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# DEVELOPMENT AND METHOD VALIDATION USING HPLC FOR ASSAY OF ZIPRASIDONE CAPSULE

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## ABSTRACT

**Objective:** To develop and validate a novel High-Performance Liquid Chromatography (HPLC) method for the determination and stability analysis of Ziprasidone, an antipsychotic medication used in treating schizophrenia and bipolar disorder.

**Methods:** An HPLC system with a C18 column was utilized, employing a mobile phase of acetonitrile and phosphate buffer (pH 3.0) in a 60:40 v/v ratio. The flow rate was 1.0 mL/min, and detection was at 315 nm. Method validation followed ICH guidelines, assessing linearity, accuracy, precision, specificity, limit of detection (LOD), and limit of quantification (LOQ). Stability studies subjected Ziprasidone to hydrolysis, oxidation, photolysis, and thermal degradation.

**Results:** The HPLC method exhibited excellent linearity over 1-100 µg/mL, with a correlation coefficient ($R^2$) of 0.999. High precision was observed, with intra-day and inter-day relative standard deviations (RSD) below 2%. Accuracy showed recovery rates between 98.5% and 101.2%. The LOD and LOQ were 0.1 µg/mL and 0.3 µg/mL, respectively. Specificity tests indicated no significant interference from excipients and degradation products. Stability studies revealed that Ziprasidone is susceptible to acidic, basic, and oxidative conditions but stable under photolytic and thermal conditions.

**Conclusion:** The developed HPLC method is simple, precise, accurate, and robust for Ziprasidone determination and stability analysis. It is suitable for routine quality control and stability testing of Ziprasidone in pharmaceutical formulations. The stability data ensure the drug's efficacy and safety throughout its shelf life.

**Keywords**:- Ziprasidone, HPLC, Stability study, Method validation, Pharmaceutical analysis

**INTRODUCTION:** Ziprasidone HCL is chemically named as 5- [2- [4- (1, 2 benzisothiazol- 3- yl) - 1- Piperazinyl] ethyl]- 6- chloro-1, 3-dihydro- 2h- indol- 2- one. It is a novel anti psychotic exhibits a potent highly selective antagonistic activity on the D2, D3, 5HT1 and $5HT_2$ receptors. Literature survey gives analytical methods of Ziprasidone HCL by HPLC, LC-MS and other pharmacokinetic studies. The present work gives simple, rapid analytical method for estimation of Ziprasidone HCL capsule.

**Experimental:**

**Chemicals and solvents:** Potassium dihydrogen phosphate (AR grade), water (HPLC grade), potassium hydroxide (AR grade), buffer solution, methanol (HPLC grade) (Qualigens), acetonitrile (HPLC grade) were used for preparing the mobile phase. Pure samples of Ziprasidone HCL (Zydus Cadila) and commercial samples of capsules containing Ziprasidone HCL namely Geobon-80 (Pfizer), were employed in the study.

**Chromatographic conditions:** A gradient HPLC system (Waters) with Alliance2690 with millennium database software, detector-PDA waters. RP $C_{18}$ column (150×4.6 mm), particle size 5µ) was used. Freshly prepared buffer solution, acetonitrile and methanol (45:40:15v/v/v) mixture was used as the mobile phase. Both methanol and phosphate buffer were filtered through 0.45 µ membrane filter and sonicated before use. The flow rate of the mobile phase was maintained at 1.5ml/min. The detection was carried out at 230 nm.

**Estimation of Ziprasidone HCl:** About 110mg of Ziprasidone HCl was weighed accurately and transferred into a 200mL volumetric flask and dissolved in 100mL methanol. The solution was sonicated for 5 min and then the volume made up with 200mL of diluent.10ml of standard stock solution was diluted to 50ml with diluent and mixed well. Filtered through 0.45µ membrane filters and filtered. The flow rate of mobile phase was fixed at 1.5ml/min and detection was carried out at 230nm and the corresponding chromatograms are shown in **Fig. 1**.

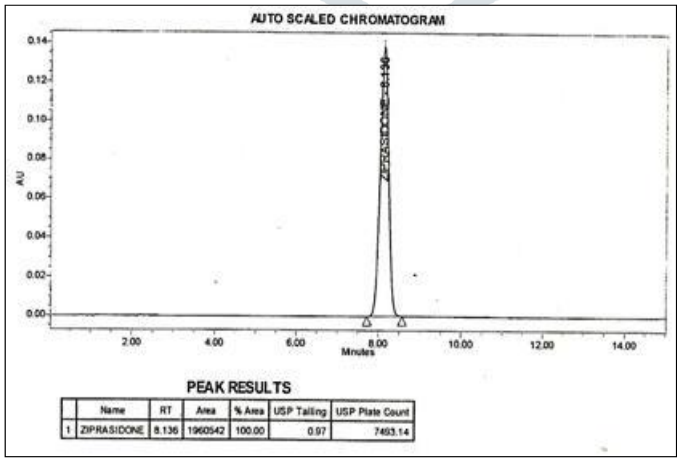


**FIG. 1: CHROMATOGRAMS OF SYSTEM SUITABILITY**

From these chromatograms, the retention times were noted and the areas under the peaks of the drug were

noted. The data regarding quantitative estimation is depicted and corresponding chromatogram were noted. The data regarding recovery studies is presented and corresponding chromatogram is depicted were noted. The specificity of methodology was confirmed by observing no shift wavelength due to placebo.

**Estimation of the Drug in Capsule Dosage Forms:** Commercial brands of capsules namely Geodon were chosen for testing the suitability of the proposed method to estimate Ziprasidone in capsule formulations. For this, 20 capsules were weighed and powdered. Capsule powder equivalent to 100 mg of Ziprasidone was transferred to a 200 mL volumetric flask. Dissolved in 100ml of diluent by sonicating it for 10min to ensure complete solubility of the drug and made upto the volume with diluents and mixed well. Further dilute 10ml to 50ml with diluent, then filtered through 0.45µ membrane filter. 10µL of the solution was then injected into the column. The mean peak area of the drug of five such determinations was calculated and the drug content in the capsules was quantified using the regression equation obtained for the pure sample.

**RESULTS AND DISCUSSION:** The present study was aimed at developing a sensitive, precise and accurate HPLC method for the analysis of Ziprasidone in pharmaceutical dosage forms. For this, mixture of buffer, acetonitrile and methanol (45:40:15v/ v/v) proportion was found to be the most suitable mobile phase as the chromatographic peaks obtained with this system were better defined and estimation of Ziprasidone Hydrochloride resolved and all almost free from tailing (**figure 2**). Under the above-mentioned conditions, Retention time obtained for Ziprasidone was 8 min.

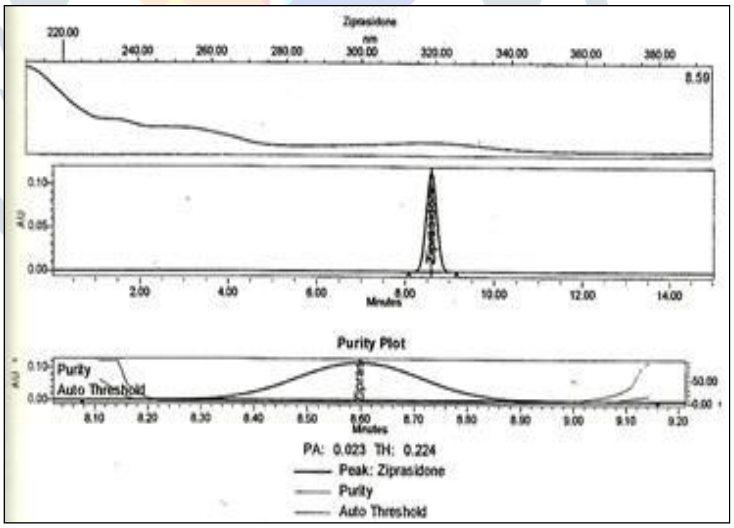


**FIG. 2: A MODEL CHROMATOGRAM OF ZIPRASIDONE HYDROCHLORIDE**

The peak areas of the drug were reproducible as indicated by low coefficient of variation (1.02%). A good linear relationship (r = 0.999) was observed between the concentrations of Ziprasidone and respective peak areas. The regression curve was constructed by linear regression fitting and its mathematical expression was. The drug content in the capsules was quantified using the proposed analytical method. The mean amount of Ziprasidone obtained in capsule dosage forms is shown in figure. This reveals that the method is quite

precise. The absence of additional peaks in the chromatogram indicates non- interference of the common excipients used in the capsules. It can be concluded that the proposed HPLC method is sensitive and reproducible for the analysis of Ziprasidone HCl in pharmaceutical dosage forms in a short analysis time. The method was duly validated by evaluation of the required parameters.

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