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METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF ZIPRASIDONE HYDROCHLORIDE IN PELLETS BY RP-HPLC

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ABSTRACT

The aim of the present work was to develop and validate a simple, efficient, economical method for the estimation of drug Ziprasidone hydrochloride in its pellets by reverse phase high pressure liquid chromatography. Chromatography was performed on Inertsil ODS C18 column (150 mm x 4.6 mm, 5 µm) with mobile phase containing methanol: 0.05%v/v ortho-phosphoric acid in water (90:10) at a flow rate of 1 mL/min and eluents were monitored at 270 nm. The retention time of drug was 3min and showed a good linearity in the concentration range of 20-60 µg/mL with a correlation coefficient of 0.9998.The developed method was validated for specificity, accuracy, precision, recovery, linearity, robustness, and system suitability and stability. The low standard deviation values and good recoveries indicate the reproducibility and accuracy of the developed method. By the overall results obtained, it was concluded that the developed method was more accurate, precise, specific and robust with ±5º C in temperature, ± 10% in flow rate.The percentage of recovery of ziprasidone was found to be 99.8% at 100.1% level.The method could be successfully used for the analysis of ziprasidone in bulk and dosage forms.

Keywords: RP-HPLC method, Ziprsidone, pellets, accuracy, precision, recovery, linearity, robustness.

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INTRODUCTION

The drug analysis plays an important role in the development, manufacture and therapeutic use of drugs. Most of the pharmaceutical industries do the Quantitative chemical analysis to ensure that the raw material used and the final product thus obtained meets certain specification and to determine how much of each component is present in the final product. Standard analytical procedure for newer drugs or formulation may not be available in Pharmacopoeias; hence it is essential to develop newer analytical method and validation of drug. For the Method Development and Validation of new drug present in dosage forms UV- Spectrophotometer, HPLC and HPTLC methods are considered to be most suitable. Since these are powerful and rugged methods and also extremely precise, accurate, sensitive, specific, linear and rapid (1, 2)

Ziprasidone an antipsychotic drug used for the treatment of schizophrenia, mania and mixed states associated with bipolar disorder. Ziprasidone's antipsychotic activity is likely due to a combination of its antagonistic function at D2 receptors in the mesolimbic pathways and at 5HT2A receptors in the frontal cortex (3).

Literature survey has revealed that various methods were reported for estimation of Ziprasidone those are Colorimetry, UV Spectrophotometry and HPLC. The objective of the proposed method is to develop simple and accurate method for the estimation of Ziprasidone in bulk and its pellets by RP-HPLC. Hence, on the basis of literature survey it was thought to develop a precise, accurate, simple and reliable, less time consuming and less cost effective method(4).

A RP-HPLC method was developed for the estimation of Ziprasidone hydrochloride in bulk and its pellets. The HPLC method was then validated to indicate that the analytical procedure used was suitable for intended use by using various parameters like specificity, linearity, precision, accuracy, range, and robustness, stability in analytical solution, system suitability and filter interference(5).

MATERIALS AND METHODS

Optimized chromatographic conditions

Instrument: Waters 2690 Seperation Module ,Column: Inertsil ODS C18, 150 x 4.6mm, 5µm, Mobile phase: Methanol:0.05%v/v o-phosphoric acid in water (90:10), Mode : Isocratic, Flow Rate : 1.0 ml/min, Injection Volume : 20 µL, Wave Length : 270 nm, Detector : PDA, Run time : 6mins

Drug sample Ziprasidone hydrochloride pellets 68%w/w, Month of Manufacture- June 2012, Month of Expiry- November 2014, Manufactured by Sereo Drugs Pvt.Ltd, Hyderabad.

Standard preparation

Weigh and transfer 50 mg of ziprasidone hydrochloride working standard into a 50 ml volumetric flask. To to this add 20ml of methanol, sonicate to dissolve and dilute with methanol to volume and mix(std.stock solution).5.0 ml of above solution was transferred into a 50 ml volumetric flask and make up to the mark with mobile phase through 0.45 µm nylon filter(6).

Sample preparation

Weigh and transfer the powdered pellets equivalent to 100 mg of ziprasidone hydrochloride into a 100 ml volumetric flask add 20 ml of mobile phase and sonicate for 30 min and make up to the mark with methanol, filter the solution through 0.45µ nylon filter. Transfer 5.0 ml of the resulting solution into a 50 ml volumetric flask and make up to the mark with mobile phase (7).

Method validation

System suitability

Plate counts (N), tailing factor (T), resolution (R_s) and reproducibility are determined from replicate injection of standard (an analyte peak and internal standard, related compound, excipient and or impurity, etc.,) compared with method specification (8, 9, 10).

Accuracy

The accuracy study was conducted by spiking the known amount of active ingredients into the placebo at three different levels (80 %, 100 % and 120 % of target concentration). The samples were analysed as per the proposed procedure and the % recovery for each spiked level was calculated.

Precision

The system precision was checked by using Ziprasidone hydrochloride standard to ensure that the analytical system was precise. Five injections of standard were taken and the retention time and area of five determinations was measured and %RSD was calculated.

Robustness

The robustness of an analytical method was a measure of its capacity to remain unaffected by small deliberate variations in method parameters and provides an indication of its reliability during normal usage. Robustness was done by changing the column temperature (± 5°C), flow rate (± 10%).

Linearity

Linearity of detector response of ziprasidone was conducted from 50% level of ziprasidone standard to 150% of the ziprasidone standard concentration. Plotted linearity graphs of standard ziprasidone concentration versus peak area level 50%, 75%, 100%,

125%, 150% and has been found linear in the prescribed range. Performed the precision study for lower and higher level solutions by injecting 6 replicate injections into HPLC system.

Solution stability

A study to establish the stability of standard and test preparation at controlled room temperature (25 ± 5^0C) and refrigerated ($2\text{-}8^0$C) condition was conducted over a period of 30hrs.The difference in percentage assay of standard and test preparations at initial, after 24hrs and after 30 hrs of room temperature and refrigerator conditions were found within the limits.

RESULTS AND DISCUSSION

The results of typical quantitative analysis can computed from two measurements. One is the mass or volume of sample to be analyzed and second is the measurement of some quantity that is proportional to the amount of analytes in that sample and normally completes the analysis. Instruments play a key role in the quantitative analysis of pharmaceutical chemistry (Fig – 1, 2).

System suitability

It was observed from the data tabulated above; the method complies with the system suitability parameters. Hence it was concluded that the system suitability parameter met the requirement of method validation (Table-1, Fig-3).

Accuracy

From the above results, it can be concluded that the recovery is well within the limit. Hence, the method is accurate (Table-2)

Precision

It was observed from the data tabulated above, that the retention time and area responses are consistent as evidenced by the values of relative standard deviation. Hence, it can be concluded that the system precision parameter meets the requirement of method validation (Table-3)

Linearity

The method for ziprasidone hydrochloride was found to be linear in the concentration range of 20µg/ml to 60µg/ml. Correlation Coefficient was found to be 0.9998. (Fig-4).

Solution stability Standard and sample solutions of Ziprasidone hydrochloride stable upto 48 hrs and there is no additional peak was observed in the solution (Table-5, Fig-5)

Table-1 System suitability results for Ziprasidone hydrochloride

Injection	RT(min)	Peak Area	Theoritical plates	Tailing factor
1	3.006	3228239	3268	1.36
2	3.008	3229234	3223	1.34
3	3.011	3228403	3224	1.35
4	3.005	3228489	3277	1.34
5	3.011	3228403	3224	1.35
	Mean	3228554		
	SD	390.9767		
	%RSD	0.012		

Table-2 Accuracy results for Ziprasidone hydrochloride

Concentration level	Amount added	Amount found	%Recovery	Average % recovery	%RSD
80%	32 32 32	32.3 32.5 32.6	101.1 101.7 101.8	101.53	0.37

100%	40 40 40	40.6 40.8 40.9	101.4 101.5 101.9	101.6	0.26
120%	60 60 60	60.5 60.4 60.7	101.7 101.6 101.8	101.7	0.10

Table-3 Method precision results for Ziprasidone hydrochloride pellets

Injection no	% Assay of Ziprasidone hydrochloride pellets
1	99.8
2	100.0
3	99.8
4	100.0
5	99.8
6	100.1
Mean	100
SD	0.12
%RSD	0.12

Table-4 Results for Robustness

Sr. No.	Parameter	Condition	System suitability results		
			% RSD	Tailing factor	Theoretical plates
1	Flow rate by ± 10%	1.0ml	0.16	1.2	5658
		0.9 ml	0.18	1.4	4155
		1.1 ml	0.31	1.3	3770
2	Column Oven temperature by ± 5°C	25°C	0.16	1.2	5625
		20°C	0.09	1.4	3528
		30°C	0.31	1.4	3460

Table -5 Solution stability results for Ziprasidone hydrochloride sample solution at refrigerator temperature

Time	Sample 1		Sample 2	
	Assay %	Difference %	Assay %	Difference %
Initial	101.1	NA	102.2	NA

After 24hrs	101.7	0.6	102.1	0.1
After 48hrs	102.2	0.5	102.7	0.5

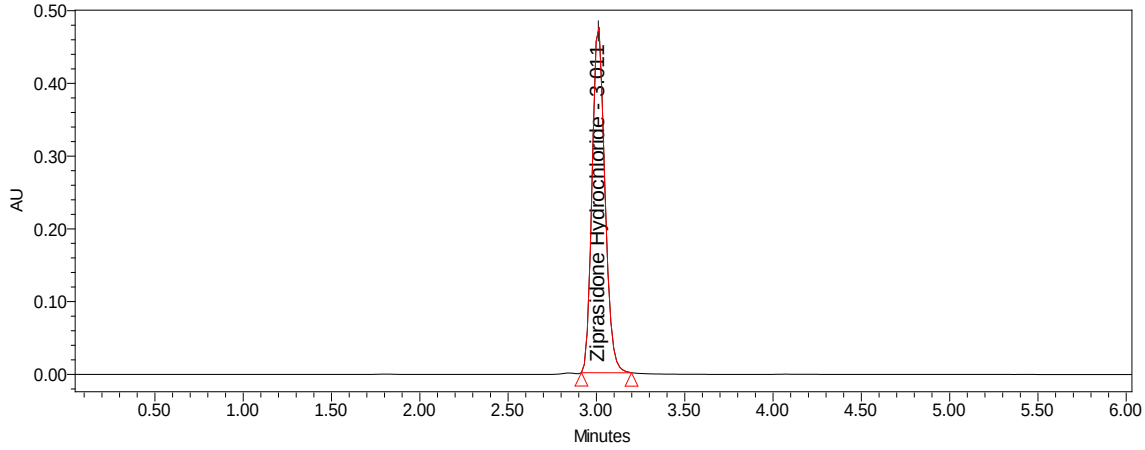

Fig-1 Chromatogram of standard solution by optimized Method

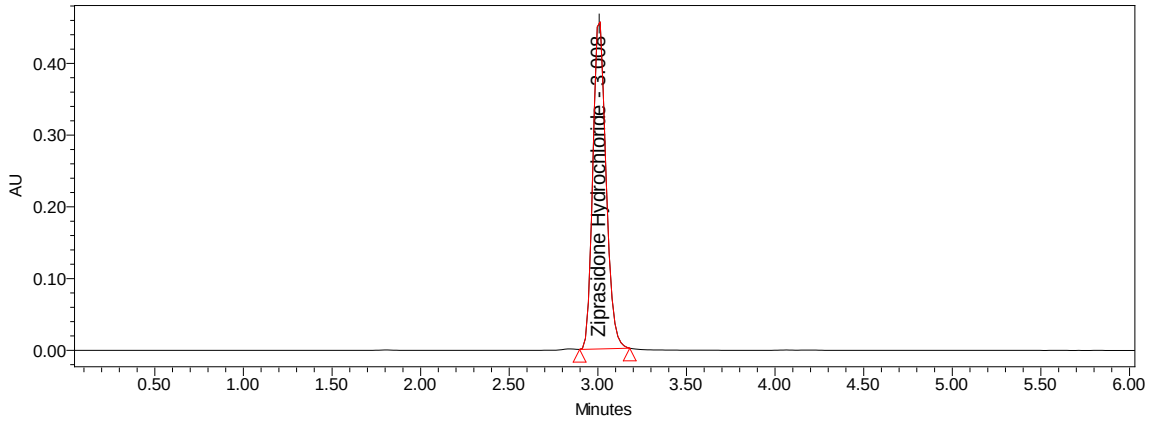

Fig-2 Chromatogram of sample solution by optimized Method

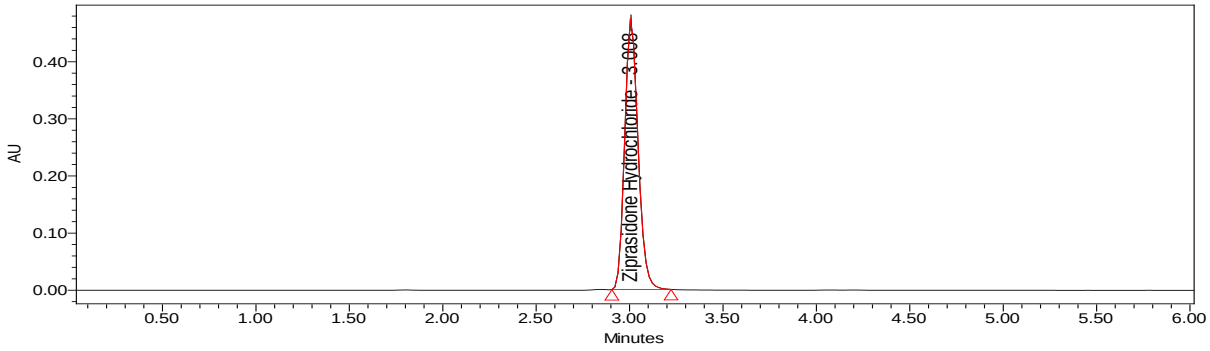

Fig-3 Chromatograms for system suitability of Ziprasidone

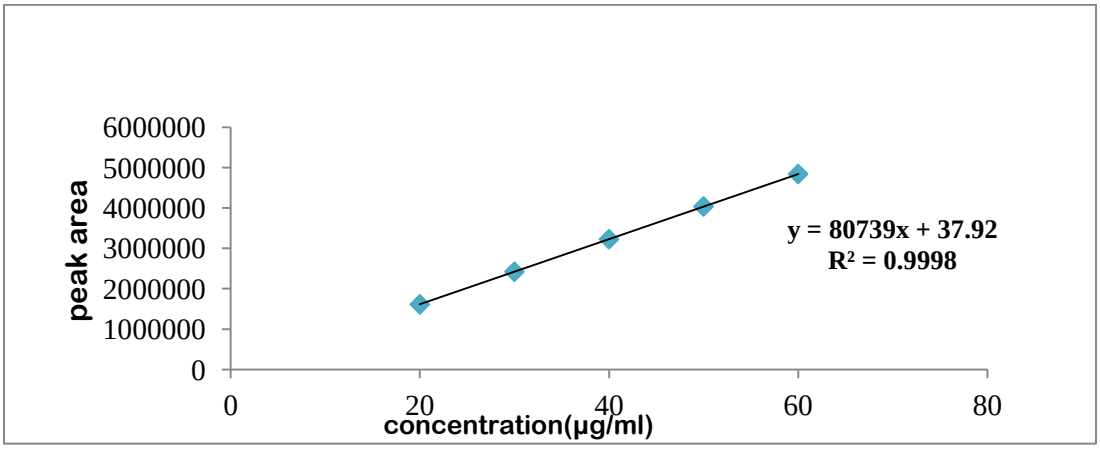

Fig-4 Linearity plot for ziprasidone hydrochloride

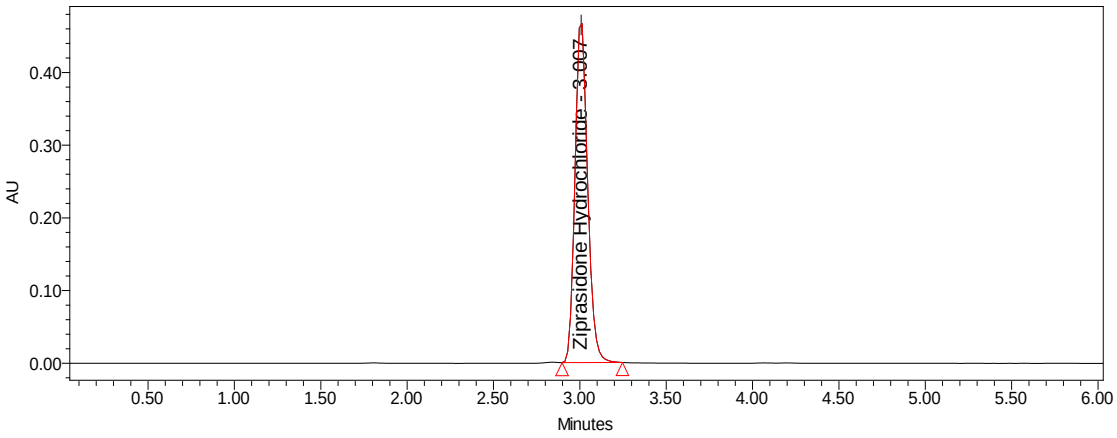

Fig-5 Chromatograms for solution stability

CONCLUSION

The developed chromatographic (RP-HPLC) method for Ziprasidone hydrochloride is said to be rapid, simple, precise, accurate, and cost effective that can be effectively applied for the routine analysis in research institution, quality control department in industries, approved testing laboratories, biopharmaceutical studies, and clinical pharmacokinetic studies and for determination of impurities in formulated products.From the overall results obtained it was concluded that the developed method was more accurate, precise, specific and robust with ±5º C in temperature, ±0.2 mL/min in flow rate

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