



## Derivative Spectrophotometric Method for Determination of Lamotrigine and Risperidone in Pharmaceutical Dosage Forms

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Received: March 28, 2020

Published: May 31, 2020

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### Abstract

This work proposes a method for simple spectrophotometric determination of Lamotrigine (LMT) in presence of Risperidone (RSP) was accomplished using second derivative spectrophotometry. In the present method, neither a chromogenic reagent nor any other reagents are required. Excipients with drug molecule do not interfere with the determination. The Lamotrigine can be determined in the range of 1.0 -20 µg/mL. All other analytical parameters are established. The proposed method was more appropriate to the pharmaceutical formulation for the determination of Lamotrigine.

**Keywords:** Lamotrigine; Risperidone; Second Derivative Spectrophotometry

### Introduction

Lamotrigine (LMT) is a 6-(2, 3-dichlorophenyl)-1, 2, 4-triazine-3, 5-diamine used for the treatment of acute epilepsy and bipolar disorder. Neurological lesions are treated with LMT as a tranquilizer [1]. Planar chromatography [2], TLC and HPLC [3], HPLC-EMS [4], GC-MS [5], capillary electrophoresis [6], radio-immunoassay [7], adsorptive stripping voltammetry [8], polymer-carbon paste electrode [9], micellar electrokinetic capillary chromatography [10], LC-tandem mass spectrometry [11] and UV-spectrophotometric method [12-14] are commonly used analytical techniques for the determination of LMT drug in pharmaceuticals.

Risperidone (RSP) is a benzisoxazole derivative used for the treatment of acute and chronic schizophrenia psychoses and other psychotic conditions. Mania in bipolar disorder treated with RSP. Analytical techniques used for the determination of risperidone are differential pulse polarography [15], chemiluminescence assay [16], HPLC-ESI [17], chiral chromatography [18], LC-MS [19,20], LC-tandem mass spectrometry [21], LC with electrochemical de-

tection [22,23], LC with UV detection [24], LC with coulometric detection [25] and visible spectrophotometric method [26].

HPLC methods are very sensitive but need sophisticated instrumentation and skilled hands. In differential pulse voltammetric methods, the adsorption of the drug on the electrode surface has not been sufficiently strong. Using absorbance ratios at certain wavelengths or solving two simultaneous equations to treat interferences [27]. However, the intrusion or overlying spectra would indeed over results that cannot be reproducible. Other approaches like pH induced differential spectrophotometry, least squares and orthogonal function methods aimed at solving this problem. The derivative spectrophotometry can be a constructive means overlying spectra and eradicating matrix interferences in the evaluation of components in a mixture by selecting the optimum working wavelength for maximum absorption spectra or zero crossing technique. In addition, the component being determined should make a reasonable contribution to the total derivative reading of the mixture at the selected wavelength. Two components mixtures analy-

sis can be accepted out without solving simultaneous equation in derivative spectrophotometric method.

This is a nonmathematical method for finding and eradicating redundant absorption during photometric studies. Spectrophotometry method has numerous advantages in UV and visible regions for differentiation of absorption spectra. It is the essential for the possible improvement of resolution of overlaid bands. It facilitates the finding of weakly determined absorption peaks occurred from commixtures or impurities in solution or due to structural rationales. It facilitates the accurate determination of  $\lambda_{\max}$  of the particular constituents and increases the sensitivity of the spectrophotometric procedure. Background exclusion method is a distinctive inclusion of Derivative spectrometry. Scattering Rayleigh significance, stable background absorbance, accessory ingredients are eliminated and the intensity of the signal to noise ratios is enhanced [28]. Ojeda, *et al.* [29] analyzed the basis, usefulness, and function of this method. This technique offers various advantages over the conventional absorbance methods such as: the discrimination of the sharp spectral features over the large bands and the enhancement of the resolution of overlapping spectra. As a result, derivative spectrophotometry usually provides much better spectra than the traditional absorbance spectra. In addition, derivative spectrophotometry has more preferences because of its simplicity, sensitivity, selectivity, rapid reaction time and unaffected by an error from various sources that affect the precision and accuracy of spectrophotometric quantification. In view of advantages of derivative spectrophotometry, in present work we reported the determination of LMT in pharmaceutical formulations not by using expensive instruments.

## Materials and Methods

### Instrument

UV-visible Spectrophotometer with 10 mm matched quartz cells were used for absorbance measurement. Absorbance was measured in 1 cm quartz cuvettes using a double beam UV-1800 ultraviolet-visible spectrophotometer (Shimadzu, Japan).

### Chemicals and reagents

All chemicals used were of analytical reagent grade. LMT and RSP were received from Jubilant Organosys Ltd., Nanjangud, Mysore, India, purity 99.6% and 99.5% respectively as a gift sample.

### Standard solution

A Standard stock solution of LMT (100  $\mu\text{g}/\text{ml}$ ) and RSP (100  $\mu\text{g}/\text{ml}$ ) were prepared by dissolving 10 mg of LMT in 0.1M sulfuric acid and risperidone in ethanol respectively diluted to 100 ml with distilled water.

### Recommended procedure

Different concentrations of the standard LMT solution (1.0 - 20  $\mu\text{g}/\text{ml}$ ) and RSP (5.0 - 20  $\mu\text{g}/\text{ml}$ ) were transferred separately into a sequence of 10 ml volumetric flasks and diluted up to the mark with distilled water. The absorbance of each solution (LMT and RSP) were measured by transferred into 10 mm quartz cuvettes.

## Results and Discussion

Absorption spectrum originating from electronic transitions between various energy states of a molecule due to absorption of energy in UV or Visible regions is the fundamental basis of UV-Vis spectrophotometry. The second derivative amplitude for LMT and fourth derivative for RSP was observed at 309 nm and 291 nm respectively. The calibration graphs were plotted (Figure 1 and 2) and the method was applied for the determination of LMT and RSP in pharmaceutical formulations.

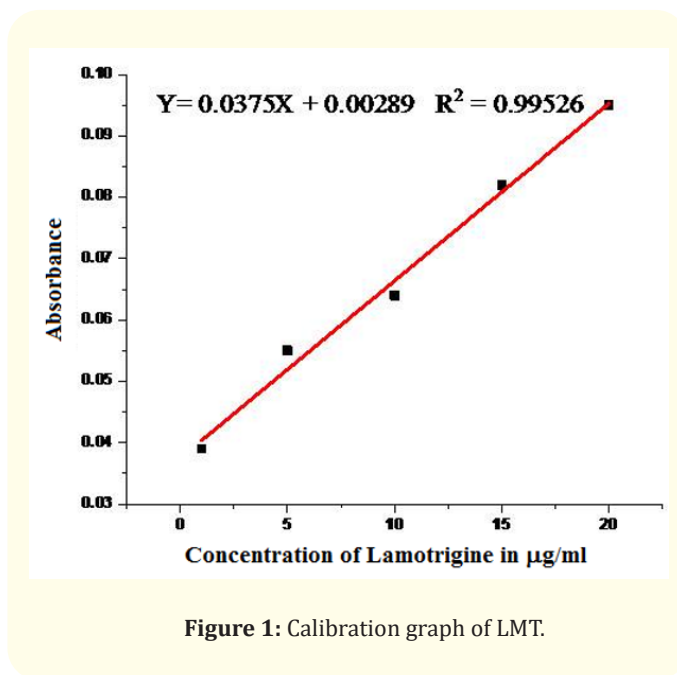


Figure 1: Calibration graph of LMT.

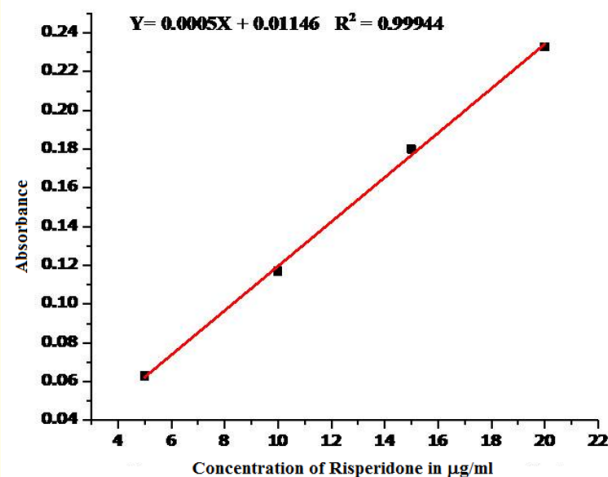
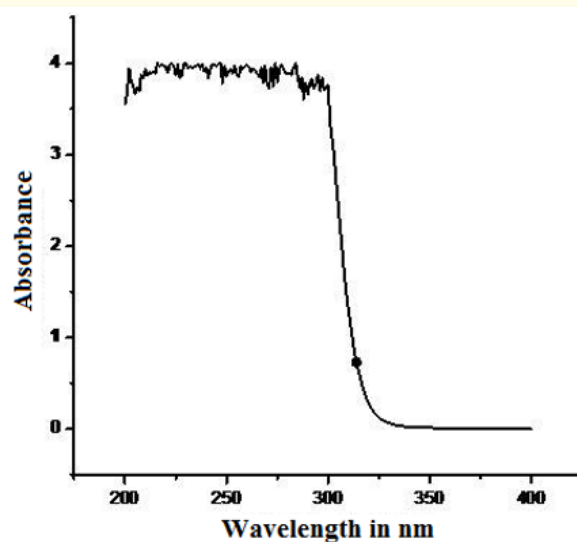


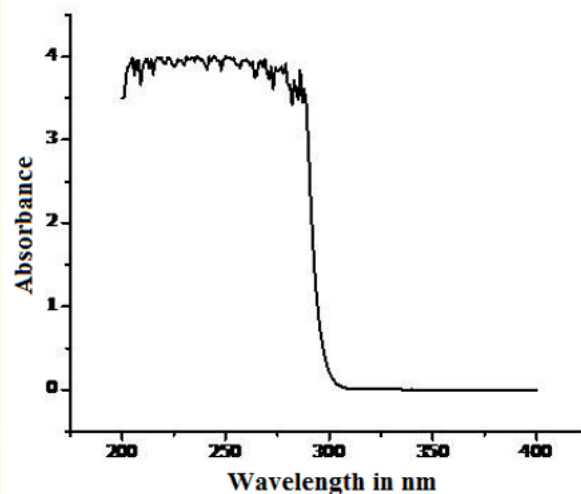
Figure 2: Calibration graph of RSP.

Figure 3a and 3b presents absorption spectra of LMT and risperidone and by a simple measurement of absorbance, it is not possible to determine the concentration of an analyte. The significant property of derivative spectrophotometry is the dependence of the derivative value of concentration of analytes. Differentiation allows us to acquire better knowledge holding in the basic absorption spectrum (Figure 3). As a result, it is possible to identify the differences in the positions of peaks (Figure 4). LMT was determined using a second derivative spectrophotometric method based on baseline-to-peak measurement of a derivative signal at 309 nm. RSP was determined using a fourth derivative spectrophotometric method with a derivative signal at 291 nm since at fourth derivative noise levels are very low. The second derivative curve shows a peak at 309 nm and the derivative amplitudes for LMT in the range of 1.0 - 20 µg/ml in the final measured solutions was plotted which gave linear plots. The fourth derivative curve shows peak at 291 nm and the derivative amplitudes for RSP in the range of 5.0 - 20 µg/ml in the final measured solutions was plotted which gave linear plots. From the second and fourth derivative curves, we were able analyzed that, LMT and RSP absorb strongly at 309 nm and at 291 nm respectively. Analytical parameters like correlation coefficient values are summarized in table 1.

The proposed method was applied to determine the LMT in pharmaceutical formulations. The powder equivalent to 10 mg of



a



b

Figure 3: Absorption spectrum of (a) LMT (b) RSP.

LMT and RSP were weighed separately and dissolved in 0.1M sulfuric acid and ethanol respectively. The residues were filtered into 100 ml calibrated flask and volume was made up to the mark with distilled water. An appropriate dilute solution was analyzed according to the suggested procedure and results agree very well with the certified as well as reported values. The values are summarized in table 2.

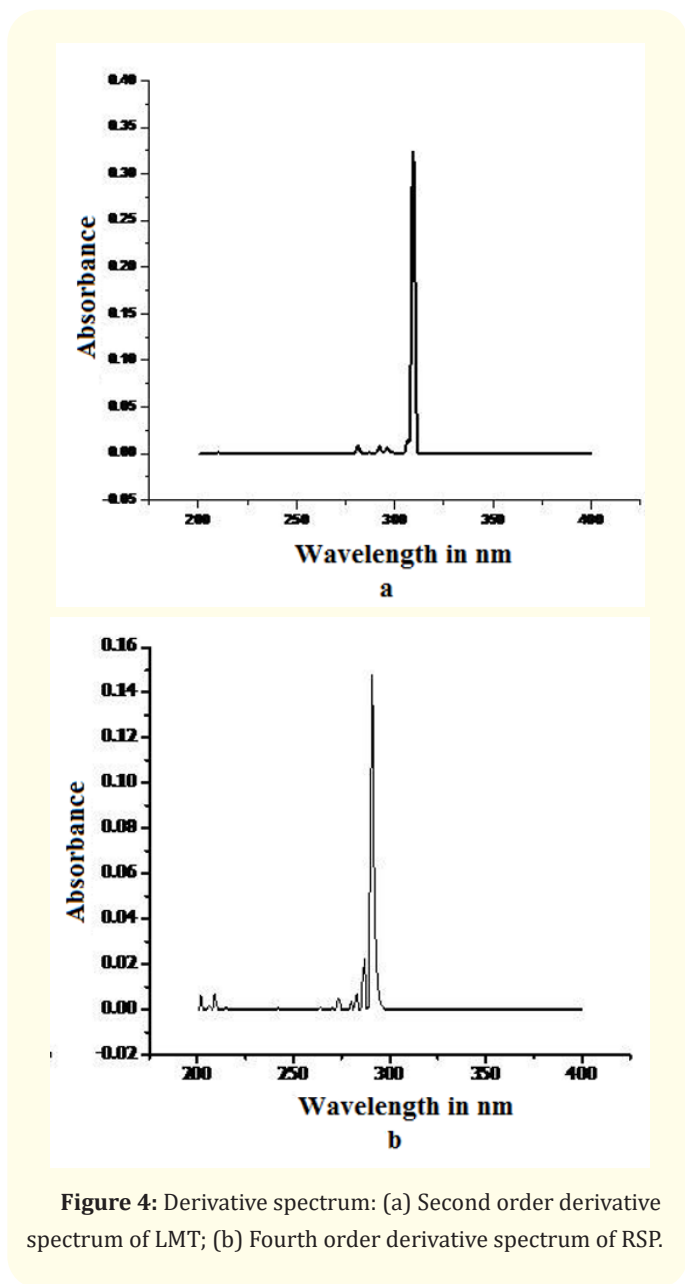


Figure 4: Derivative spectrum: (a) Second order derivative spectrum of LMT; (b) Fourth order derivative spectrum of RSP.

Parameters	LMT	RSP
Concentration range (µg/ml)	1.0 - 20	5.0 - 20
Wavelength λ, nm	309*	291*
Derivative order	2	4
Correlation coefficient (r)	0.99526	0.99944
<b>Regression equation</b>		
Slope (b)	0.03752	0.0055
Intercept (a)	0.00289	0.01146

Table 1: Analytical characteristics of the proposed procedure.

\*Peaks used in Second order derivative.

Pharmaceutical formulation	Label Claim (mg)	Amount found (mg) <sup>a</sup> Proposed Method
<sup>b</sup> Lamosyn-100	100	99.90
<sup>b</sup> Lamosyn-25	25	24.50
<sup>c</sup> Lamotec-50 DT	50	49.40
<sup>d</sup> Lamepil	50	49.70
<sup>e</sup> Lamez OD	50	49.60
<sup>f</sup> Lamidus-DT	50	50.20
<sup>g</sup> Lamitor	50	49.30
<sup>h</sup> Lamone	50	49.40
<sup>i</sup> Risperdal	2	2.02
	1	1.05
<sup>j</sup> Rispond	2	2.03
	3	3.01

Table 2: Analysis of pharmaceutical formulations.

<sup>a</sup>: Mean of five determinations.

Marketed by: <sup>b</sup>: Sun Pharma; <sup>c</sup>: Cipla; <sup>d</sup>: Innova; <sup>e</sup>: Intas; <sup>f</sup>: Zydus Cadila; <sup>g</sup>: Torrent; <sup>h</sup>: Bondane Pharma; <sup>i</sup>: Johnson and Johnson and <sup>j</sup>: Micro labs.

### Effect of excipients

The effect of excipients on the derivative amplitude were investigated by observing any interference encountered from common dosage from excipients such as starch, glucose, cellulose, lactose and talc present in tablet formulations. It was shown that these compounds at different concentrations did not interfere with results in the second-order derivative method.

### Conclusion

A Second derivative spectrophotometric method based on baseline-to-peak measurement techniques of a derivative signal was proposed for the determination of LMT in pharmaceutical solutions. The proposed method requires neither reagents nor any toxic or costly solvents, only doubled distilled water was used throughout the experiments. The determination was carried out at normal laboratory temperature. The method is accurate since experimental values are in accord with the certified values. This method could be regarded as a useful alternative to the earlier reported methods in the routine quality control of pharmaceutical formulations, allowing qualitative and quantitative determinations and rapidly achieved with a relatively inexpensive instrumentation.

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