



## Spectrophotometric Determination of Ziprasidone in Pharmaceutical Formulations

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**Abstract:** A simple and reproducible spectrophotometric method has been developed for the determination of Ziprasidone hydrochloride monohydrate (ZPS) in bulk and in dosage forms. The method is based on the extraction of the drugs into organic layer of the dye TPooo in presence of 0.1 N hydrochloric acid and the absorbances were measured at 490 nm. Results indicate that the proposed method was simple, sensitive, accurate and reproducible.

**Key words:** Ziprasidone, spectrophotometric method, ZPS, TPooo

### Introduction

Ziprasidone is chemically known as 5-[2-[4-(1,2 benzisothiazol-3-yl)-1-piperazinyl]ethyl]-6-chloro-1, 3-dihydro-2h-indol-2-one. Ziprasidone hydrochloride is a novel antipsychotic with a unique pharmacological profile. Ziprasidone exhibits a potent and highly selective antagonistic activity on the D<sub>2</sub> and 5HT<sub>2A</sub> receptors<sup>1</sup>. It also has a high affinity for the 5HT<sub>1a</sub>, 5HT<sub>1d</sub> and 5HT<sub>2c</sub> receptors subtypes that could contribute to the overall therapeutic effect<sup>2</sup>.

The metabolic fate of Ziprasidone has been studied in both rats and humans and found to be extensively metabolized in both species<sup>3-5</sup>. 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 3A<sub>4</sub><sup>6</sup>.

Over a dosing range of 80 to 160 mg/day, linear increases have been observed in both the maximum concentration ( $C_{max}$ ) and area under the concentration-time curve (AUC) of Ziprasidone. The  $C_{max}$  observed 6 hrs after multiple oral dosing with food. Absorption of Ziprasidone is increased upto 2-fold in the presence of food. No difference in absorption has been found with low- or high- fat meals or with administration up to 2 hrs after a meal.]. Oral dose of Ziprasidone has a mean terminal elimination half-life of 6.6 hrs. There are several published procedures that describe the quantization of Ziprasidone in plasma. Liquid chromatography with UV detection at 215 nm proceeded with a solid-phase extraction with a structurally similar analog as the internal standard was reported <sup>7</sup>. A method for serum Ziprasidone using LC-APCI-MS was reported with an emphasis on automated sample preparation <sup>8</sup>. It is 99 % bound to plasma proteins, binding primarily to albumin and alpha-1-acid glycoprotein <sup>9</sup>. HPLC with column switching also reported <sup>10</sup>.

## Experimental

Spectral and absorbance measurements were made on a Elico UV-Visible Spectrophotometer (Model-164) with 10 mm-matched quartz cells. Solutions of 0.2 % TPooo and 0.1 N hydrochloric acid were prepared using distilled water. AR grade chloroform was used All the chemicals used were of AR grade.

### *Preparation of Standard solution*

100 mg of ZPS (Bulk or formulation) is accurately weighed and dissolved in 100 ml of methanol. The solution is suitably diluted with methanol to get 100 µg/ml.

### *Preparation of sample solution*

Two commercial brands of capsules were chosen. For this, 20 capsules were weighed and powdered. An accurately weighed portion of this powder equivalent to 50 mg of Ziprasidone was transferred to a 50 ml volumetric flasks containing 25 ml methanol. The contents were allowed to stand for ½ h with intermittent sonication to ensure complete solubility of the drug and then filtered through 0.45 µm membrane filter. The volume was made to the mark with methanol. The solution is suitably diluted with methanol to get 100 µg/ml.

### *Preparation of the reagents*

Tpooo (0.2%) was prepared by dissolving 200 mg of Tropaeolin ooo in 100 ml of distilled water. HCl solution was prepared by dissolving 8.6 ml of con. HCl to 1000 ml of distilled water and Standardized.

### *Method*

Into a series of 125 ml separating funnels containing aliquots of standard drug solution (0.5-2.5 ml) and 6.0 ml of HCl solution and 2 ml of dye solution were added. The total volume of aqueous phase in each separating funnel was adjusted to 15 ml with distilled water and 10 ml of chloroform was added. The contents were shaken for 2 min. the two phases were allowed to separate and the absorbances of the separated organic layer were measured at 490 nm against a reagent blank prepared under identical conditions.

## Results and Discussion

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation and percent range of error were calculated for the method and the results are summarized in Table 1 and Beers plot was shown in

Figure 1. The accuracy of the method was ascertained by comparing the results of the proposed methods with that of reported method (Table 2).

Table 1. Optical characteristics

Parameters	Method
Beer's law limits ( $\hat{c}$ )	2-10
Sandell's sensitivity ( $\mu\text{g}/\text{cm}^2/0.001$ absorbance unit)	0.010
Molar absorptivity (E max)	55277
%Relative standard deviation	0.3572
<b>% Range of error</b>	
0.05 Confidence limits	0.253
0.01 Confidence limit	0.452
Correlation coefficient	0.99940
<b>Regression equation (Y=b+ac)*</b>	
Slope (a)	0.09860
Intercept (b)	0.00580

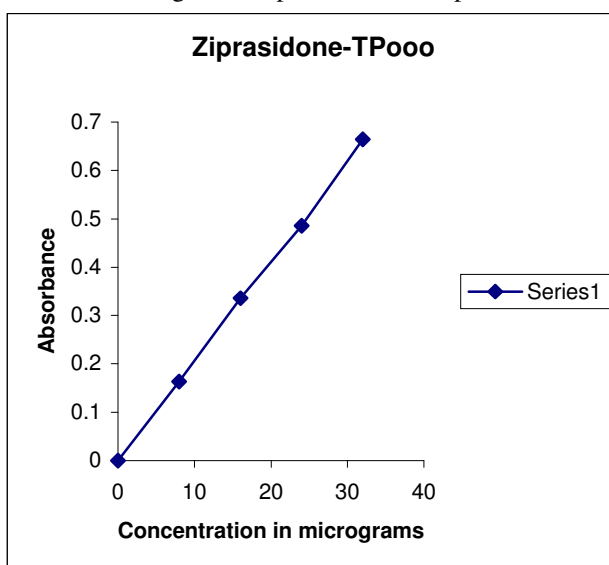
\*Where C is the concentration in  $\mu\text{g}/\text{ml}$  and Y is absorbance unit

Table 2. Assay of Ziprasidone in Pharmaceutical Formulations

Formulation	Labeled amount (mg)	Amount found by proposed method (mg)	Reference method (mg)	% Recovery by the proposed Method
1. Azona-20	20	19.99	19.98	99.95
2. Zipsydon	40	40.02	40.01	100.05

\*UV method developed by authors

Figure 1. Ziprasidone Beers plot



In order to justify the reliability and suitability of proposed methods, a known amount of pure drug was added to its various pre analyzed dosage forms and was analyzed by the proposed method. The result presented in Table 2 indicates that the proposed method can be successfully applied for the analysis of Ziprasidone in dosage forms. The additives and excipients usually present in pharmaceutical preparations did not interfere.

Thus the proposed method was simple, sensitive, accurate and reproducible and can be used for the routine analysis of Ziprasidone hydrochloride monohydrate in bulk and in pharmaceutical dosage forms.

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