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ESTIMATION OF ZIPRASIDONE BY A NEWLY DEVELOPED AND VALIDATED ANALYTICAL METHOD USING RP–HPLC WITH UV DETECTION

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ABSTRACT

A simple, sensitive, accurate, precise and reproducible high performance liquid chromatographic method was developed for the estimation of Ziprasidone hydrochloride in bulk drug and capsule dosage form. In this method, chromatography was carried using Sunsil C_{18} (x 150x4.6mm, 5µ) column using a mixture of water: methanol (55:45) as the mobile phase at a flow rate of 1.0 ml/min, and the detection wavelength was 261 nm. The linearity was observed in the range of 2-10 µg/ml with a correlation coefficient of 0.999. The proposed method was validated for its linearity, accuracy, precision and robustness and found to be simple, rapid, accurate, and precise. LOD and LOQ values were found to be 0.09 µg/ml and 0.29 µg/ml respectively. Hence can be applied for routine quality control analysis of Ziprasidone hydrochloride in capsule dosage forms.

INTRODUCTION

Ziprasidone[1]is a novel antipsychotic agent and is indicated for the treatment of schizophrenia, as monotherapy for the acute treatment of bipolar manic or mixed episodes, and as an adjunct to lithium or valproate for the maintenance treatment of bipolar disorder. Chemically, it is 5-[2-[4-(1, 2-benzisothiazol-3-yl)-1-piperazinyl] ethyl]-6-chloro-1, 3-dihydro-2H-indol-2-one (Fig.1). The action of Ziprasidone is mediated through a combination of dopamine type 2 (D2) and serotonin type 2 (5HT2) antagonisms. Ziprasidone exhibited high in vitro binding affinity for the dopamine D2 and D3, the serotonin 5HT2A, 5HT2C, 5HT1A, 5HT1D, and α1-adrenergic receptors and moderate affinity for the histamine H1 receptor. Ziprasidone is functioned as an antagonist at the D2, 5HT2A, and 5HT1D receptors, and as an agonist at the 5HT1A receptor. Ziprasidone inhibited synaptic reuptake of serotonin and norepinephrine. A few spectrophotometric[2-3], HPLC[4-7], LC-MS[8-10] and capillary electrophoresis [11,12] methods were reported earlier for the determination of Ziprasidone Hcl in bulk and pharmaceutical formulations. In the present study the authors report a rapid, sensitive, accurate and precise HPLC method for the estimation of Ziprasidone Hcl in bulk samples and in capsule dosage forms.

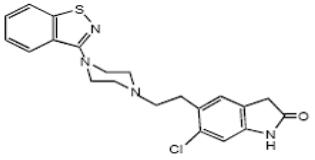

Fig.1: Chemical structure of Ziprasidone

Materials and methods

Instrument: The Analysis of the drug was carried out on WATERS hplc system equipped with a sunsil C18 (4.6mm x 150,5 µ)column with 1525 Binary pump and 2487 dual absorbance detector.Software used was Empower 3.0.

Chemicals and solvents: Ziprasidone hydrochloride was supplied by TCI chemicals Ltd., Hyderabad. Commercial capsules of ziprasidone were procured from local market, which were manufactured by sun pharma laboratories Ltd, Sikkim. HPLC grade methanol and water purchased from Lichrosolv (Merck) were used throughout the study.

Preparation of mobile phase and diluent: Measured quantities of HPLC grade water and Methanol were filtered through 0.45 µ filter under vacuum and degassed in digital ultrasonicater for 10 minutes. Filtered and sonicated HPLC grade methanol was used as Diluent.

Standard preparation: Stock I: Accurately weigh and transfer 10 mg of Ziprasidone working standard into a 10ml clean dry volumetric flask,add about 7ml of Methanol, sonicate to dissolve and removal of air completely and make volume up to the mark with the same.(1000µg/ml) Stock II: Pipette out 1ml stock solution into a 100ml volumetric flask, dilute up to the mark with diluent.(10µg/ml)

Results and Discussion

Selection of wavelength: Establishing a maximum absorbance was the initial step which was observed at 261nm using UV spectrophotometer (Figure2).

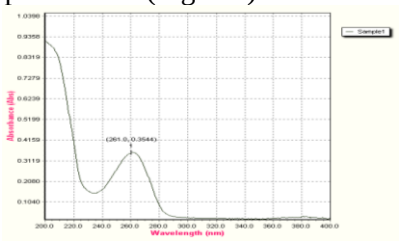

Fig. 2: UV Spectrum of Ziprasidone Hcl

Method Development: Optimized chromatographic conditions were established on a trial and error basis by varying organic and aqueous phase. The column was equilibrated by pumping the mobile phase consisting water: methanol (55:45%v/v) for at least 30 min prior to the injection of the drug solution at a flow rate of 1 ml/min. The column oven temperature being ambient, detection of ZPS was monitored at 261 nm. The run time was set to 10min. Under these optimized chromatographic conditions a sharp peak meeting all the system suitability criteria was retained at 3.08 min. The optimized chromatogram was shown in Figure 3.

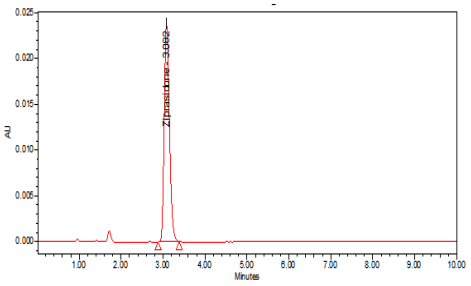

Fig.3: Optimized chromatogram of Ziprasidone Hcl Validation[13]

System Suitability: Five replicate injections of standard solution (5µg/ml) were injected into the chromatographic system. The system suitability parameters like theoretical plates, resolution and asymmetric factor were evaluated and the values are depicted in Table 1.

RepeatabilityPrecision of the method was determined by measuring the %RSD of six replicate injections of stock II solution. Values obtained are presented in table 2.

Intraday &Inter day: Solutions containing various concentrations of Ziprasidone Hcl was carried out to check intra-day and inter-day variation of the method and the results are furnished in Table 3.High values of mean assay and low values of standard deviation (% RSD < 2.0) within a day and day to day variations revealed that the proposed method is precise.

Linearity and Range

Linearity of the method was performed by preparing serial dilutions of standard Ziprasidone Hcl solution(stock II) to obtain a final concentration ranging from 2-10 µg/ml. Peak areas obtained were tabulated (Table 4) , a straight line obtained in the calibration curve (Fig 4) shows the method is linear. Regression analysis (r^2=0.999) by the least square method meets acceptance criteria. This regression equation was later used to estimate the amount of Ziprasidone hydrochloride in capsule dosage forms.

Accuracy of the method was assessed by spiking of Ziprasidone hydrochloride API at 50%, 100% and 150% of the labeled amount. Each spike level was injected in triplicate and average % recovery was calculated for the same. The results are furnished in Table 5The Minimum concentration level at which the analyte can be reliably detected (LOD) and quantified (LOQ) were found to be 0.09 and 0.29 µg/ml respectively.

Table 1: System Suitability Results for Ziprasidone Hcl

Replicate	Retention time	Peak Area	USP plate count	USP Tailing
1	3.08	204753	4506	1.3
2	3.08	204331	4674	1.2
3	3.07	204753	4298	1.2
4	3.08	204331	4032	1.0
5	3.08	204753	4812	1.3
Mean	3.078	204584.2		
Std. Dev	0.0045	231.1389		
% RSD	0.15	0.11		

Precision

Table.2: Repeatability results for ziprasidone HCL

Replicate	Rt	Peak Area	USP plate count	USP Tailing
1	3.082	404754	4755	1.3
2	3.082	407332	4814	1.3
3	3.082	404754	4822	1.3
4	3.082	407332	4709	1.3
5	3.082	404754	4704	1.3
6	3.082	404754	4704	1.3
Mean	3.082	405613.33		
Std. Dev		1215.281		
% RSD		0.30		

Table.3: Intra-Day and Inter-Day Results

Conc.Of ZiprasidoneHcl (API) (µg/ml	Intra-Day		Inter-Day	
	Mean (n=6)	% RSD	Mean (n=6)	**% RSD**
5	5.03	0.25	5.95	**0.21**
10	10.49	0.36	10.02	**0.32**
15	15.14	0.14	15.30	**0.19**

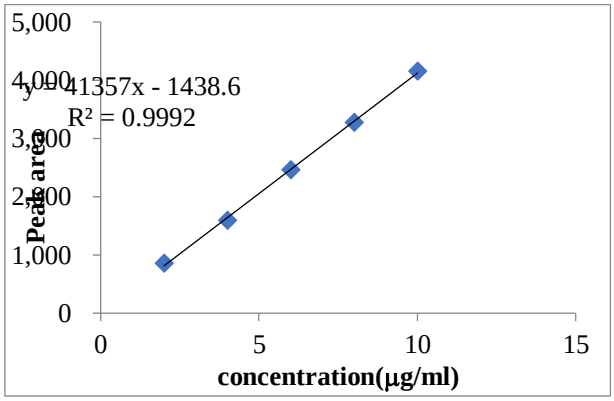

Fig.4: Linearity plot of Ziprasidone Hcl

Table.4: Linearity data
Accuracy

S.NO	Conc. (µg/ml)	Average Peak Area
1	2	85535
2	4	159277
3	6	246375
4	8	327185
5	10	415154

Table.5: Accuracy Results

Spike level	Replicates	Amount spiked (ppm)	Amount Found (ppm)	Peak Area	% Recovery	Mean %Recovery
50%	Replicate 1	2	2.03	249991	100.54	
	Replicate 2	2	1.92	248236	99.48	100.0
	Replicate 3	2	1.91	248722	99.78	
100%	Replicate 1	4	3.69	331176	99.43	
	Replicate 2	4	3.79	332098	99.98	100.0
	Replicate 3	**4**	**3.81**	**332140**	**100.01**	
150%	Replicate 1	6	5.78	413214	99.22	
	Replicate 2	6	5.82	414987	99.93	99.44
	Replicate 3	6	5.76	413054	99.16	

LOD and LOQ

Assay

Preparation of sample solution: Take average weight of 10 capsules and transfer them in a mortar, 10mg equivalent of Ziprasidone sample was weighed and transferred into a 10mL clean dry volumetric flask and add about 7mL of diluent and sonicate to dissolve it completely and make volume up to the mark with the same diluent. Pipette out 0.5ml stock solution was taken in a 100ml of volumetric flask dilute up to the mark with diluents. (5µg/ml)

Label claim = 206361/ 204754× 10/1000× 1000/68.675 × 100/100 × 275/40× 100
= 100.2%

CONCLUSION

A delicate and specific, sensitive RP-HPLC strategy has been created and approved for the investigation of Ziprasidone Hcl API. Facilitate the proposed RP-HPLC strategy has amazing affectability, exactness and reproducibility.

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