VISIBLE SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF ZIPRASIDONE IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

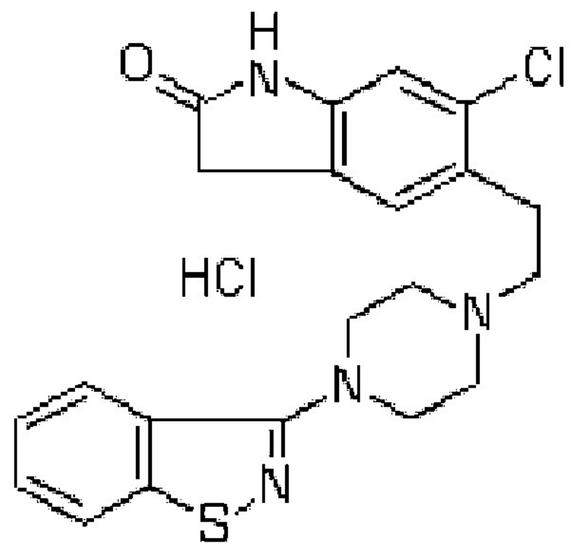
Ziprasidone is a typical antipsychotic agent. Two simple, sensitive and accurate spectrophotometric methods have been developed for the determination of Ziprasidone hydrochloride (ZPD) in pure state and in its pharmaceutical formulations. The developed Method A is based on the oxidation of the drug with Fe(III) and subsequent chelation of Fe(II) produced with 2,2[1] Bipyridyl to produce colored chromogen having maximum absorption at λ_{max} 510 nm and Linearity in the range of 40-200 µg/mL. Method B involves oxidation followed by complex formation of the drug with Bathophenanthroline and it exhibits maximum absorption at λ_{max} 630 nm; Linearity in the range of 4-20 µg/mL. The results obtained were statistically evaluated and were found to be accurate and reproducible.

KEY WORDS: Ziprasidone, Spectrophotometric, ZPD.

1.INTRODUCTION

Ziprasidone (5-[2-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]ethyl]-6-chloro-1, 3-dihydro-2H-indol-2-one), is the most commonly prescribed benzothiazoyl piperazine derivative for the treatment of positive, negative and depressive symptoms associated with schizophrenia. Ziprasidone exhibits a potent and highly selective antagonistic activity on the D_2 and $5HT_{2A}$ receptors (Fort,1999). It also has a high affinity for the $5HT_{1a,}$ $5HT_{1d,}$ $5HT_{2c}$ receptors subtypes that contribute to the overall therapeutic effect (Geis and Scand,1999).

Literature survey reveals that a few analytical methods published that describe the quantification of ziprasidone in plasma by spectrophotometric (Srinubabu,2006), liquid chromatography with uv detection at 15 nm proceeded with a solid-phase extraction with a structurally analog as the internal standard was reported (Sajeev,2000). A method for serum ziprasidone using LC-APCI-MS was reported with an emphasis on automated sample preparation (Rose and Woolf,2000). A rapid stability-indicating LC method for ziprasidone hydrochloride (Singh,2007). Determination of ziprasidone in human plasma by LC- MS method was reported (Manickam,2007). Automated determination of ziprasidone by HPLC with column switching and spectrophotometric detection (Sachse,2005) also reported. In the present investigation two simple, sensitive and accurate visible spectrophotometric methods have been developed for the estimation of ziprasidone hydrochloride in pharmaceutical dosage forms and in bulk drug. Method A shows λ_{max} at 510 nm and Linearity in the range of 40-200 µg/mL. Method B exhibits λ_{max} at 630 nm and Linearity in the range of 4-20 µg/mL.



Structure of Ziprasidone

2.EXPERIMENTAL

Spectral and absorbance measurements were made on systronics Double beam UV-Visible spectrophotometer model 2201 with 1cm matched quartz cells. Ziprasidone was procured from a local pharmaceutical industry. All other reagents used were of analytical grade.

Reagents Preparation

For Method A, 2, 2[1] Bipyridyl solution :-

156 mg of 2, 2[1] Bipyridyl was dissolved in 100 mL of 0.1N hydrochloric acid.

$FeCl_3$ stock solution :- (For method A and B)

162 mg of anhydrous ferric chloride was dissolved in 100 mL of distilled water. 33.3 mL of above stock solution was further diluted to 100 mL with distilled water.

O-Phosphoric acid :- (For method A and B)

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1.3 mL of orthophosphoric acid is diluted to 100 mL with distilled water.

For Method B, Bathophenanthroline :-

332 mg of bathophenanthroline was dissolved in 100 mL of 0.1 N Hcl.

Standard preparation

For Methods A and B, About 400 mg of the ZPD was accurately weighed and first dissolved in small amount of methanol in a 100 mL volumetric flask and then make up to volume with water to give a stock solution of 4 mg/mL. From this stock solution, 10 mL was taken and further diluted to 100 mL with water to get the working standard of concentration 400 µg/mL. This working standard concentration can be used for Methods A and B.

Preparation of sample solution

The content of twenty capsules was transferred to a mortar by carefully emptying each capsule. The capsule powder was mixed and thoroughly ground with mortar. For Methods A and B, The powder equivalent to 40 mg was taken in a 100 mL volumetric flask and first dissolved in methanol and it was extracted and further diluted with water to get 400 µg/mL.

Procedure for estimation

Methods A and B: Aliquots of standard ZPD solution (400 µg/mL) containing from 40 to 200 µg for Method A and 4 to20 µg for Method B were transferred into a series of 10 mL volumetric flasks and equalize to a certain level with water. 2.0 mL of 0.003 M ferric chloride and 1.0 mL of 2, 2^1 Bipyridyl solution for Method A and 2.0 mL of bathophenanthroline solution for Method B was added to each flask. The contents were gently boiled for 40 minutes for Method A and 15 min for Method B. The flasks were cooled to room temperature and 2.0 mL of orthophosphoric acid was added to all and final volume of all volumetric flasks was brought to 10 mL with water. The absorbance was measured at 510 nm for Method A and 630 nm for Method B against corresponding reagent blanks. The amount of ZPD sample was estimated from corresponding calibration graph.

3.RESULTS AND DISCUSSION

The developed Methods A and B are based on the reducing property of ziprasidone due to the presence of functional moieties vulnerable to oxidation selectively with oxidizing agents such as Fe (111) under controlled experimental conditions. When treated with known excess of oxidant, giving products of oxidation besides unreacted oxidant. The reduced form of Fe 111 (Fe11) has a tendency to give colored complex on treatment with 2, 2^1 Bipyridyl solution and bathophenanthroline.

The interference studies revealed that the common excipients usually present in the dosage forms do not interfere in the proposed method.

The optical characteristics and validation parameters were given in Table 1. To evaluate the accuracy and reproducibility of the method, known amounts of the pure drug was added to the previously analyzed pharmaceutical formulations and the mixture were reanalyzed by the proposed methods and the recoveries (average of six determinations) were given in Table 2.

Table -1 :Optical characteristics, regression data, Precision and accuracy of the proposed methods for Ziprasidone

Parameter	Method A	Method B
λ_{max} (nm)	510	630
Beer's law limits (µg/mL)	40-200	4-20
Molar absorptivity (Lit.mole^{-1}.cm^{-1})	1.094 x 10^3	1.86 x 10^4
Detection limits (µg/mL)	2.599	0.3353
Sandell's Sensitivity (µg/cm^2/0.001 abs. unit)	0.37559	0.022161
Optimum photometric range	39.5-199.5	3.5-19.5
Regression equation (Y=a+bc) : Slope (b)	0.025	0.02895
Standard deviation of slope (Sb)	3.74 x 10^{-5}	2.22 x 10^{-4}
Intercept (a)	0.025	0.0136
Standard deviation of intercept (Sa)	4.53 x 10^{-3}	2.94 x 10^{-4}
Standard error of estimation (Se)	6.27 x 10^{-3}	2.8 x 10^{-3}
Correlation coefficient (r)	0.9991	0.9995
% Relative standard deviation*	0.6938	0.4068
% Range of Error* (confidence limits) 0.05 level 0.01 level	 0.1177 0.1547	 0.1178 0.154
% Error in bulk samples**	0.31	-0.34

* Average of six determinations

** Average of three determinations

The values obtained for the determination of ziprasidone in several pharmaceutical formulations (capsules) and bulk drug by the proposed and reference methods were compared (Table 2). The results indicate that the proposed methods are simple, sensitive, accurate and reproducible and can be used for the

routine determination of ziprasidone in bulk and pharmaceutical dosage forms.

TABLE 2: Assay and recovery of Ziprasidone in dosage forms

Method	Pharmaceutical Formulation	Labelled Amount (mg)	Proposed Method			Found by reference method ± S.D	% recovery by Proposed methods** ± S.D
			Amount found* (mg) ± S.D	T (value)	F (value)		
A	Capsule-I	20	19.98 ± 0.012	0.719	2.531	18.99 ± 0.009	99.26 ± 0.55
	Capsule-II	40	39.08 ± 0.009	0.541	1.233	40.06 ± 0.018	100.04 ± 0.12
B	Capsule-I	20	18.99 ± 0.009	0.672	1.249	20.02 ± 0.011	100.29 ± 0.13
	Capsule-II	40	40.06 ± 0.018	0.811	1.204	40.07 ± 0.013	99.98 ± 0.37

* Average ± Standard deviation of six determinations, the t and F values refer to comparison of the proposed method with reference method.

Theoretical values at 95 % confidence limits t = 2.571 and F = 5.05

** Average of five determinations.

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