Digest Journal of Nanomaterials and Biostructures Vol. 5, No 1, March 2010, p. 279 – 283

DEVELOPMENT OF RAPID UV SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF ZIPRASIDONE HYDROCHLORIDE IN BULK AND FORMULATIONS

Y. ANAND KUMAR*, M.ANITHA, A.HEMANTH, S. SRINIVAS
V.L.College of Pharmacy. Manik prabhu temple road, Raichur. 584103. India

Simple, sensitive, accurate, precise and rapid ultraviolet (UV) Spectrophotometric method was developed for the estimation of Ziprasidone HCl in pure form, formulations and stability samples. For the estimation of Ziprasidone HCl, solvent system employed was saline buffer pH 7.4 and wavelength of detection (λ_{det}) was 318nm.The developed method was used to estimate the total drug content in two commercially available oral formulations of Ziprasidone HCl and recovery studies were also carried out. Sample recovery in both the formulations using the above method was in good agreement with their respective label claims, thus suggesting the validity of the method and noninterference of formulation excipients in the estimation. The developed method was found to be stability specific and was validated as per ICH guidelines-2005, USP-2000 and statistical methods.

(Received February 2, 2010; accepted March 15, 2010)

Keywords: Spectrophotometric determination, Methanol, Ziprasidone HCl, Saline buffer pH 7.4

1. Introduction

Ziprasidone HCl is an Antipsychotic agent used in the management of CNS disorders. Chemically Ziprasidone HCl is 5-[2-[4-(1,2-benzothiazol-3-yl)piperazin-1-yl]ethyl]-6-chloro-1,3-dihydroindol-2-one hydrochloride. Ziprasidone HCl is a white or pale pink powder with a molecular weight of 449.4. It is freely soluble in methanol, ethanol and chloroform, soluble in ether, sparingly soluble in acetonitrile and octanol, and practically insoluble in water. It should be kept in a well closed container, protected from light [1-6].

Literature survey revealed that only few methods available for the estimation of Ziprasidone HCl alone, in combination with other drugs, in its dosage form and in plasma [7-10] .The present investigation was undertaken to develop simple UV spectrophotometric method for the estimation of Ziprasidone HCl in bulk and its formulations.

2. Material and methods

A Hitachi-U2000 spectrophotometer with a pair of matched quartz cells was used to measure absorbance of the resulting solutions. Ziprasidone HCl was gifted by Strides Arco (pvt) Ltd Bangalore. All the other reagents used were of analytical grade and obtained from S.D Fine chem, Mumbai.

2.1. Preparation of standard curve

* Corresponding author: neeru241586@yahoo.co.in

A 100µg/ml stock solution of Ziprasidone HCl was prepared in saline buffer pH 7.4 by first dissolving 10 mg of the drug in 10 ml of methanol and then, making up the final volume with saline buffer pH 7.4.

The λ_{max} of Ziprasidone HCl was determined by scanning suitable dilutions with high correlation coefficient. From the stock solution, various standard dilutions were made to obtain solutions of 2,4,6,8 and 10 µg/ml and their respective absorbance values were measured at fixed λ_{max} with parameter set at 0.5nm for bandwidth as well as data pitch. Average absorbance values, standard deviation and % coefficient of variance for each concentration were calculated. One way ANOVA test for linearity was carried out by picking five sets of calibration curves on random basis.

2.2. Sample preparation (Bulk drug)

Ziprasidone HCl 50mg was accurately weighed and taken into 100ml volumetric flask containing 10ml of methanol and further it was made upto the volume 100ml with saline buffer pH 7.4 solution. This solution was further serially diluted with saline buffer pH 7.4 solution to get 10, 20, 40, 50,100µg/ml solution. The Ziprasidone HCl content was further determined by measuring the absorbance at 318nm.

2.3. Sample preparation (Dosage forms)

Twenty capsules were weighed and the powder equivalent to 50mg of Ziprasidone HCl was taken in 100 ml volumetric flask containing 50ml of methanol. The contents were shaken well for 30 minutes and made upto the volume with 100 ml with methanol. This solution was further suitably diluted with saline buffer pH 7.4 solutions and determined the Ziprasidone HCl content by measuring the absorbance at 318nm.

2.4. Recovery experiments

To keep an additional check on the accuracy of the developed method and to study the interference of formulation additives, analytical recovery experiments were performed by adding known amount of pure drug to the previously analyzed pharmaceutical preparation and analyzed by the developed method. The concentration levels used were 10 µg/ml.

3. Results and discussion

3.1. Method development

To develop accurate, precise and sensitive UV spectrophotometric method for Ziprasidone HCl various solvent systems such as water, methanol etc. were tried alone and in combinations or in the presence of surfactants at different proportions. Selection of saline buffer pH 7.4 was based on sensitivity, minimal interference, ease of preparation, suitability for drug content estimation, stability, analysis time and cost. The λ_{max} for Ziprasidone HCl in saline buffer pH 7.4 (Figure 1) showed linear relationship (with correlation coefficient of 0.9988) in the concentration range of 2-10 µg/ml (Table 1and 2).

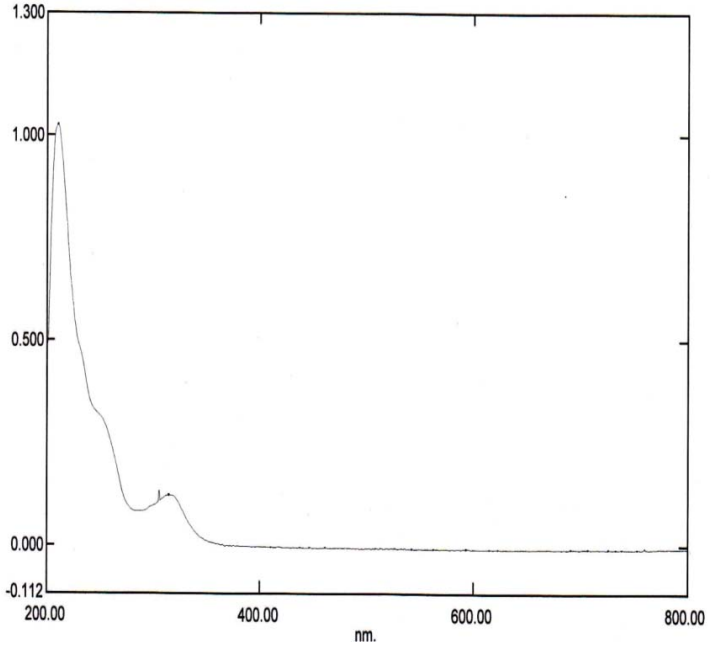

Fig. 1. Scan of 5µg/ml solution of Ziprasidone HCl in saline buffer pH 7.4

Table 1. Calibration curve points of the proposed method for the estimation of Ziprasidone HCl

Concentration (µg/ml)	Absorbance*±SD	CV (%)
2	0.025±0.0016	1.20
4	0.051±0.0010	1.23
6	0.075±0.0026	1.38
8	0.101±0.0028	1.52
10	0.124±0.0005	1.21

*Average of five reading

Table 2. Results of least square regression analysis of UV method for the estimation of Ziprasidone HCl

Absorption maxima	318
Beers law limit(µg/ml)	1-20
Molar absorptivity (1 $mole^{-1}/cm^{-1}$)	1.25×10^{-2}
Coefficient of correlation	0.9998
Best-fit values	
Slope	0.01246 ± 0.00009828
Y-intercept when X=0.0	0.0003810 ± 0.0005951
X-intercept when Y=0.0	-0.03058
1/slope	80.28
95% Confidence Intervals	
Slope	0.01218 to 0.01273
P value	< 0.0001

3.2. Sample solution stability studies

Overlay scans obtained at zero time, 12, 24, and 48 h revealed no degradation upto 48h in the selected solvent at controlled (25±2^{o}C; 65±5%RH) and accelerated (40±2^{o}C; 75±5 %RH) conditions . Drug was stable for more than 48 hours, thus there can be time lap between collection of the sample and analysis of the same.

3.3. Recovery studies

The method developed for the estimation of Ziprasidone HCl in bulk and in its dosage forms was found to be simple, accurate, economical and rapid. Table 3, 4, 5 clearly indicate that drug content was uniform ranging from 98 to 99.99% and SD, CV values were found to be satisfactorily low. Recovery studies were also carried out and found to be 98.89 to 99.89% for the both batches of capsules. The method requires only measuring the absorbance of sample solution at the selected wavelength followed by simple calculations. Hence, it was further employed for our study.

Table 3. Ziprasidone HCl estimation in dosage form by proposed method

Tablet sample	Label Claim (mg/capsule)	Actual content found mg±S.D	Percent Actual content found ±S.D	CV
Sample-1 **Ziprasidone HCl Cap**.(Generic)	20	19.75±0.153	99.00±0.153	0.939
Sample-2 **Ziprasidone HCl Cap**.(Generic)	40	39.50±2.04	99.35±0.74	0.669

Table 4. Ziprasidone HCl estimation in bulk by developed method.

S.NO	**Ziprasidone HCl taken(µg/ml)**	**Ziprasidone HCl found(CV)**	**% of Ziprasidone HCl found(CV)**
1	10	9.89(0.935)	98.9(0.76)
2	20	19.88(0.884)	99.40(0.85)
3	40	39.56(0.845)	98.9(1.12)
4	50	49.50(0.765)	99.1(0.99)
5	100	98.0 (0.928)	98.0(0.10)

Table 5. Ziprasidone HCl estimation in dosage form in recovery studies by developed method.

Tablet sample	**Concentration of added amount of drug in the final dilution (µg/ml ±S.D)**	**Recovery (µg/ml ±S.D)**	**Percent recovery ±S.D**	**CV**
Sample-1 Ziprasidone HCl Cap(Generic)	10	9.87 ±0.0123	98.7 ±0.989	0.979
Sample-2 Ziprasidone HCl Cap.(Generic)	10	9.9 ±0.0142	99.1 ±0.975	0.918

3.4. Method validation

The developed estimation method proved to be accurate (accuracy varies between 10.2-5.5%) and precise (Intra day precisions were less than 4.5%).The method has was validated in the range 2-10µg/ml using saline buffer pH 7.4 solution. The method was linear over this concentration range as indicated by the F-test for lack of fit. Analyte recovery was better than 90% at all points on the standard curve, Intraday precision was better than 5% CV while accuracy was between 98-100% of nominal over this range of the estimation.

4. Conclusions

The developed UV spectrophotometric method for the estimation of Ziprasidone HCl was found to be simple and useful with high accuracy, precision, and reproducible. Sample recoveries in all formulations using the above method were in good agreement with their respective label claim or theoretical drug content, this suggesting the validity of the method and non interference of formulation excipients in the estimation. In the selected solvent system, drugs were stable for more than 48 hours, thus suggesting that samples need not be estimated immediately after collection. The developed method was found to be stability specific and was validated as per ICH guidelines (2005) and statistical method.

References

[1] S.H. Preskorn. Clinical Pharmacokinetics. **44**(11), 1117-1133(2005).
[2] M.Tatsumi, K. Jansen, R.D.Blakely, E.Richelson. Eur. J. Pharmacol. **368**(2-3), 277 (1999).
[3] T.F.Seeger, PA.Seymour, A.W.Schmidt, S.H.Zorn, D.W.Schulz, L.A. Lebel, S. McLean, V.Guanowsky, H.R.Howard, J.A.Lowe. J Pharmacol Exp Ther. **275**(1), 101(1995).
[4] J.J.Miceli, P.Glue, J. Alderman, K. Wilner. Psychopharmacology Bull. **40**(3), 58 (2007).
[5] J.J.Miceli, R.J.Anziano, L.Robarge, R.A. Hansen, A. Laurent. Br. J. Clin. Pharmacol. **49**(1), 65 (2000).
[6] J.J.Miceli, M. Smith, L. Robarge, T. Morse, A. Laurent. Br. J. Clin. Pharmacol. **49**(1), 71 (2000).
[7] B.Sudharani, P.Venkatareddy. E.J.Chem. **3**(12), 169 (2006).
[8] G.Srinubabu, B.Sudharani, J.V.L.N.Seshagiri rao. E.J.Chem. **3**(10), 9 (2006).
[9] C.S.Chauhan, P.K. Choudhury. Asian Journal of Chemistry. **19**(1), 819 (2007).
[10] A.Singh, B.M. Rao,G.R. Deshpande,S. Sangaraju,M.K. Srinivasu,M. Lalitha Devi, P.V.V. Satyanarayana, K.B.Chandrasekhar. Chromatographia. **65**, 191 (2007).