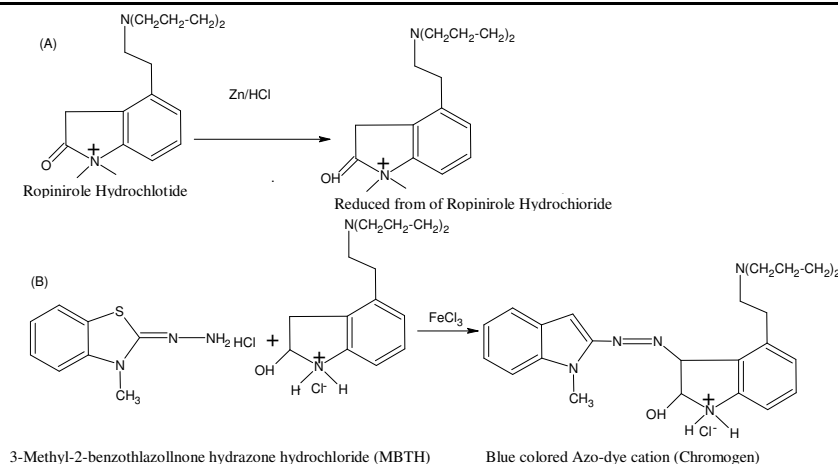
Parameter	Method A	Method B
λ_{max} , nm	680	420
Beer's law limit, $\mu\text{g/mL}$	5-50	5-50
Sandell's sensitivity, $\mu\text{g/cm}^2/0.001$ abs. unit	0.02380	0.02739
Molar absorptivity (litre/mole/cm)	22570	19160
Correlation coefficient (r^2)	0.9999	0.9999
Regression equation ($Y = b + ac$)		
Intercept (b)	-0.000518	-0.001268
Slope (a)	0.00423	0.00366
% RSD	0.72528	0.98640
% Range of error		
Confidence limit with 0.05 level	± 0.6064	± 0.8248
Confidence limit with 0.01 level	± 0.8972	± 1.2200

ROPARK, REQUIP and ROPITOR tablets containing RPH were successfully analyzed and the values obtained by the recommended methods for formulations were compared

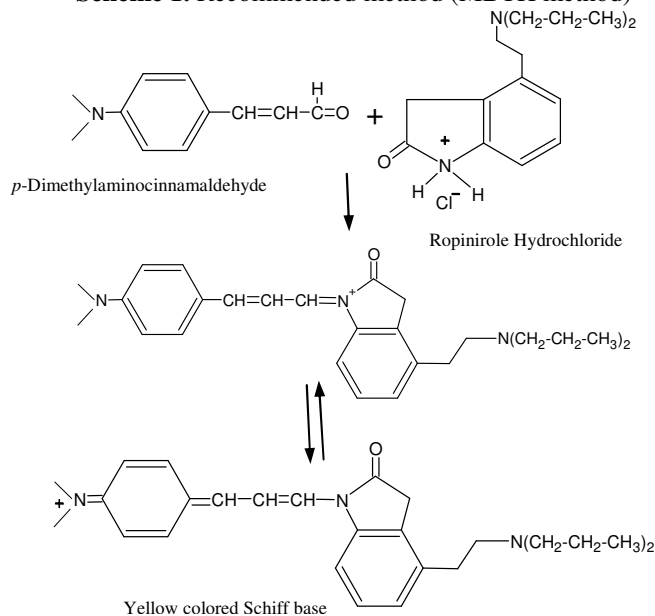
statistically by the *t*- and *f*-test with reported UV reference method and found not to differ significantly. The assay results for tablets containing RPH are shown in Table 2.

Table 2. Analysis of ropinirole hydrochloride in marketed pharmaceutical dosage forms

Sample	Formulations	Label claim, mg/tab	Estimated amount, mg/tab		% Recovery	
			Method A	Method B	Method A	Method B
Ropinirole Hydrochloride Tablets	ROPARK	5	5.02	4.99	100.4	99.8
	REQUIP	5	5.03	4.97	100.6	99.4
	ROPITOR	5	5.01	5.02	100.2	100.4



Scheme 1. Recommended method (MBTH method)



Scheme 2. Recommended method (PDAC method)

Chemistry of colored species

In the proposed method-A, the RPH can be reduced under media of zinc and conc. HCl to get reduced form RPH. Under the specified experimental conditions MBTH on oxidation with ferric chloride loses two electrons and one proton forming an electrophilic intermediate, which is the active couple rapidly with reduced form of RPH at 3rd position (most active) forming a blue colored azodye cation (Scheme 1). In the method-B, the reaction of PDAC with aromatic amine of the RPH in the presence of strong acid to form yellow colored Schiff base (Scheme 2).

Conclusion

The recommended methods are applicable for the assay of drug in wider range under Beer's law limits and possess reasonable precision, accuracy and simple, sensitive. The statistical parameters and recovery study data clearly indicate the reproducibility of this method. Analysis of the authentic sample containing RPH showed no interference from the common excipients. Hence, these methods could be considered for the determination of RPH in the quality control laboratories.

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