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FIRST AND SECOND DERIVATIVE SPECTROPHOTOMETRIC METHODS FOR DETERMINATION OF OLANZAPINE IN PHARMACEUTICAL FORMULATION

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ABSTRACT: Simple, fast and reliable derivative spectrophotometric methods were developed for determination of olanzapine in bulk and pharmaceutical dosage forms. The solutions of standard and the sample were prepared in methanol. The quantitative determination of the drug was carried out using the first derivative values measured at 222 nm and the second derivative values measured at 230 nm (n=6). Calibration graphs constructed at their wavelengths of determination were linear in the concentration range of olanzapine using 2-10 µg/ml for first and second derivative spectrophotometric method. The calibration graphs constructed at their wavelength of determination were found to be linear for UV and derivative spectrophotometric methods. All the proposed methods have been extensively validated as per ICH guidelines. There was no significant difference between the performance of the proposed methods regarding the mean values and standard deviations. Developed spectrophotometric methods in this study are simple, accurate, precise, specific, sensitive, reproducible and can be directly and easily applied to pharmaceutical dosage form.
Keywords: Olanzapine, Derivative spectrophotometric, First derivative spectrum,Second derivative spectrum.

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 in biological fluids and tissues[2, 3, 4, 5]. Most analyses were based on the use of HPLC with UV[6, 8,] electrochemical[9, 10] coulometric detection[11] and mass spectrometric[12], amperometric detection[13]. There are no derivative spectrophotometric methods reported for the analysis of olanzapine in pharmaceutical formulation. Derivative spectrophotometry is an analytical technique of great utility for extracting both qualitative and quantitative information from spectra composed of unresolved bands, and for eliminating the effect of baseline shifts and baseline tilts. It consists of calculating and plotting one of the mathematical derivatives of a spectral curve. Derivative spectrophotometry is now a reasonably prized standard feature of modern micro-computerized UV spectrophotometry. The aim of the present research work was to develop simple, sensitive and validated derivative spectrophotometric methods for the determination of olanzapine in pharmaceutical formulation.

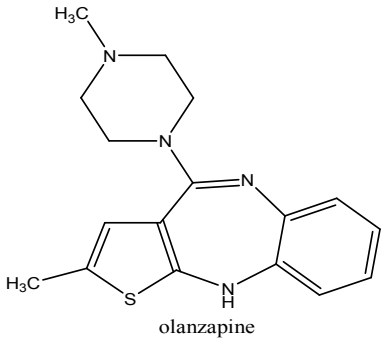

Figure 1. Chemical structure of olanzapine

EXPERIMENTAL

MATERIALS AND METHODS

Ranbaxy Laboratories Ltd. (Dewas, India) kindly supplied pure drug sample of olanzapine as a gift sample of Batch No.: 1764032. It was used without further purification and certified to contain 99.5 % (w/w) on dry weight basis. All chemicals and reagents used were of analytical grade and were purchased from Merck Chemicals,
India.

INSTRUMENTATION

UV and derivative spectra of the solutions were recorded on double beam UV–Vis spectrophotometer Jasco V-530 using 10mm path length quartz cells with fixed slit width of 2 nm at a scanning speed of 1000 nm/min scan range of 200–400 nm, data
pitch 0.5 nm.

PREPARATION OF STANDARD AND SAMPLE SOLUTIONS:

Stock solution of 1000 µg/ml of olanzapine was prepared in methanol, for first and second derivative spectrophotometric analysis. The standard solutions were prepared by dilution of the stock solution with methanol in a concentration range of 2, 4, 6, 8 and 10 µg/ml with methanol for first and second derivative spectrophotometric methods. Methanol was used as a blank solution.

ASSAY PROCEDURE:

A total of 20 tablets of olanzapine were accurately weighed and powdered. An amount of tablet triturate equivalent to label claim of olanzapine was weighed and transferred in 10 ml calibrated volumetric flask, diluted with methanol stirred for about 45 min and then volume made up with methanol. This solution was filtered to remove any insoluble matter. The filtrate was collected in a clean flask. Appropriate dilutions were made to obtain 10 µg/ml with methanol from stock solution for both UV and derivative spectrophotometric methods.

RESULTS AND DISCUSSION

The UV, first and second derivative spectra for olanzapine were recorded at the wavelength of 270nm, 222 nm, 230nm respectively (Figures 2-4).

LINEARITY AND RANGE:

Under the experimental conditions described, the graph obtained for UV, first, second derivative spectra showed linear relationship. Regression analysis was made for the slope, intercept and correlation coefficient values. The regression equations of calibration curves were $y = 0.1784x + 0.0195$ ($r^2 = 0.9989$) at 222 nm, and $y = 0.183 x -$
0.0145 ($r^2 = 0.9994$) at 230 nm for first and second derivative spectrophotometry respectively. The range was found to be 2-12 µg/ml for first and second derivative spectrophotometric methods. The statistical parameters given are the regression equation calculated from the calibration graphs (Table 1).

PRECISION:

To determine the precision of the method, olanzapine solutions at a concentration of 2, 4, 6 µg/ml were analyzed each six times. Solutions for the standard curves were prepared fresh everyday (Table 2).

ROBUSTNESS AND RUGGEDNESS:

For robustness and ruggedness of analytical methods the tests mentioned below were carried out. The robustness of developed methods was tested by changing parameters such as degree of derivation, wavelength range and N value and the optimum parameters were chosen for this study. The UV and derivative spectrophotometric determinations of olanzapine were carried out by two different analysts on the same instrument with the same standard. The results showed no statistical differences suggesting that the developed methods were robust and rugged (Table 3).

SPECIFICITY:

Comparison of the UV spectrum with first and second derivative spectrum of olanzapine in standard and drug formulation solutions showed that the wavelength of maximum absorbance did not change. According to the results obtained by recovery study (Table 4), the derivative spectrophotometric method is able to access the analyte
in presence of excipients and hence, it can be considered specific.

SENSITIVITY:

The limit of detection (LOD) and limit of quantification (LOQ) were calculated by using the equations $LOD = 3 \times \sigma / S$ and $LOQ = 10 \times \sigma / S$, where σ is the standard deviation of intercept, S is the slope. The LOD and LOQ were found to be 500 ng/ml and 166.6 ng/ml respectively for first derivative and The LOD and LOQ were found to be 499 ng/ml and 159.2 ng/ml for second derivative respectively.

RECOVERY STUDY

To study the accuracy of the proposed methods, and to check the interference from excipients used in the dosage forms, recovery experiments were carried out by the standard addition method. This study was performed by addition of known amounts of olanzapine to reanalyzed solutions of commercial tablets (Table 4).

ANALYSIS OF THE MARKETED FORMULATION

The drug samples extracted from tablets. There was no

interference from the excipients commonly present in the tablets. The drug content was found to be 100.64± 0.88% and 100.11± 0.70% for first derivative and second derivative spectrofotometry respectively with a % R.S.D. of 0.69 and 0.95 for first derivative and second derivative spectroscopy respectively. It may therefore be inferred that degradation of olanzapine had not occurred in the marketed formulations that were analyzed by this method. The low
% R.S.D. value indicated the suitability of this method for routine analysis of olanzapine in pharmaceutical dosage form (Table 5).

The summary of the validation parameters is depicted in (Table 6).

CONCLUSION

No UV or derivative spectrophotometric methods have been described for the determination of olanzapine. Therefore simple, fast and reliable derivative spectrophotometric methods were developed for the routine determination of olanzapine. The developed methods can be concluded as accurate, sensitive and precise and can be easily applied to the pharmaceutical formulation.

Table 1: Stastical data for the calibration graphs for determination of olanzapine by proposed methods

Parameters	First derivative	Second derivative
Linearity range (μg.mL^{-1})	2-12	2-12
r^2 ± S.D.	0.9989	0.9994

[a] n=6.

Table 2: Results of Intra and Inter Day Precision

Parameters	Intra Day Precision		Inter Day Precision	
	S.D of areas	% RSD	S.D of areas	% RSD
First derivative	0.0031	0.82	0.0029	0.75
Second derivative	0.0084	0.96	0.0056	0.83

[a] n = 6

[b] Average of three concentrations 2, 4, 6 μg/ml.

Table 3: Data of recovery studies

Original concentration (μg mL^{-1})	Excess drug added to the analyte (μg.mL^{-1})	Drug found (μg.mL^{-1})	Recovery (%)	% RSD
First derivative spectrophotometric method				
10	8	17.96	99.82	0.82
10	10	20.14	100.70	1.20
10	12	22.04	100.20	0.96
Second derivative spectrophotometric method				
10	8	18.05	100.29	1.02
10	10	19.94	99.97	0.69
10	12	22.11	100.50	0.58

[a] n = 6,

[b] Matrix containing 5 mg drug.

Table 4: Results of analysis of olanzapine by different analyst

Parameters	X			Y		
	Found	SD	RSD	Found	SD	RSD
Standard ($10\mu g\ ml^{-1}$) First derivative	10.329	0.093	0.52	9.93	0.104	0.58
Standard ($10\mu g\ ml^{-1}$) Second derivative	10.007	0.49	0.85	9.45	0.110	0.61

X and Y are different analyst
SD is standard deviation
RSD is relative standard deviation

Table 5: Assay results for the determination of olanzapine in pharmaceutical formulation

Parameters	Tablet brand name	Drug Content (%)	%RSD
First derivative method	Oleanz 5mg	100.64	0.69
Second derivative method	Oleanz 5mg	100.11	0.95

[a] n=6, Average of three concentrations 2, 4, 6 µg/ml

Table 6: Summary of validation parameters

Parameters	Results	
	First Derivative	Second derivative
Wavelength (nm)	222	230
Linearity range (µg/ml)	2-12	2-12
Correlation coefficient	0.9989	0.9994
Recovery (n=6) Mean recovery % RSD %	 100.24 0.9933	 100.01 0.7633
Precision (n=6) Intraday (RSD %) Interday (RSD %) LOD (ng/ml) LOQ (ng/ml)	 0.82 0.75 500 166.6	 0.96 0.83 499 159.2

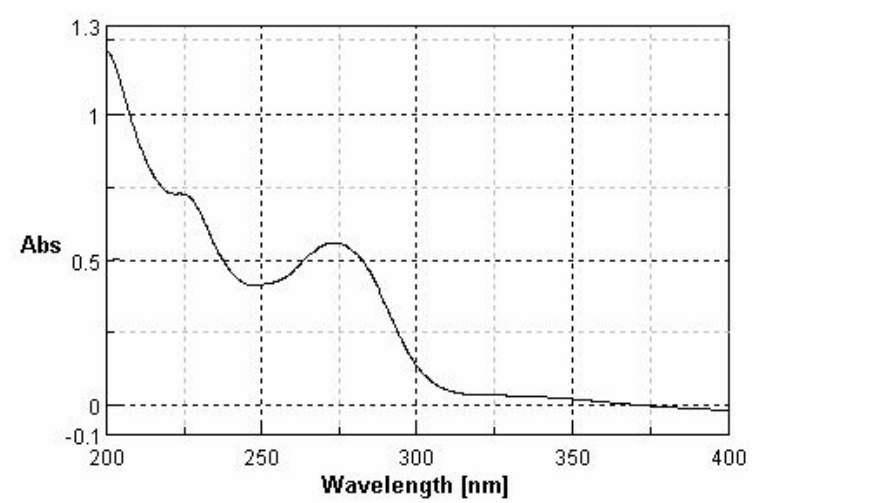

Figure 2. UV spectrum of 10 µg.mL^{-1}olanzapine in methanol

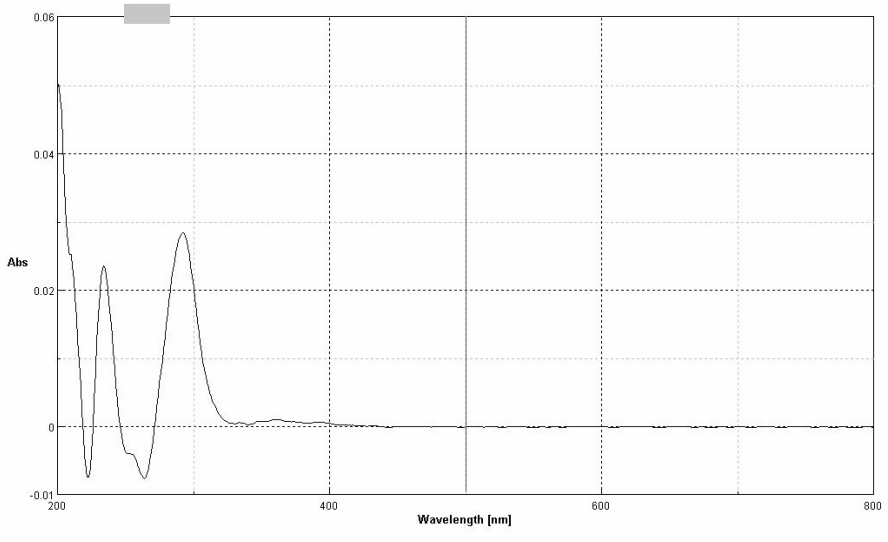

Figure 3. First derivative spectrum of 10 µg.mL^{-1}olanzapine in methanol

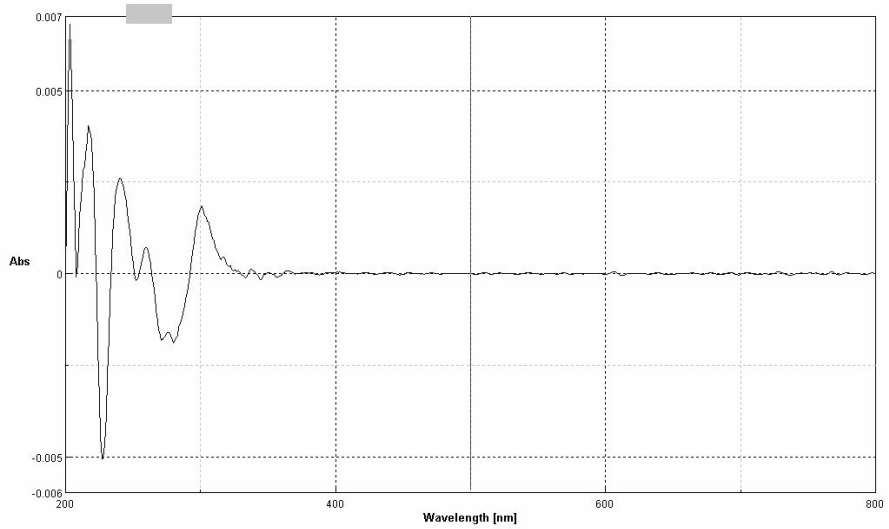

Figure 4. Second derivative spectrum of 10 µg.mL^{-1}olanzapine in methanol

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