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Stability indicating and validation by RP-HPLC for the estimation of Ziprasidone in bulk and its dosage Form

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Abstract

A new simple, sensitive and stability indicating RP-HPLC method for the determination of ziprasidone in pharmaceutical dosage form was developed. Chromatographic separation was carried on RP-C8 column (symmetry 250x4.6mm;5µm) with a mobile phase composed of potassium dihydrogen phosphate buffer (pH 4.5) and acetonitrile (70:30) at an absorption maxima 247nm. Linearity for detector response was observed in the concentration range of 50-150% of test concentration. Correlation coefficient found to be 1.0. Retention time was found to be 4.1min. Percent recovery studies were found in the range 50-150% of test concentration. Drug product was exposed to acid, base, heat, oxidation and photolytic stress conditions and the samples were analysed by the proposed validated method. Results of the analysis were validated statistically and by recovery studies. The developed method was found to be precise for the determination of ziprasidone in bulk and capsule dosage form.

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Introduction

Ziprasidone is chemically 5-[2-[4-(1, 2-benzisothiazol-3-yl)-1-piperazinyl] ethyl]-6-chloro-1, 3-dihydro-2*H*-indol-2-one. It is an atypical antipsychotic drug mainly acts through dopamine receptor, specifically D_2 and $5\text{-}HT_{2A}$ receptor. [1-2]

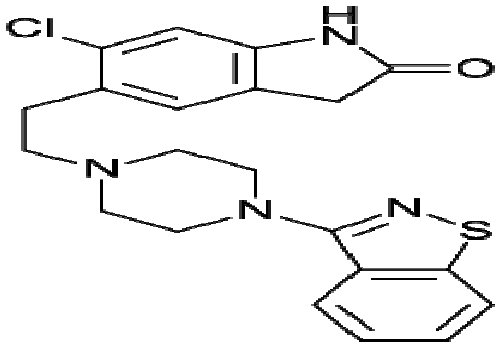

Fig 1 Structure of ziprasidone

Experimental

Materials

Ziprasidone was gift sample from the Dr.Reddy's laboratories, Hyderabad and the chemicals potassium dihydrogen phosphate, acetonitrile and methanol (fine chemicals Ltd, Mumbai, Maharashtra) were used for the study.

Instrument

A Waters high performance liquid chromatography (model 2695) with PDA detector (model 2998) with auto sampler was used for the method development and validation.

Buffer preparation:

Weighed 13.6g of potassium dihydrogen phosphate and dissolve it in 1000 ml of milli-Q water and filter through 0.45µm filter and degas.

Mobile phase preparation:

Buffer solution and acetonitrile were mixed in the ratio of 70:30 and degassed.

Standard stock preparation:

8gm of ziprasidone was weighed and transferred into 25 ml of volumetric flask and make up the volume with methanol.

Sample preparation:

Capsule powder equivalent to average weight (304mg) was taken and transferred into 50 ml flask and 20 ml of methanol was added and sonicated for 30min and the solution was made up with methanol. The solution then filtered through 0.45µm filter and diluted 5ml of the above solution to 25ml with methanol.

Table 1: Optimised parameters

Parameters	Results
Mobile phase	Potassium dihydrogen phosphate buffer:acetonitrile (70:30)
Stationary phase	Symmetry RP-C8 column (250*4.6, 5µm)
Lambda max	247nm
Retension time	4.1min
Flow rate	1ml/min
Injection volume	20µl
Run time	7min
Temperature	45°C

Linearity:

Linearity of detector was found by injecting five standard solutions with concentration ranging from 50% to 150% of the test concentration and a graph was plotted for concentration versus peak area. The results were shown in fig :2

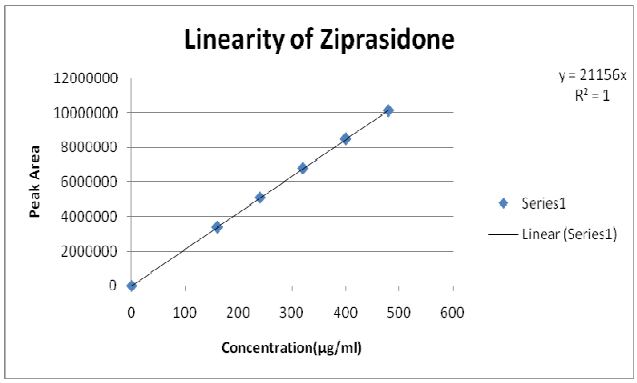

Figure 2: Linearity of ziprasidone

Precision:

The precision of an analytical procedure expresses the closeness of agreement between a series of measurements. [10] The precision of test method was determined by preparing six test preparations and the relative standard deviation of assay results was calculated and shown in table 2.

Table 2: Precision of ziprasidone

S. No	Sample area	%Assay
1	6783720	101
2	6598016	98
3	6742584	100
4	6759035	100
5	6760123	100
6	6732576	100
%RSD		0.99

Accuracy:

Recovery studies are performed in the concentration range of 50, 100 and 150% keeping the average weight constant and varying the quantity of active ingredient as per spike levels. Lower and higher concentrations are prepared six times and triplicate at other levels to accurately quantify and to validate the accuracy.

Table 3: Accuracy of ziprasidone

Spiked level	Amount µg/ml added	Amount µg/ml found	%Recovery	%Mean
50%	160	159.84	100	99
50%	160	159.37	100	
50%	160	159.24	99	
100%	320	320.28	100	100
100%	320	320.38	100	
100%	320	318.23	99	
150%	480	482.68	101	100
150%	480	482.19	100	
150%	480	482.19	100	

Robustness:

Effect of variation in flow rate and temperature

System suitability parameters were checked by injecting sytem suitability preparation into HPLC system with 0.9ml/ml and 1.1ml/min and temperature at 38°C and 42°C to get the robustness of the assay method. The results were shown in table 4.

Table 4: Robustness of ziprsidone

Parameter	Variation	%Recovery of ziprasidone
Standard	1ml/min	100
Flow rate	0.9ml/min	99.4
	1.1ml/min	99.7
Temperature	38°C	99.4
	42°C	99.2

Limit of detection and Limit of quantification

The parameter LOD and LOQ was determined on the basis of the height of the signal and the noise of response. The LOD and LOQ for this method were found to be 0.376 and 1.255µg/ml respectivelyz. [10]

Forced degradation studies

The zipsydon capsule containing (Ziprasidone 80mg) were subjected to various forced degradation conditions to effect partial degradation of the drug. Forced degradation studies were performed to show the method is suitable for the degraded products. Moreover, the studies provide information about the conditions in which the drug is unstable so that measures can be taken during formulation to avoid potential instabilities. [9]

Acid degradation

Capsule powder equivalent to average weight was transferred into 25ml volumetric flask. To that 10ml of 0.1N HCl was added and made up to the mark with methanol and sonicated for 60min. Then the solution was filtered through 0.45µm filter and diluted 5ml of the above solution to 25ml with methanol.

Base degradation

Capsule powder equivalent to average weight was transferred into 25ml volumetric flask. To that 10ml of 0.1N NaOH was added and made up to the mark with methanol and sonicated for 60min. Then the solution was filtered through 0.45µm filter and diluted 5ml of the above solution to 25ml with methanol.

Heat degradation

Capsule powder equivalent to average weight was transferred into 25ml volumetric flask and made up to the mark with methanol and kept at 60°C for 60min. Then the solution was filtered through 0.45µm filter and diluted 5ml of the above solution to 25ml with methanol.

Light degradation

Capsule powder equivalent to average weight was transferred into 25ml volumetric flask and made up to the mark with methanol and kept in U.V chamber for 60min. Then the solution was filtered through 0.45µm filter and diluted 5ml of the above solution to 25ml with methanol.

Peroxide degradation

Capsule powder equivalent to average weight was transferred into 25ml volumetric flask. To that 2ml of

0.1N H_2O_2 solution was added and made up to the mark with methanol and sonicated for 60min. Then the solution was filtered through 0.45µm filter and diluted 5ml of the above solution to 25ml with methanol. The results were shown in table 5.

Table 5: Forced degradation studies of ziprasidone

S. No	Sample	Peak Area	% Assay
1	Standard	6749906	99
2	Acid	4021035	60
3	Base	3933836	58
4	Light	4284504	63
5	Heat	4530057	67
6	Peroxide	5129108	76

Results and discussion:

The proposed method for the determination of Ziprasidone in pharmaceutical dosage form was found to be precise, selective and economical the present study describes the RP-HPLC method development and validation for the estimation of Ziprasidone in capsules. The dosage form was analysed symmetry C8 column (250mmx4.6mm) using phosphate buffer of analysis pH (4.5) and Acetonitrile in an isocratic programme with flow rate 1.0ml/min and UV detection was performed at 247nm. The retention times observed as 4.1 min. The linearity for detector response was observed in the concentration range of 50 to 150% of the concentration and the correlation coefficient(r) for calibration curve was found to be 1. The results of the recovery studies between 50 to 150% were in the range of 98 to 102% indicating accuracy of the method. The %RSD for the capsule analysis is less than 2 which is indicating high degree of precision. The results of the robustness study indicates that the method is robust and is unaffected by small variations in the chromatographic conditions. The LOD and LOQ were calculated and were found to be 0.376 and 1.255µg/ml respectively. Forced degradation studies were performed and degradation was found within the 20-80% range. The assay of the sample shows the purity indicates the purity of the formulation. Hence, it can be concluded that the developed RP-HPLC method is accurate, precise rapid and selective and can be employed successfully for the estimation of Ziprasidone in bulk and its dosage form.

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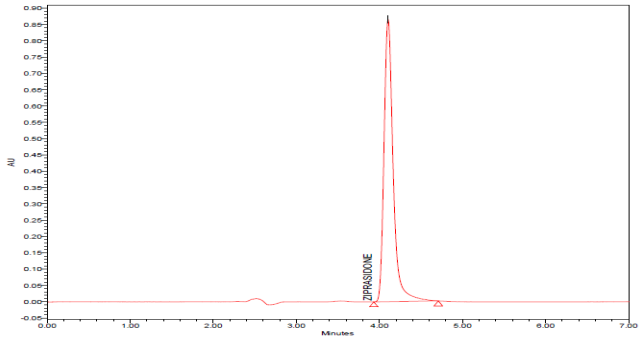
Table 5: Assay of Ziprasidone capsules

Brand name	Drug	Label claim	Amount found	%Assay	%RSD
zipsydon	ziprasidone	80mg	79.90mg	99.8%	0.17

Fig 3: Chromatogram of API



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