Int. J. Chem. Sci.: 8(4), 2010, 2168-2172

DETERMINATION OF OLANZAPINE IN TABLETS BY HPLC

J. V. L. N. SESHAGIRI RAO* and N. USHA RANI

Pharmaceutical Analysis Division, College of Pharmaceutical Sciences, Andhra University, VISAKHAPATNAM – 530 003 (A.P.) INDIA

ABSTRACT

An accurate and reproducible reverse phase high performance liquid chromatographic method has been developed for the estimation of olanzapine in its pure form as well as in its tablet dosage forms. The chromatography was carried out on a Kromasil C-18 column using a mixture of acetonitrile and phosphate buffer (30 : 70 v/v) as the mobile phase at a flow rate of 1.5 mL/min. The detection was done at 258 nm. The retention time obtained for the drug was 1.850 min. The method produced linear responses in the concentration range of 10 to 50 μg /mL of olanzapine. The method was found to be reproducible for analysis of the drug in tablets.

Key words: Olanzapine, Determination, Tablets, HPLC.

INTRODUCTION

Olanzapine (2–methyl–4–(4–methyl–1–piperzinyl)–10H–thieno [2,3b] [1,5] benzodiazepine is the most commonly prescribed second generation neuroleptic drug for the treatment of psychiatric patients suffering from schizophrenia[1,2]. A few HPLC methods have been reported earlier for the estimation of olanzapine[3-5]. The authors made an attempt to develop a more accurate, sensitive and validated HPLC method for estimation of olanzapine. The applicability of this method in determining the drug in commercial tablet dosage forms was also studied.

EXPERIMENTAL

Chromatographic conditions

A Shimadzu LC-2010 CHT high-performance liquid chromatographic instrument provided with a Shimadzu LC 2010 C series HPLC pump and a SIL LC 2010 C series auto sampler equipped with a 20 μL sample loop was employed in the study. A Kromasil ODS

*Author for correspondence; E-mail: jvlnsrao@gmail.com

reverse phase column (250 mm x 4.6 mm; 5μ) was used for the separation. Detection was done using an SPD LC 2010 C dual absorbance detector and the output signal was monitored and integrated using Shimadzu CLASS-VP Version 6.12 SPI software. Enertech ultra sonicator was used for sonication.

HPLC grade acetonitrile (Qualigens), A.R grade potassium dihydrogen phosphate and sodium hydroxide (Qualigens) were used for preparing the mobile phase. A freshly prepared 30 : 70 (v/v) mixture of acetonitrile and phosphate buffer (6.7 pH) was found to be the most suitable mobile phase for separation of the drug. The mobile phase was filtered through a 0.45 μm membrane filter and sonicated before use. The flow rate of the mobile phase was maintained at 1.5 mL/min. The column temperature was maintained at 50^0C. The detection of the drug was carried out at 258 nm.

Estimation of olanzapine

About 100 mg of working standard sample of olanzapine was weighed accurately, transferred into a 100 mL volumetric flask and dissolved in 50 mL of the mobile phase. The solution was sonicated for 15 min and then the volume was made up with a further quantity of the mobile phase to get a 1 mg/mL solution. Subsequent dilutions of this solution ranging from 10 to 50 μg/mL were made in 10 mL volumetric flasks with the mobile phase. Twenty micro liters of the solution was injected each time into the column. Each of the dilutions was injected five times into the column and the corresponding chromatograms were recorded. From these chromatograms, the retention times and the areas under the peaks of the drug were noted. The regression equation of the drug concentrations was computed. This equation was later used to estimate the amount of olanzapine in tablet dosage forms

Estimation of the drug in tablet dosage forms

Two commercial brands of tablets containing the drug (Olapin of Crescent Therapeutics and Olexar of Cipla) were chosen for testing the suitability of the proposed method to estimate olanzapine in tablet formulations. For this, twenty tablets were weighed and powdered. An accurately weighed portion of this powder equivalent to 100 mg of olanzapine was transferred into a 100 mL volumetric flask and dissolved in 50 mL of the mobile phase. The contents were allowed to stand for 30 min with intermittent sonication to ensure complete solubility of the drug and the volume was made up with a further quantity of the mobile phase. This solution was then filtered through a 0.45 μm membrane filter. Three mL of this filtrate was transferred to a 100 mL volumetric flask and the volume was made up with the mobile phase to get a 30 μg/mL solution. Twenty microlitres of this solution was then injected into the column. The mean peak area of the drug of five such

determinations was calculated and the drug content in the tablets was quantified using the regression equation obtained for the reference sample.

RESULTS AND DISCUSSION

The present study was aimed to develop a sensitive, precise and accurate HPLC method for the analysis of olanzapine in tablet dosage forms. For this, a binary mixture of acetonitrile and phosphate buffer (30 : 70 v/v) was found to be the most suitable mobile phase as the chromatographic peaks obtained with this system were better resolved and were almost free from tailing. Under the above mentioned conditions, the retention time obtained for olanzapine was 1.850 min. A typical chromatogram of the drug is shown in Fig. 1. The peak areas for different concentrations were calculated and are shown in Table 1.

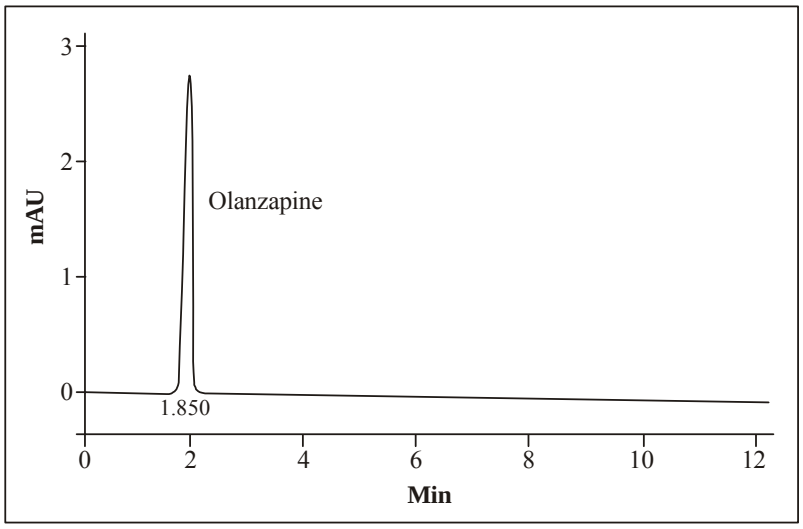

Fig. 1: A typical chromatogram showing separation of olanzapine

Table 1: Calibration of the proposed method

Concentration (μg/mL)	Peak area
10	5620312
20	11240625
30	16860937
40	22481250
50	25667593

A good linear relationship (r = 0.991) was observed between the concentrations of olanzapine and the respective peak areas. The curve shown in Fig. 2 was constructed by linear regression fitting and its mathematical expression is y = 51335 x + 97358 (where y is the peak area and x, the concentration of olanzapine). The intra-day and inter-day drug variation studies by the proposed method showed low coefficient of variation as shown in Table 2. The drug content in the tablets was quantified using the proposed method of analysis. The mean amount of olanzapine obtained in tablet dosage form is shown in Table 3. This reveals that the method is quite precise. The absence of additional peaks in the chromatogram indicated non-interference of the common excipients used in the tablets.

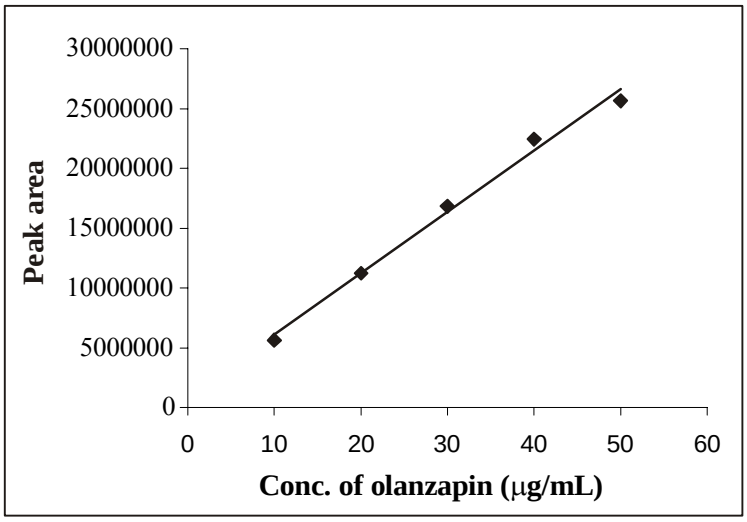

Fig. 2: Calibration curve for olanzapine

Table 2: Intra- and inter-day precision of the proposed method

Concentration of olanzapine (μg/mL)	Observed concentration of olanzapine (μg/mL)			
	Intra-day		Inter-day	
	Mean (n = 5)	Coefficient of variation (%)	Mean (n = 5)	Coefficient of variation (%)
2	1.970	0.066	1.970	0.055
4	3.944	0.072	3.960	0.065
6	5.970	0.071	5.960	0.056

Table 3: Recovery of olanzapine from tablet dosage forms

Brand name of the tablet	Labelled amount of drug (mg)	Mean (± S.D.) amount found by the proposed method (n = 5)	Mean (± S.D.) % of labelled amount (n = 5)
Olapin	10	9.944 ± 0.073	99.978 ± 0.081
Olexar	10	9.948 ± 0.071	99.960 ± 0.073

It can be concluded that the proposed HPLC method is accurate and reproducible for the analysis of olanzapine in tablet dosage forms in a short analysis time. The method was duly validated by evaluation of the required parameters.

ACKNOWLEDGEMENTS

The authors are thankful to M/s Nosch Labs Private Limited for providing a reference sample of olanzapine. They also acknowledge the laboratory facilities provided by M/s Startec Laboratories, Hyderabad for this study.

REFERENCES

1. S. H. Snyder, Am. J. Psychiatry., **133**, 197 (1976).
2. Goodman and Gilman's, The Pharmacological Basis of Therapeutics, 11th Edn., Mc Graw -Hill Co Inc. USA (2006) p. 482.
3. A. Manickam, A. Donna, C. W. William and R. M. Stephen, Therapeutic Drug Monitoring., **19**, 307 (1997).
4. J. A. Chiu and R. B. Franklin, J. Pharm. Biomed. Anal., **14**, 609 (1996).
5. T. C. John, D. B. Richard, C. Matt, A. G. Todd, G. Michael and P. S. Steven, J. Chromatogr. B. Biomed. Appl., **668**, 85 (1995).

Accepted : 12.04.2010