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Research Article

HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC ESTIMATION OF ZIPRASIDONE IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

A simple, sensitive and rapid reverse phase high performance liquid chromatographic method was developed for the estimation of Ziprasidone HCl (ZPR) in pure and in pharmaceutical dosage forms. Phenomex C_{18} column (250x4.6mm, 5µ) was used with a mobile phase containing a mixture of 0.02M $KH2PO_4$ (pH-3), methanol and aetonitrile in the ratio of 40:30:30. The flow rate was 1.5ml/min and effluents were monitored at 219nm and eluted at 3.37min. Calibration curve was plotted with a range from 10-50 µg/ml. The assay was validated for the parameters like accuracy, precision, robustness and system suitability parameters. The proposed method can be useful in the routine analysis for the determination of ziprasidone in pharmaceutical dosage forms.

Key words: Ziprasidone, Reverse phase HPLC, Pharmaceutical dosage forms

INTRODUCTION

Ziprasidone (ZPR) is chemically known as 5-[2-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl] ethyl]-6-chloro-1, 3-dihydro-2H-indol-2-one (Fig 1). The drug is not official in any pharmacopoeia. Ziprasidone hydrochloride is a novel antipsychotic with a unique pharmacological profile. Ziprasidone exhibits a potent and highly selective antagonistic activity on the D_2 and $5HT_{2A}$ receptors[1]. It also has a high affinity for the $5HT_{1a}$, $5HT_{1d}$ and $5HT_{2c}$ receptor subtypes that could contribute to the overall therapeutic effect[2].

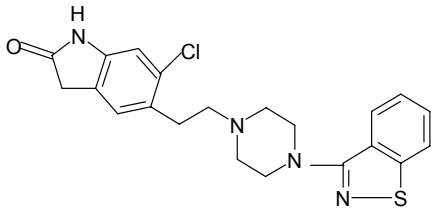

Fig. 1: Chemical structure of ziprasidone

Literature survey reveals that reports are available for the estimation of ZPR in biological fluids and pharmaceutical formulations. Most of them are based on visible spectrophotometric methods[3, 4], HPLC[5-8], LC-MS[9-12], HPLC-MS[13] and mass[14]. The objective of the present work was to develop a rapid and accurate HPLC method with UV detection in bulk drug and its dosage forms. The developed method was simple, precise, sensitive and very useful for the determination of ziprasidone in bulk and pharmaceutical dosage forms.

MATERIALS AND METHODS

Reagents

Ziprasidone (ZPR) obtained as gift sample from Dr. Reddy's laboratories, Hyderabad. Commercial capsule formulations Zipsydon (Sun Pharma) and Azona (Pfizer) containing 20mg of ziprasidone were procured from local market. HPLC grade methanol, acetonitrile, tri ethylamine and water were purchased from Merck, Mumbai, India. All other chemicals used were of HPLC grade.

Chromatographic equipment

The HPLC system consisted of a Shimadzu Class LC-10AT vp and LC-20AD pumps connected with SPD-10A vp UV-Visible detector. The data acquisition was performed by Spincotech 1.7 software.

Chromatographic conditions

The HPLC system consisted of Shimadzu Class LC-10AT vp and LC-20AD pumps connected with SPD-10A vp UV-Visible detector. The data acquisition was performed by Spincotech 1.7 software. Analysis was carried out at 219nm using a phenomenex C18 reverse phase column of 250x 4.6 mm i.d., 5 µm dimensions at ambient temperature. The mobile phase consisted of 0.02M KH_2PO_4 solution pH 3: methanol: Acetonitrile in the ratio of 40: 30: 30 that was set at a flow rate of 1.5ml/min. The column performance parameters for the method have been summarized in Table 1.

Table 1: Column performance parameters

Parameters	Result
Retention time (min)	3.37
Column length (cm)	25
Theoretical plates (n)	4387
Theoretical plates per meter (N)	17546
Ht equivalent to theoretical plates (HETP) (mm)	0.0569
Tailing factor	0.63

Preparation of stock and sample solutions

The standard stock solution of the ziprasidone was prepared with methanol to give the final concentration of 1000 µg/ml. The working standard solution of ZPR was prepared by taking suitable aliquots of drug solution from the standard solution and the volume was made up to 10 ml with mobile phase to get concentrations of 1-50 µg/ml. The solutions were filtered through 0.45µm membrane filter and then 20 µL of filtrate was injected three times into the column at flow rate of 1.5mL/min. Evaluation of drug was performed with UV detector at 219nm. Peak areas were recorded for all peaks. A plot of peak area versus the respective concentration gives the calibration curve. The regression of drug concentration over the peak area was computed. The regression equation was used to estimate the amount of ZPR in capsules.

For the analysis of pharmaceutical dosage forms, ten capsules were weighed, powder was collected and mixed. A quantity equivalent to 20 mg of ZPR was transferred into extraction flask, to this suitable amount of methanol was added and the mixture was subjected to vigorous shaking for 30 min for complete extraction of drug in an ultrasonic bath. The solution was filtered into 100ml volumetric flask and made up to the mark with mobile phase. From this, different aliquots were taken in separate 10ml volumetric flasks. The contents of the flask were made up to the volume with mobile phase and mixed well. Each of the solutions 20 µL was injected six times into the column. From the peak areas, the drug content in the capsule was quantified using the regression equation obtained from pure sample.

Method validation

The method was validated by International Conference on Harmonization (ICH) guidelines for linearity, range, precision, specificity and accuracy parameters.

RESULTS AND DISCUSSION

A reversed-phase column procedure was proposed as a suitable method for the determination of ziprasidone from dosage form. A typical chromatogram obtained by using the aforementioned mobile phase from 20 µL of the assay preparation is illustrated in Figure 2.

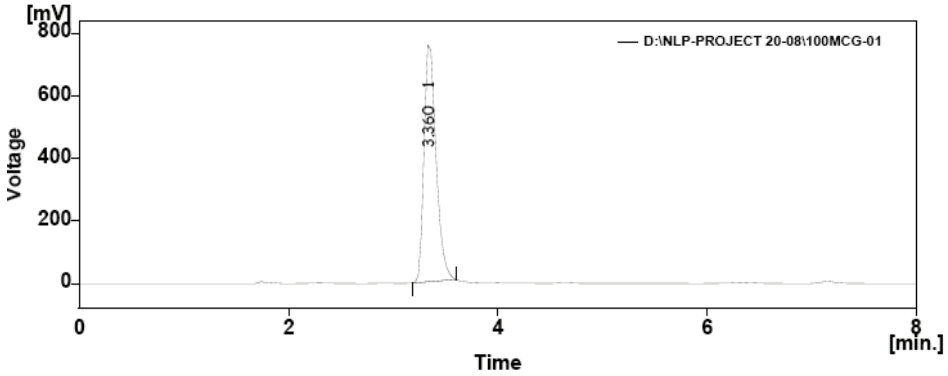

Fig. 2: A typical chromatogram showing the peak of ziprasidone

The retention time for ziprasidone was 3.3min. The linearity of the method was tested from 1-50 µg/ml. Linearity solutions were injected in triplicate and the calibration graphs were plotted as peak area of the analyte against the concentration of the drug in µg/ml. The peak areas from such different concentrations set up above were calculated and are shown in Table 2.

The calibration graph was found to be linear in the mentioned concentrations and the correlation coefficients for the regression line was 0.9998. The accuracy of the method was studied by recovery experiments. The recovery experiments were performed by adding known amounts of the drug to the placebo. The recovery was determined at three levels, viz. 50%, 100% and 150% of the selected concentration. Three samples were prepared for each recovery level. The recovery values ranged from 99.5-100.5% and the values are shown in Table 3.

The precision (repeatability and intermediate precision) of the method was determined from one lot of dosage form. Intra and Inter day studies were performed in triplicate of four concentrations. The results are shown in Table 4. The limit of detection (LOD) and limit of quantitation (LOQ) was 30ng/ml and 90ng/ml respectively.

Table 2: Calibration curve of the proposed method

Drug concentration (µg/ml)	Peak area
10	651
15	973
20	1321
25	1623
30	1891
35	2204
40	2527
45	2841
50	3189

Regression equation from 10-50 µg/mL is Y = 62.946X + 22.461

Table 3: Recovery of ziprasidone (n=3)

Amount of drug added (µg/ml)	Recovery from drug solution		Recovery form tablet formulation	
	Mean amount found	Mean % recovery	Mean amount found	Mean % recovery
15	14.99	99.93	15	100
30	29.97	99.90	30.04	100.1
45	45.09	100.20	44.97	99.90

Table 4: Precision data of ziprasidone (n=3)

Concentration of ziprasidone (µg/ml)	Observed concentration of ziprasidone (µg/ml)			
	Intra-day		Inter-day	
	Mean	CV (%)	Mean	CV (%)
10	9.99	0.52	9.97	0.74
20	19.96	0.53	19.95	0.69
30	29.98	0.42	29.97	0.71
40	39.99	0.31	39.95	0.53

Application of the method to pharmaceutical dosage forms

The method is sensitive and specific for the quantitative determination of ziprasidone and also subjected to validation for different parameters, hence has been applied for the estimation of drug in pharmaceutical dosage forms. Capsules from two different manufacturers were evaluated for the amount of ZPR present in the formulations. Each sample was injected six times after extracting the drug as mentioned above in experimental section. The amount of ZPR was found to be within the range of 99.85%-100.1%. None of the capsule excipients were found to interfere with the analyte peak and the results were shown in Table 5.

Table 5: Results of the determination of ziprasidone in capsules (n=6)

Sample ID	Labeled amount of drug (mg)	Mean amount found	Mean labeled amount
Capsule 1	20	19.97±0.106	99.85±0.075
Capsule 2	20	20.02±0.078	100.1±0.034

CONCLUSION

The proposed method was found to be simple, precise, accurate and rapid for determination of ziprasidone from pure and in pharmaceutical dosage forms. The mobile phase is simple to prepare. The sample recoveries in all formulations were in good agreement with their respective label claims and they suggested non-interference of formulation excipients in the estimation. Hence, the method can be easily and conveniently adopted for routine analysis of ziprasidone from dosage forms and can also be used for dissolution or similar studies.

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