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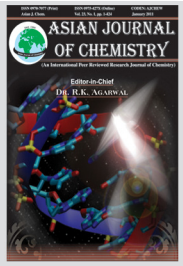

NOTE

Extractive Spectrophotometric Method for Determination of Acipimox in Capsule

B. THANGABALAN[1,*] and P. VIJAYARAJ KUMAR[2]

[1]Department of Pharmacy, Southern Institute of Medical Sciences, Mangaldas Nagar, Guntur-522 001, India
[2]Bharat Institute of Pharmacy, Mangalpally Village, Ibrahimpatnam-501 506, India

*Corresponding author: Fax: +91 86 32327766; E-mail: bthangabalan@gmail.com

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A sensitive and rapid extractive spectrophotometeric method has been developed for the assay of acipimox in pharmaceutical formulation. The method is based on the formation of a chloroform soluble ion-pair complex between acipimox and methylene blue in a basic medium. The complex shows absorption maximum at 662 nm and the system obeys Beer's law in the concentration range of 2-10 µg/mL. The results obtained by the proposed method were validated statistically and by recovery studies.

Key Words: Acipimox, Capsules, Ion-pair complex.

Acipimox, chemically 5-methylpyrazine carboxylic acid 4-oxide, is a nicotinic acid analogue, which is an antilipolytic drug used in the management of different forms of hyperlipidemia[1,2]. Literature survey reveals that the drug can be estimated by HPLC[3], UV estimation in formulation[4] and no visible spectrophotometric method has been reported. The present study describes a simple, sensitive, accurate and precise extractive spectrophotometric method for estimation of acipimox in bulk and capsule formulation.

A Elico UV-SL146 UV-VIS spectrophotometer (Bombay) with 1 cm quartz cells was used for all absorbance measurements. Spectra were automatically obtained by Elico UV-SL146 system software. A calibrated digital pH meter was used for pH measurements.

All the chemicals were of analytical reagent grade of E. Merck unless otherwise specified. Doubly distilled water was used to prepare all solutions. Freshly prepared solutions were always employed. Ammonia-ammonium chloride buffer (pH 9.8) and 0.2 (% w/v) methylene blue solution were prepared.

Standard solution of the drug: A stock standard solution of 1000 µg/mL was prepared by dissolving acipimox in doubly distilled water. Working standard solution was then prepared by suitable dilution of the stock standard solution with doubly distilled water.

Procedure for the assay of bulk sample: From the 100 µg/mL solution, 0.2, 0.4, 0.6, 0.8 and 1 mL was transferred to a series of separating funnels and 2 mL of pH 9.8 buffer was added to each and then 0.4 mL of 0.2 % w/v methylene blue solution was added and shaken well and 10 mL of chloroform was added to each and shaken well and kept for few minutes. The chloroform layer was separated and treated with anhydrous sodium sulphate and the absorbance of the solution at 662 nm was measured against reagent blank. Final concentrations of analyzed solutions were 2 to 10 µg/mL. The standard calibration plot was prepared to calculate the amount of the analyte drug in unknown samples.

Procedure for formulation: Twenty capsules containing acipimox were weighed accurately. The powder equivalent to 100 mg acipimox was dissolved in 20 mL of distilled water, sonicated for 15 min and filtered through Whatman No. 41 filter paper. The residues were washed thoroughly with distilled water and further diluted with distilled water to 100 µg/mL concentration. Convenient aliquots from this solution were taken for the determination of acipimox by methylene blue in the range 2 to 10 µg/mL.

Spectral characteristics: Absorption spectra of the drug-methylene blue ion-pair complex with its λ_{max} at 662 nm shown in the Fig. 1. The colourless blank is practically negligible absorbance.

Optimization of variables: Optimum conditions necessary for rapid and quantitative formation of coloured ion-pair complexes with maximum stability and sensitivity were established by a number of preliminary experiments. ammonia-ammonium chloride buffer buffer was found to be suitable for this method. Chloroform was preferred to other solvents (carbon tetrachloride, dichloromethane and ether) for this method for its selective and quantitative extraction. Optimum conditions

TABLE-2
ASSAY RESULTS AND PRECISION STUDIES

Formulation	Labeled amount (mg/ capsule)	Amount found (mg/ capsule)	Label claim[a] ± S.D (%)	Precision[b]		
				Repeatability	Inter-day	Intra-day
Acipimox capsules	250	249.86	99.94 ± 0.4776	0.2861	0.3548	0.2779

a. Average of six determinations; b. % RSD of six determinations.

TABLE-3
RECOVERY STUDY

Formulation	Label claim (mg/ capsule)	Formulation (µg/mL)	Amount of drug added (µg/mL)	Amount of drug recovered (µg/mL)	Percentage recovery ± SD[a]
Acipimox capsules	250	4	3.2	3.18	99.43 ± 0.2352
		4	4.0	4.01	100.33 ± 1.0567
		4	4.8	4.80	100.07 ± 0.3136

a. Mean of six determinations.

were fixed by varying one parameter at a time while keeping other parameters constant and observing its effect on the absorbance at 662 nm for methylene blue. A volume of 0.4 mL of 0.2 % w/v methylene blue solution was found to be optimal for complete complexation.

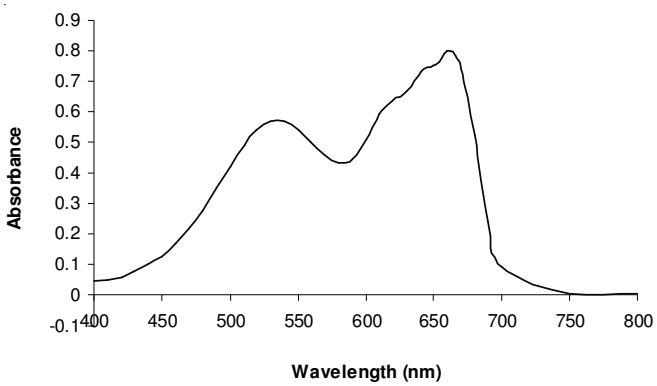

Fig. 1. Absorption spectra of Acipimox-methylene blue complex extracted into 10 mL chloroform

Linearity and range: Beer's law range, molar absorptivity, Sandell's sensitivity, regression equation and correlation coefficient determined for this method are given in Table-1. A linear relationship was obtained in the concentration range of 2 to 10 µg/mL. Regression analysis of the Beer's law plots reveals a good correlation. The graphs show negligible intercept and are described by the regression equation, Y = a + bc, where, Y is the absorbance of 1 cm layer, b is the slope, a is the intercept and c is the concentration of the measured solution in µg/mL. The high molar absorptivities of the resulting complexes indicate the high sensitivity of this method.

Validation of the method: Samples of pure acipimox were prepared and tested at four levels of drug using the proposed procedure. The complete set of validation assay was performed for drug by the proposed methods. The results obtained for formulation are given in Table-2. The precision and accuracy of this method were tested by analyzing six replicates of the drug. The standard deviation, relative standard deviation, recovery were determined from the calibration curve (Table-2). The accuracy of the method is indicated by the excellent recovery (99.43-100.33 %).

TABLE-1
OPTICAL CHARACTERISTICS OF PROPOSED METHOD

Parameters	Values
λ_{max} (nm)	662
Beer's law limit (µg/mL)	2-10
Sandell's sensitivity (µg/cm^2/0.001 absorbance unit)	1.001×10^{-2}
Molar absorptivity (l/moL/cm)	1.5289×10^4
LOD (µg/mL)	0.0240
LOQ (µg/mL)	0.0721
Regression equation (Y = a + bc)	
Slope (b)	0.0996
Intercept(a)	0.0015
Correlation coefficient (r^2)	0.9999

Capsule analysis: The proposed method was applied to the determination of acipimox in commercial capsules. The applicability of the proposed method for the assay of acipimox in capsule formulation was examined by analyzing various formulations and the results obtained were tabulated in Table-2. Satisfactory results were obtained for drug and were in a good agreement with the label claims (Table-2). The average per cent recoveries obtained were indicating good accuracy of this method. The results of analysis of the commercial capsules and the recovery study of drug (Table-3) suggested that there is no interference from any excipients.

Conclusion

The newly developed method is sensitive enough to enable quantization of the drug at low concentrations. This method is simple rapid and has great sensitivity and accuracy. Proposed method makes use of simple reagent, which an ordinary analytical laboratory can afford. This method is suitable for routine quality control analysis of acipimox in pharmaceutical formulations.

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