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Spectrophotometric Determination of Olanzapine in Pharmaceutical Preparations

K.V. SIVA PRASAD, J.M. RAJENDRA KUMAR, M.V.V.N. REDDY, G. PRABHAKAR* and D.G. SANKAR

Pharmaceutical Analysis Division, Department of Pharmaceutical Sciences Andhra University, Visakhapatnam-530 003, India

Two simple and sensitive visible spectrophotometric methods (method A and B) have been described for the assay of olanzapine (OLP) in pure form and in pharmaceutical formulations. These methods are based on the oxidation followed by complexation between OLP and *o*-phenanthroline or potassium ferricyanide in presence of ferric chloride to form a coloured product with λ_{max} at 520 nm for method A and 760 nm for method B respectively. Beer's law limits, precision and accuracy of these methods are checked by the UV reference method. The results obtained are reproducible and are statistically validated and so found to be suitable for the assay of OLP in bulk and pharmaceutical formulations.

Key Words: Spectrophotometric, Determination, Olanzapine.

INTRODUCTION

Olanzapine (OLP) is an antipsychotic agent that belongs to the thienbenzodiazepine class. The chemical designation is 10H-thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl). The mechanism of action of OLP, as with other antipsychotic drugs, is unknown. However, it has been proposed that this drug's antipsychotic activity is mediated through a combination of dopamine and serotonin type 2 ($5HT_2$) antagonism. Antagonism at receptors other than dopamine and $5HT_2$ with similar receptor affinities may explain some of the other therapeutic and side effects of OLP. OLP's antagonism of muscarinic M_{1-5} receptors may explain its anticholinergic effects. OLP's antagonism of histamine H_1 receptors may explain the somnolence observed with this drug. OLP's antagonism of adrenergic alpha$_1$ receptors may explain the orthostatic hypotension observed with this drug.

A number of methods such as HPLC[1–5], mass[6,7] were reported for the estimation of OLP. Literature survey revealed that visible spectrophotometric methods are not reported for its quantitative determination in bulk and pharmaceutical formulations. Although spectrophotomeric methods are the instrumental methods of choice commonly used in industrial laboratories, no colorimetric method has been reported so far for the determination of OLP. Therefore the need for a fast, low cost and selective method is obvious, especially for routine quality

control analysis of pharmaceutical formulations, containing OLP. Ferric salts (ferric chloride) play a prominent role in the colorimetric determination of organic compounds. Acting as an oxidant a ferric salt converts into ferrous salt. They can be easily detected by the usual reagent for divalent iron, potassium ferricyanide $K_3[Fe(CN)_6]$, *ortho*-phenanthroline (*o*-PTL), bipyridyl or triazine. We have applied the above two reagents (*o*-PTL-Fe(III) and Fe(III)-$K_3[Fe(CN)_6]$ for the determination of OLP in bulk sample and pharmaceutical formulations.

EXPERIMENTAL

A Systronics model 117 UV-visible spectrophotometer with 1 cm matched quartz cells was used for spectral and absorbance measurements in the UV and visible regions respectively. All the reagents and chemicals used were of analytical grade. Aqueous solutions of Fe(III) (Wilson, 1.10×10^{-2}), $K_3[Fe(CN)_6]$ (BDH, 3.02×10^{-3}), *o*-PTL (Merck, 1.10×10^{-2}), orthrophosphoric acid (Qualigens, 2.0×10^{-2}) were prepared by dissolving the required amounts in triple distilled water. The commercially available tablets were procured from the local market.

Standard and sample solutions: Stock solution (1 mg/mL) of OLP was prepared by dissolving 100 mg of OLP (bulk or tablet powder equivalent) initially in 10 mL of 0.1 M HCl followed by dilution to 100 mL with distilled water. Working solutions of OLP were prepared by stepwise dilution of each stock solution with distilled water to get suitable concentrations of OLP (20 μg/mL) for methods A and B respectively.

Assay

Method A: Aliquots (10–50 μg/mL) of the standard OLP solution were transferred into a series of 10 mL calibrated flasks. Then solution of 1.5 mL of Fe(III) and 2.0 mL of *o*-PTL was added successively. The total volume in each flask was brought to 10.0 mL with distilled water and heated for 30 min in a boiling water bath. After cooling to room temperature, 2.0 mL of orthophosphoric acid was added; the volume in each flask was made up to the mark with distilled water. The absorbances of the coloured complex solution were measured after 5 min at 520 nm against a reagent blank prepared similarly. The amount of the drug was computed from the Beer-Lambert plot.

Method B: Into a series of 10 mL calibrated tubes, aliquots of standard OLP solution (10–50 μg/mL) were transferred and 1.0 mL of Fe(III) solution was added. The tubes were stoppered immediately and shaken well for 5 min. Then 0.5 mL of $K_3[Fe(CN)_6]$ solution was added into each tube. After 5 min 1.0 mL of 1 N HCl was added and final volume was made up to 10 mL with distilled water. The absorbance of the solution in each tube was measured immediately at 740 nm against the similar reagent blank.

Assay of pharmaceutical formulation

Tablets powder equivalent to 100 mg was taken and the sample solution prepared as described for the standard solution and filtered if insoluble material was present prior to analysis as described for pure samples.

RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, molar absorptivity and Sandell's sensitivity for these methods are given in Table-1. The precision of each method was found by measuring absorbances of six replicate samples containing known amounts of drug and the results obtained are incorporated in Table-1. Regression analysis using the method of least squares was made to evaluate the slope (b), intercept (a) and correlation coefficient (R) for each system (Table-1). The relative standard deviation and % range of error at 95% confidence level are also given in Table-1. The accuracy of the methods was ascertained by comparing the results by reference method (UV) statistically. This comparison shows that there is no significant difference between the results of studied methods and those of reference ones. The similarity of the results is an obvious evidence that during the application of these methods, the excipients that are usually present in pharmaceutical formulations do not interfere in the assay of proposed methods.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

Parameters	Method A	Method B
λ_{max} (nm)	520	760
Beer's law limit (μg/mL)	1–6	1–6
Sandell's sensitivity (μg/cm^2/0.001 abs. unit)	0.0093	0.0094
Molar absorptivity (L mole^{-1} cm^{-1})	3.34×10^4	3.31×10^4
Regression equation (Y*)		
Slope (b)	0.108	0.107
Intercept (a)	–0.0012	–0.0049
Correlation coefficient (r)	0.9997	0.9999
% RSD	0.732	0.653
% Range of error (0.05 level confidence limit)	0.768	0.682

Y = a + bX where X is the concentration of OLP in μg/mL and Y is the absorbance at the respective λ_{max}.

TABLE-2

Sample* (Tablets)	Labeled method (mg)	Amount obtained (mg)				
		UV* method	Proposed method		Recovery (%)	
			A	B	A	B
T_1	5	4.92	4.94	4.92	98.8	98.4
T_2	10	9.86	9.82	9.88	98.2	98.8

*Tablets from different manufactures

Chemistry of coloured species: Methods A and B depend upon the oxidation of OLP with Fe(III) and subsequent coloured complex formation of the resulting Fe(II) ion with *o*-PTL or $K_3[Fe(CN)_6]$. *o*-PTL forms a complex of low

tinctorial value with Fe(III) which in turn functions as a better oxidant than Fe(III), well known as ferrion. In conclusion the proposed methods are simple, sensitive, accurate and useful for the routine determination of OLP in pure samples and in pharmaceutical formulation.

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