

DEVELOPMENT AND VALIDATION OF A RAPID UV-SPECTROSCOPIC METHOD FOR THE ESTIMATION OF ZIPRASIDONE HYDROCHLORIDE MONOHYDRATE IN DRUG SUBSTANCE AND ITS DOSAGE FORMS

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ABSTRACT

A rapid and sensitive UV-Visible spectroscopic method was developed for the estimation of Ziprasidone HCl Monohydrate [ZHM] in pure and its capsule dosage forms. The method was validated as per International Conference on Harmonization [ICH] guidelines. The Ziprasidone Hydrochloride was monitored at 260nm with UV detection and there is interference of diluent at 260nm for Ziprasidone. The method was linear ($r^2 = 0.999$) at concentration ranging from 10 to 30 $\mu\text{g/ml}$, precise (intra-day relative standard deviation [RSD] and inter-day RSD values < 1.0%), accurate (mean recovery = 100.4%), specific and robust. The results showed that the proposed method is suitable for the precise, accurate and rapid determination of ZHM in bulk, its capsule dosage forms.

Keywords: Ziprasidone, UV-Visible spectroscopy, Validation, Dosage form.

INTRODUCTION

Ziprasidone^{5, 7} Hydrochloride Monohydrate [ZHM] is an atypical antipsychotic drug that is chemically unrelated to phenothiazine or butyrophenone antipsychotic agents^{5, 7}. It is a benz-isothiazoyl-piperazine derivative and it is used in the treatment of schizophrenia, mania and mixed states associated with bipolar disorder. Ziprasidone HCl has a potent selective antagonist activity for the serotonin Type 2 (5HT₂), dopamine Type 2 (D₂), 1 and 2 adrenergic, and H₁ histaminergic receptors¹. ZHM is chemically known as 5-[2-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]ethyl]-6-chloro-1,3-dihydroindol-2-one hydrochloride [Figure 1].

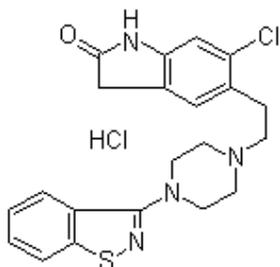


Fig. 1: Chemical Structure of ZHM

A few analytical methods published that describe the quantification of Ziprasidone in plasma by liquid chromatography, fluorescence detection, and UV detection. In the present investigation the authors propose a simple, sensitive and reproducible method for the determination of Ziprasidone hydrochloride monohydrate.

The target of this study is to develop a new, simple and fast analytical method by UV-Visible spectroscopy to quantify ZHM in bulk and its capsule dosage forms. This validation study is carried out as per ICH guidelines.

MATERIALS AND METHODS

Instrumentation

Perkin Elmer UV-Visible Spectrometer (Model-Lambda-35) was used for carrying out the current study.

Standards and chemicals

Commercial capsule formulations Zipsydon (Sun Pharma) were used for present study containing 20mg, 40mg and 80mg of ZHM,

respectively. HPLC grade Acetonitrile and water A.R. grade was purchased from Fisher scientific, Mumbai, India. All other chemicals used were of HPLC grade or A.R. grade.

Preparation of standard drug solutions

About 21.6mg of Ziprasidone HCl monohydrate was weighed accurately and transferred into a 100mL volumetric flask and dissolved in water and acetonitrile in the ratio of 50:50 v/v (used as diluent). The solution was sonicated for 15min and then the volume made up with a further quantity of diluent to give 20 $\mu\text{g/mL}$. This solution was scanned against blank solution and extracted the spectrum Based on the spectrum a λ_{max} of 260nm was selected for analysis.

Preparation of sample solutions

For the preparation of sample solutions, twenty capsules were weighed, powder was collected and mixed. A quantity equivalent to 20 mg of Ziprasidone Hydrochloride was transferred into 100mL flask, to this 25mL of methanol, was added and sonicated for 10 min for dispersion of drug from its excipients. Then about 50mL of diluent was added and sonicated for 30minute to get extraction of the drug and finally diluted to 100mL volume to get 20 $\mu\text{g/mL}$ solution. The solutions were filtered through 0.45 μ membrane filter before using for spectroscopic analysis. From the data amount of Ziprasidone Hydrochloride was calculated as monohydrate.

Method validation

The objective of method validation is to demonstrate that the method is suitable for its intended purpose as it is stated in ICH guidelines Q2A and Q2B. Recommend validation characteristics depend on the type of analytical procedure. Method validation characteristics were tested in accordance with ICH guidelines. Method specificity was verified by comparing the Spectrum of sample of pharmaceutical preparation, standard solution and blank. Method precision, Recovery in the range of 50% to 150% of label claim of the drug using the blend, Linearity was tested in the range 10–30 $\mu\text{g/ml}$. Intra and inter-day instrumental system Precision as well as repeatability and intermediate method precision were obtained using six replicates per day. Limits of detection and quantification were provided for Ziprasidone Hydrochloride. Calculation was made by means of RSQ (Residual Square of regression).

RESULTS AND DISCUSSION

UV method development and optimization

The UV method was optimized by changing various parameters, such as Diluent composition, various Concentration levels for getting good results within beers law limit.

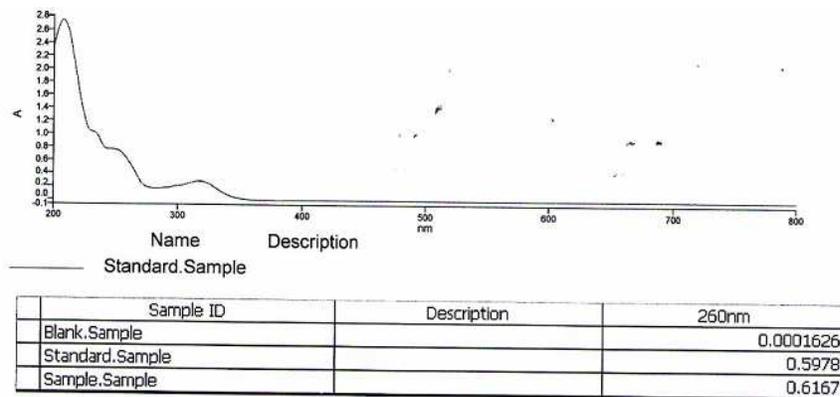


Fig. 2: A typical UV spectrum showing the spectral profile of Ziprasidone Hydrochloride

Method validation

The analytical method was validated as per ICH guidelines with respect to parameters such as precision, accuracy, specificity, Linearity, range and robustness.

Table 1: System suitability parameters for Ziprasidone Hydrochloride by proposed method

% RSD	Result observed in %	Proposed Limit in %
Precision (Inter Day)	0.02	Not more than 1.0
Precision (Intra Day)	0.03	

Specificity

The UV spectrum recorded for the blank showed no interference at the working wavelength of Ziprasidone Hydrochloride. The absorbance for Ziprasidone Hydrochloride is about 0.6. As there is no blank interference is not observed at the working wavelength of 260nm for Ziprasidone Hydrochloride, the UV spectroscopic method presented in this study is specific for Ziprasidone Hydrochloride.

Precision

In the study of the instrumental system precision where, a RSD of 0.02% was obtained for the absorbance obtained corresponding to the first day, being 0.03% and 0.04% for the second day, respectively. The method precision study for six sample preparations in marked samples showed a RSD of 1.2% and the 95% confidence interval of 1.3.

For the intermediate precision, a study carried out by the same analyst working on different day. The results calculated as inter-day RSD corresponded to 0.8%. The same study was carried out for different analysts (n = 6 number of samples per analyst) obtaining a

System suitability

For system suitability, five replicates of standard solution readings were taken and studied the parameters %RSD. The represented data was shown in table-1.

RSD of 1.1%. Both results together with the individual results are showing that the proposed analytical technique has a good intermediate precision.

Accuracy

The accuracy of the method was determined on three concentration levels by recovery experiments. The recovery studies were carried out in triplicate preparations on composite blend collected from 20 capsules of Zipsidone and analyzed as per the proposed method. The percentage recoveries with found in the range of 99.2 to 101.6 with an overall %RSD of 0.8. From the data obtained which given in table-2 the method was found to be accurate.

Table 2: Recovery studies for Ziprasidone Hydrochloride by proposed method

% Level	Recovery Range	% RSD at each level	Over all %RSD
50	99.2-100	0.4	0.8
100	99.7-100.9	0.6	
150	101.0-101.6	0.3	

Linearity

The standard curve was obtained in the concentration range of 10-30µg/ml. The linearity of this method was evaluated by linear regression analysis. Slope, intercept and correlation coefficient [r²] of standard curve were calculated and given in figure-3 to demonstrate the linearity of the method.

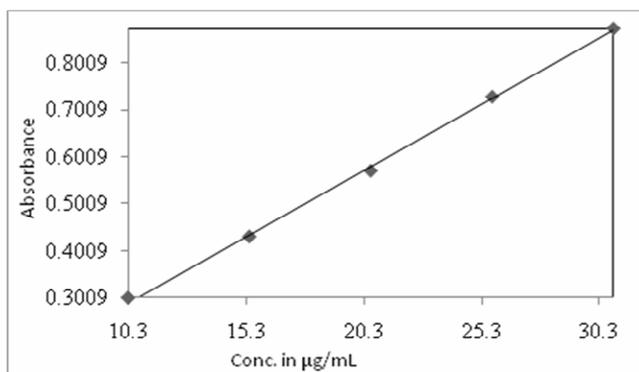


Fig. 3: Calibration curve for Ziprasidone Hydrochloride

Assay of the Marketed Samples

The method is sensitive and specific for the quantitative determination of Ziprasidone Hydrochloride and also validated for different parameters, hence has been applied for the estimation of drug in capsule dosage forms. Capsules from one manufacturer of

three strengths were evaluated for the amount of Ziprasidone Hydrochloride present in the formulations. Each sample was analyzed in duplicate preparations after extracting the drug as mentioned above under section 5.5. The results for assay of capsules are given in table-3.

Table 3: Assay results for capsules

Ziprasidone Strength	Avg. Assay for duplicate Sample in mg	Avg. Assay for duplicate Sample in %	% RSD
20mg	20.10	100.53	1.0
40mg	40.14	100.37	0.7
80mg	80.39	100.50	0.3

CONCLUSION

We have developed a fast, simple and reliable analytical method for determination of Ziprasidone Hydrochloride in pharmaceutical preparation using UV-Visible spectroscopy. As there is no interference of blank at the working wavelength, it is very fast, with good reproducibility and good response. Validation of this method was accomplished, getting results meeting all requirements.

The method is simple, reproducible, with a good accuracy and precision. It allows the analysis of Ziprasidone Hydrochloride in bulk, its capsules with a short period of time.

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