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Simple spectrophotometric methods for the determination of ziprasidone hydrochloride in pharmaceuticals using folin-ciocalteau and potassium ferricyanide

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ABSTRACT

Two simple, sensitive and reproducible spectrophotometric methods (Method A and B) were developed for the determination of Ziprasidone in bulk and in tablet dosage forms. Method A is based on reduction of Folin-Ciocalteau reagent by the drug Ziprasidone Hydrochloride in the presence of sodium bicarbonate to form a blue colored chromogen having maximum absorption at 436 nm. Method B is based on the oxidation of the drug by potassium ferricyanide reagent to form a blue colored chromogen having maximum absorption at 733 nm. Beer's law is obeyed in the range of 0.5 – 3 and 1-5 µg/ml for Method A & B respectively. Results of analysis were validated statistically and by recovery studies. These Methods are successfully employed for the determination of Ziprasidone in various pharmaceutical tablet dosage forms.

Key words: Ziprasidone Hydrochloride (ZPD), Spectrophotometric determination, FC reagent, Potassium ferricyanide.

INTRODUCTION

Ziprasidone hydrochloride is a new anti-psychotic agent, with a chemical name 5-[2-[4-(1,2-Benzisothiazol-3yl)-1-piperazinyl]ethyl]-6-chloro-1,3-dihydro-2H-indol-2-one. Clinically it is effective in the treatment of schizophrenia and management of acute mania in patients with bipolar disorder[1].The metabolic fate of ziprasidone has been studied in both rats and humans and found to be extensively metabolized in both species [2-4].The principle routes of biotransformation in humans involve N-dealkylation,oxidation to form the sulfone and sulfoxide metabolites, reductive cleavage of the benzisothiazole moiety and the hydration of C-N double bond followed by sulfur oxidation or N-dealkylation . Subsequent invitro studies indicated that ziprasidone is predominantly metabolized in human liver microsomes by the CYP isoform 3_{A4}[5] The drug has been determined by spectrophotometry [6]HPLC, [7-15] HPLC-MS/MS [16-19]and Capillary zone electrophoresis[20] techniques. In the present study the author had developed two simple and sensitive spectrophotometric methods for the determination of ZPD in pharmaceutical formulations

EXPERIMENTAL

Materials and Method

ELICO UV-Visible Double beam spectrophotometer model SL164

All the chemicals used were of analytical grade. All the solutions were freshly prepared using double distilled water.

Folin Ciocalteau reagent

This reagent is commercially available. The original stock reagent was diluted to 1:2 ratio with water(Method A).

Sodium bicarbonate

Prepared by dissolving 20 g of sodium bicarbonate in 100mL of distilled water (Method A).

Potassium Ferricyanide

Prepared by dissolving 100 mg of Potassium Ferricyanide in 100 ml of distilled water (Method B).

Preparation of standard and sample solutions

Accurately weighed 100 mg of Ziprasidone was dissolved in 30 ml of methanol and made up to 100 mL with methanol to give a concentration of 1mg/mL. The final concentration was brought to 100 µg/mL for Method A and B.

General procedure for the determination of Ziprasidone Hydrochloride

Method A

Aliquots of the working standard solution of Ziprasidone (100 µg/ml) were transferred into a series of 10 ml calibrated flasks. To all the flasks 1.5 ml of 1N Folin-Ciocalteau reagent and 0.5 ml of sodium bicarbonate were added. The solution was made up with distilled water, mixed well and kept aside for 5 min. The absorbance of the yellow colored solution was measured at 436 nm against the corresponding reagent blank.

Method B

Aliquots of (0.5ml) reagent were transferred into a 10 ml volumetric flasks. To all the flasks 0.5 ml of potassium ferricyanide and 1 ml of Ziprasidone were added. The solution was made up to the mark with distilled water, mixed thoroughly and after 5 min the absorbance was measured at 733 nm against a reagent blank, and the calibration graph was constructed.

Assay of pharmaceutical tablets

Five tablets were powdered and mixed thoroughly. An amount equivalent to 59.2 mg of the Ziprasidone was dissolved in water and filtered. The filtrate was made up to 5 ml and appropriate aliquots of the drug solution were treated as described above for the determination of Ziprasidone.

RESULTS AND DISCUSSION

Spectral characteristics

Method A involves reduction of the Folin Ciocalteau by the Ziprasidone in the presence of sodium bicarbonate, Method B involves the oxidation of Ziprasidone, followed by coupling with potassium ferric cyanide. The absorption spectra of reduced Folin Ciocalteau and Ziprasidone – potassium ferric cyanide complex have absorption maxima at 436 and 733 nm respectively.

Analytical data

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar absorptivity were calculated for both the methods and the results are summarized in Table 1. Regression and correlation coefficient were calculated for all the methods and are shown in Table 1.

Table 1: Optical characteristics of of the proposed methods

Parameters	Method A	Method B
λmax (nanometers)	436	733
Beer's law limits (µg/ml)	50-250	10-50
Molar extinction coefficient (1mo cm)	4.7×10^{6}	2.5×10^{5}
Sandell's sensitivity (µg/cm^2/0.001 absorbance Unit)	0.010	0.023
Regression equation *(Y)		
Slope (m)	0.0082	0.012
Intercept (c)	0.00124	0.003
Correlation coefficient (r)	0.9998	0.9997

*Y=mx+c, where x is the concentration in µg/ml and Y is absorbance unit.

Analysis of pharmaceutical preparations

Application of the proposed methods to the determination of Ziprasidone in its dosage forms was successfully made: The results are presented in Table 2. The excellent recoveries obtained indicated the absence of any interference from the excipients.

Table 2: Results of analysis of tablet formulations containing ZPD

Sample (capsule)	Labeled amount mg	Amount obtained mg*		**%Recovery by the proposed method	
		Method A	Method B	Method A	Method B
1	20	19.98	19.99	99.95	99.96
2	20	19.96	19.95	99.94	99.95

*Average of three determinations; ** After spiking the sample.

CONCLUSIONS

The proposed methods were found to be simple, economical, selective and sensitive. The statistical parameters and recovery study data clearly indicate the reproducibility and accuracy of the methods. Analysis of the authentic samples containing Ziprasidone showed no interference from the common excipients. Hence, these methods could be considered for the determination of Ziprasidone in the quality control laboratories.

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