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RP-HPLC METHOD FOR QUANTITATIVE ESTIMATION OF OLANZAPINE IN TABLET DOSAGE FORMS

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ABSTRACT

A simple RP-HPLC method for the determination of olanzapine in pharmaceutical dosage forms. Numerous HPLC conditions were tested for determination of olanzapine. The best result was achieved by using Capcell pak C-18 (250×4.6mm) 5µm column and a mobile phase consisting of Acetonitrile: Water: Tri ethylamine (60:40:0.1 v/v/v), a flow rate of 1.0 ml/min with ultraviolet detection at 270nm. The retention time of the drug was 6.53 min. The method produced liner responses in the concentration range of 2 to 12µg/ml of olanzapine. The method was found to be applicable for determination of the drug in tablets.

KEYWORDS: **Olanzapine, Estimation, RP-HPLC, Validation, Tablets.**

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INTRODUCTION

Olanzapine, a thienobenzodiazepine derivative with chemical name 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2-3-b][1-5]benzodiazepine, (Figure 1) is a synthetic atypical antipsychotic agent used to treat schizophrenia and related disorders [1]. Olanzapine has high affinity for serotonin (5-HT_{2A}, 5-HT_{2C}), dopamine (D_1-D_4), muscarinic (M_1- M_5), α_1- adrenergic & histaminergic (H_1) receptor. Literature survey reveals that there were several papers on analysis of olanzapine by using UV-spectrophotometry[2], visible spectrophotometry[3,4,5], HPLC[6,7,8], HPLC-MS[9,10], GC-MS[11], electrochemical[12], and some analytical methods for determination of olanzapine in biological fluids and tissues [13,14,15].

Now the authors report a simple, reliable and reproducible RP-HPLC method which was duly validated by statistical parameters precision, accuracy and recovery. The method has been satisfactorily applied to the determination of olanzapine in pharmaceutical preparations.

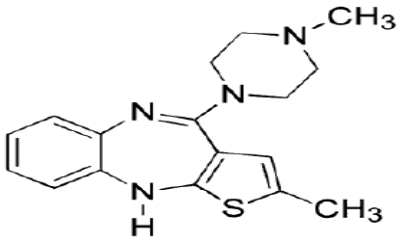

Figure- 1
Chemical structure of olanzapine

EXPERIMENTAL

Chemicals and solvents

HPLC grade Acetonitrile, HPLC grade Water and Tri ethylamine was used for mobile phase preparation. Pure sample of Olanzapine was a gift sample from a local pharmaceutical industry. Commercial samples of tablets containing the drug olanzapine were purchased from the local pharmacy.

Chromatographic Conditions:

A High pressure liquid chromatography (Cyber lab HPLC**)** with LC-P 100 pump, variable wavelength programmable UV-Visible detector LC- UV 100, system controller (Cyber lab) and Capcell pak C- 18 column was used. The HPLC system was equipped with the soft ware WS- 100 workstation (Cyber lab). A freshly prepared 60:40:0.1 v/v/v mixture of acetonitrile, water and tri ethylamine was used as the mobile phase. Acetonitrile, water and tri ethylamine were filtered through a 0.45 µm membrane filters and sonicated before use. The flow rate of the mobile phase was maintained at 1ml/min. The detection was carried out by UV detector at 270 nm.

Table 1
Method development conditions

CONDITION	MOBILE PHASE-A	MOBILE PHASE-B	RATIO OF A/B	OLANZAPINE RETENTION TIME	TAILING FACTOR
1	Acetonitrile	Water	50:50	6.78	1.57
2	Acetonitrile	Water	60:40	10.20	1.45
3	Acetonitrile	Water/Tri ethylamine	60:40:0.1	6.53	1.07

Estimation of Olanzapine

About 100 mg of olanzapine was weighed accurately and transferred into a 100 ml volumetric flask and dissolved in 50 ml mobile phase. The solution was sonicated for 20 min and then the volume was made up with a further quantity of the mobile phase to get a 1mg/ml solution. Subsequent dilutions of this solution ranging from 2 to 12µg/ml were made in 10 ml volumetric flasks with the mobile phase. 20 µl of the solution was injected each time into the column, at a flow rate of 1ml/min. Each of the dilutions was injected 5 times into the column and the corresponding chromatograms were obtained. 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 pharmaceutical dosage forms. To check the intra-day an interday variation of the method, solution containing 6 and 8 µg/ml of olanzapine were subjected to the proposed HPLC method of analysis and the recoveries were noted.

Estimation of the Drug in Tablet Dosage Forms:

Twenty tablets were weighed and powdered. An accurately weighed portion of this powder equivalent to 50 mg of olanzapine was transferred into a 50 ml volumetric flask containing 25 ml mobile phase. The contents were allowed to stand for half an hour with intermittent sonication to ensure complete solubility of the drug and then filtered through a 0.45µm membrane filter. Appropriate volume of this filtrate equivalent to 10 µg/ml of the drug was taken in a 10 ml volumetric flask. The contents of the flask were made up to the volume with the mobile phase and mixed well. 20 µl of the 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 pure sample.

RESULTS AND DISCUSSION

The present study was aimed at developing a sensitive, precise and accurate HPLC method for the analysis of olanzapine in pharmaceutical dosage forms. For this, a binary mixture of acetonitrile, water and tri ethylamine (60:40:0.1 v/v/v) portion was found to be the most suitable mobile phase as the chromatographic peaks obtained with this system were better defined and resolved and all almost free from tailing. Under the above mentioned conditions, the retention time obtained for olanzapine was 6.53min. A model chromatogram was shown in Figure 2. A good linear relationship (r = 0.9999) was observed between the concentration of olanzapine and respective peak areas. Table 2. The intra-day inter-day drug variation studies by the proposed method as shown in Table 3.The drug content in the tablets was quantified using the proposed method of analysis. The mean amount of olanzapine obtained in tablet dosage forms is shown in Table 4. The recovery studies by the proposed method as shown in Table 5. This reveals that the method is quite precise. The absence of additional peaks in the chromatogram indicated no interference of the common excipients used in the tablets. It can be concluded that the proposed HPLC method is sensitive and reproducible for the analysis of olanzapine in pharmaceutical dosage forms in a short analysis time. The method was duly validated by evaluation of the required parameters.

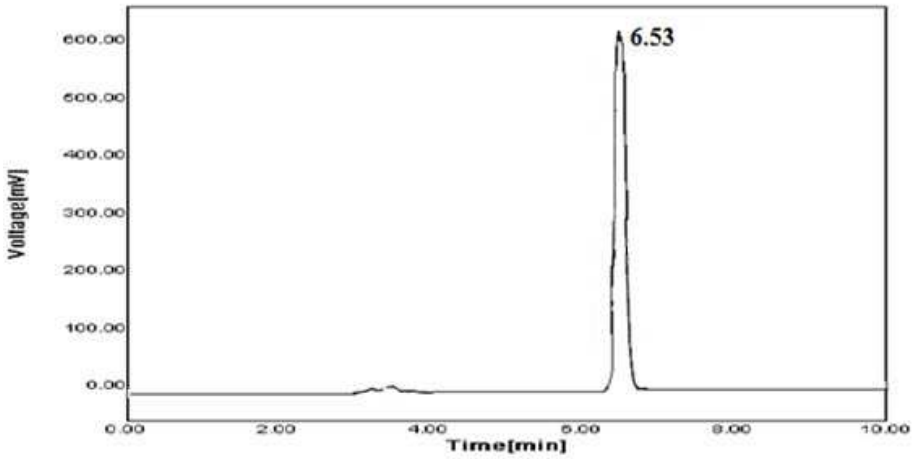

Figure – 2
A model chromatogram of Olanzapine

Table 2
Calibration of the proposed method

Linearity range (µg/ml)	2-12(µg/ml)
r^2 ± S.D.	0.9999

Table 3
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 *	%RSD	Mean *	%RSD
6	6.09	0.94	5.96	0.89
8	7.97	1.04	8.05	0.99

Table 4
Assay of Olanzapine in Tablet Dosage Forms

Brand	Labelled amount of drug(mg)	Amount found by proposed method (µg)	Amount found by proposed method (%)
Olip	5	4.9±0.2	99.85

Table 5
% Recovery Results for Olanzapine

Original concentration (µg mL^{-1})	Excess drug added to the analyte (µg.mL^{-1})	Drug found (µg.mL^{-1})	Recovery (%)	% RSD
10	8	17.98	99.92	0.86
10	10	19.85	99.95	0.94
10	12	22.02	100.05	1.25

CONCLUSION

A method was developed for the determination of olanzapine in tablets which is simple, quick, reliable, inexpensive and simple. The results indicate that the described method can be used for quantitative analysis of the compound.

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