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DEVELOPMENT OF HPLC METHOD FOR THE DETERMINATION OF OLANZAPINE IN BULK AND DOSAGE FORMS

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ABSTRACT : A reverse phase HPLC method is developed for the determination of olanzapine in pharmaceutical dosage forms. Chromatography was carried out on an inertsil C18 column using a mixture of ammonium phosphate buffer and methanol (70:30 v/v) as the mobile phase at a flow rate of 1 ml/min. Detection was carried out at 220 nm .The retention time of the drug was 3.447min. The method produced linear responses in the concentration range of 2 to 10µg/ml of olanzapine. The method was found to be applicable for determination of the drug in tablets.
KEY WORDS: HPLC, Olanzapine, Estimation, tablets.

INTRODUCTION:

Olanzapine(2-methyl-4-(4-methyl-1-piperazinyl)-10*H*-thieno-[2,3*b*][1,5]benzodiazepine), is the most commonly prescribed second-generation neurloteptic for the treatment of psychiatric patients suffering from schizophrenia. Since its introduction in a therapy of psychiatric disorders in 1997, the need for reliable, sensitive and fast methods for its analysis in bulk samples and pharmaceutical preparations is obvious. Several methods have been already reported for the determination of olanzapine, including hyphenated techniques: spectrophotometric[1-4], HPLC-MS[5,6], HPLC[7] , Capillary zone electrophoresis[7] and GC-MS[8].

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.

EXPERIMENTAL:

Chemicals and solvents:

Ammonium dihydrogen orthophosphate and orthophosphoric acid (AR grade, Qualigens) were used for preparing the buffer. HPLC grade methanol (Qualigens) 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 chromatograph (Shimadzu HPLC class VP series) with two LC-10 AT VP pumps, variable wavelength programmable UV-Visible detector SPD-10 A VP, SCL-10A VP system controller (Shimadzu) and C-18 column was used. The HPLC system was equipped with the soft ware Class VP series version 5.03 (Shimadzu).

A freshly prepared 70:30 v/v mixture of Ammonium phosphate buffer (2.5 pH) and methanol was used as the mobile phase. Buffer solution was prepared by dissolving 3 gms of Ammonium dihydrogen orthophosphate in 900ml of water. To this add 2mL of Triethyl amine and dilute to 1000ml with water. Adjust the pH to 2.5 with orthophosphoric acid. Both Ammonium phosphate buffer and methanol were filtered through a 0.45 µm membrane filter 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 220 nm.

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 15 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 10µg/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, solutions containing 4 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

Three commercial brands of tablets 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 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 ammonium phosphate buffer and methanol (70:30 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 3.447min. A model chromatogram was shown in Figure 1.

A good linear relationship (r = 0.9999) was observed between the concentration of olanzapine and respective peak areas. The regression curve was constructed by linear regression fitting and its mathematical expression was y =387136.2 - 5989.23 x (where 'y' is peak area and 'x' is the concentration of olanzapine). The regression characters were given in Table 2.

The intra-day inter-day drug variation studies by the proposed method showed low coefficient of variation, 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. 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.

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.

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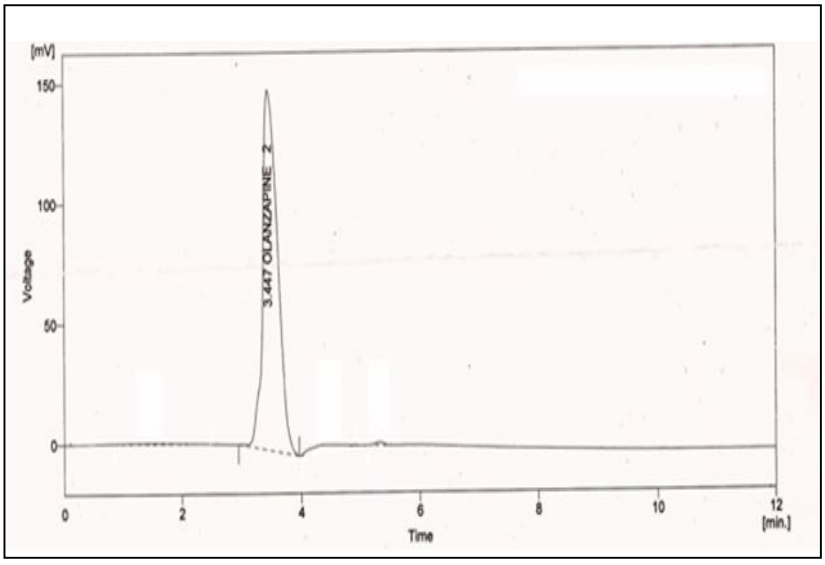

Figure - 1. A model chromatogram of Olanzapine

Table -1. Calibration of the proposed method

Concentration of Olanzapine (µg/ml)	**Mean Peak area(n=5)**
2	2658.731
4	5317.462
6	7976.193
8	10634.92
10	13293.66

Table - 2. Regression Characters of the Proposed HPLC Method

Parameters	**Value**
Relative standard deviation (%)	0.652
Regression equation	
Intercept (a)	0.808
Slope (b)	1.306 x 10^3
Standard deviation slope	0.657
Standard deviation of intercept	0.769
% Range of errors (95% confidence limits)	0.5450
0.05 significance level	0.8065
0.01 significance level	0.9999
Correlation coefficient®	

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***
4	3.97	1.09	4.04	0.89
8	8.06	0.98	7.93	0.94

Table - 4. Assay of Olanzapine in Tablet Dosage Forms

Brand	**Labelled amount of drug(mg)**	**Mean(±s.d) amount(µg) found by proposed method(n=5)**	**Mean (±s.d)% of recovery (n=5)**
Tablet I	2.5	2.48 ± 0.16	99.84 ± 0.39
Tablet II	5	5.01 ± 0.11	100.15 ± 0.22
Tablet III	7.5	7.49 ± 0.24	99.86 ± 0.10

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