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ESTIMATION OF DOMPERIDONE IN BULK AND FORMULATION BY FIRST ORDER DERIVATIVE AREA UNDER CURVE UV-SPECTROPHOTOMETRY METHODS

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Abstract

Simple, fast and reliable spectrophotometric methods were developed for determination of Domperidone 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 order Derivative Area under Curve method values measured at 289-307nm. Calibration graphs constructed at their wavelengths of determination were linear in the concentration range of Domperidone using 5-25µg/ml (r^2=0.999) for first order Derivative Area under Curve spectrophotometric method. 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. The developed methods were successfully applied to estimate the amount of Domperidone in pharmaceutical formulations.

Keywords: Domperidone, First order Derivative, Area under Curve (AUC), Accuracy, Precision.

Introduction

Domperidone is chemically known as 5-Chloro-1-[1-[3-(2-oxo-2, 3-dihydro-1H benzimidazol-1-yl)propyl]-4-piperidyl]-1,3-dihydro-2H-benzimidazol-2-one.[1,2] Domperidone is an Antiemetic drug used to treat nausea and vomiting and to stimulate lactation in women. It is used in the inhibition of receptive relaxation, causes enhancement of coordinated antral-duodenal motility and results acceleration of transit in the small intestine. [3, 4] It stimulates gastro-intestinal motility and is used as an antiemetic for the short term treatment of nausea and vomiting of various aetiologies, including that associated with cancer therapy and with levodopa or bromocriptine therapy for Parkinsonism. In our Literature survey reveals that for Domperidone Spectrophotometric [5] methods and HPLC [6, 7] methods have been reported for its determination in commercial formulation. To our notice, no UV-

spectrophotometric method using First Order Derivative Area under Curve has been reported for the determination of Domperidone in bulk and tablets. Hence an attempt has been made to develop new First Order Derivative Area under Curve spectrophotometric method for estimation of Domperidone in bulk and pharmaceutical formulations with good accuracy simplicity, precision and economy.

Materials and Methods

Derivative Spectrophotometric Methods

The first derivative spectrophotometry was used in the wavelength ranges from 289 and 307 nm.

[$dA/d\lambda = f(\lambda)$: first order, The first derivative spectrum of an absorption band is characterized by a maximum, a minimum, and a cross-over point at the λ max of the absorption band.

Area under curve (Area calculation)

In this study area was integrated between wavelength ranges from 289 &307 nm.

$$\text{Area calculation: } (\alpha+\beta) = \int_{\lambda 2}^{\lambda 1} A d\lambda$$

Where, α is area of portion bounded by curve data and a straight line connecting the start and end point, β is the area of portion bounded by a straight line connecting the start and end point on curve data and horizontal axis, λ1 and λ2 are wavelength range start and end point of curve region.[8]

Apparatus and instrumentation: A shimadzu 1800 UV/VIS double beam spectrophotometer with 1cm matched quartz cells was used for all spectral measurements. Single Pan Electronic balance (CONTECH, CA 223, India) was used for weighing purpose. Sonication of the solutions was carried out using an Ultrasonic Cleaning Bath (Spectra lab UCB 40, India). Calibrated volumetric glassware (Borosil®) was used for the validation study.

Materials

Reference standard of Domperidone API was supplied as gift sample by Cipla Pharmaceutical Company, Pune. Methanol was obtained from Research-Lab Fine Chem Industries, Islampur, Mumbai, and Maharashtra. Tablet sample with label claim 125 mg per Tablet were purchased from local market Mangalwedha, Solapur, Maharashtra, India.

Method development

Preparation of Standard and Sample Solutions: Stock solution of 10µg/ml of Domperidone was prepared in Methanol, for First Order Derivative Area under Curve spectrophotometric analysis. The standard solutions were

prepared by dilution of the stock solution with Methanol in a concentration range of 5, 10, 15, 20 and 25µg/ml with Methanol for First Order Derivative Area under Curve spectrophotometric methods. Methanol was used as a blank solution.

Calibration curve for Ranitidine

The dilutions were made from Standard Stock solution to get concentration of 5, 10, 15, 20, and 25µg/ml respectively. These solutions were scanned from 400 to 200 nm and First Order Derivative Area under Curve values was integrated in the range of 289-307 nm. The calibration curve was plotted between areas under curve values against concentration.

Assay of tablet formulation

Twenty tablets each containing 10 mg of Domperidone were weighed crushed to powder and average weight was calculated. Powder equivalent to 10 mg of Domperidone was transferred in 100 ml of volumetric flask. A 50 ml of Methanol was added and sonicated for 15 minutes. Then solution was further diluted up to the mark with Methanol. The solution was filtered using Whatmann filter paper no. 41, first 5 ml of filtrate was discarded. This solution was further diluted to obtain 10µg/mL solution with water, subjected for UV analysis using Methanol as blank. This procedure was repeated three times.

Method Validation: The above method was validated for various parameters such as Accuracy, Linearity, Precision, Limit of detection (LOD) and Limit of Quantitation (LOQ) according to ICH guideline. [(9)]

Accuracy

The accuracy for the analytical method was evaluated at 80%, 100% and 120% levels of 10 µg/ml Sample solution. First Order Derivative Area under curve (AUC) was measured in wavelength range 289-307 nm and results were obtained in terms of percent recovery. Three determinations at each level were performed and % RSD was calculated for each level. [(9)]

Precision

The precision of an analytical procedure expresses the closeness of an agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions intraday precision was studied by integrating area of standard solution of 10 µg/ml concentration at six independent series in the same day. Interday precision studies were performed by integrating area of standard solution of 10µg/ml concentration on three consequent days. The %RSD Was calculated. [(9)]

Limit of Detection and Limit of Quantification

The Limit of Detection (LOD) is the smallest concentration of the analyte that gives the measurable response. LOD was calculated using the following formula

$$LOD = 3.3\ \sigma / S$$

The Limit of Quantification (LOQ) is the smallest concentration of the analyte, which gives response that can be accurately quantified. LOQ was calculated using the following formula

$$LOQ = 10\ \sigma / S$$

Where, σ is standard deviation of the response and

S is the slope of the calibration curve.

LOD& LOQ of Domperidone was found to be 0.84 µg/ml &2.58µg/ml respectively. [9]

Results and Discussion

The UV visible spectroscopic method for the Domperidone by First order derivative Area under Curve was found to be simple, accurate, economical and reproducible. The drug concentrations were found to be linear in the range of 5-25 µg/ml and the correlation coefficient value of 0.999 indicates that developed method was linear. For Precision the percent relative standard deviation (% RSD) was found to be 0.0441 while, intra-day and inter-day precision results in terms of percent relative standard deviation values were found to be 0.9871 and 0.9573 respectively thus the method is observed as precise. The accuracy of the method was assessed by recovery studies at three different levels i.e. 80%, 100%, 120%. The values of standard deviation were satisfactory and the recovery studies were close to 100%. The % RSD value is ≤ 2 indicates the accuracy of the method. The Limit of Detection and Limit of Quantitation values were found to be 0.84µg/ml & 2.58µg/ml respectively. The result of the analysis for pharmaceutical formulation by the developed method was consistent with the label claim, highly reproducible and reliable. The method can be used for routine quality control analysis of Domperidone in bulk and pharmaceutical formulations.

Table 1: Assay of tablet dosage form

Sr.No.	Sample Solution Concentration (µg/ml)	Amount found (%)	Mean % found*	%RSD*
1	10	100.22		
2	10	100.39	99.91	0.0359
3	10	99.14		

*n=3, % RSD = % Relative Standard Deviation.

Table 2: Accuracy results for Domperidone

Accuracy level	Sample conc (µg/ml)	Std. conc	Total amount. Added (µg/ml)	% Recovery	Mean % Recovery	% RSD
80	10	12	8	98.12		
100	10	15	10	102.16	100.70	0.0441
120	10	18	12	101.83		

Table 3: Precision Study

Parameter	Intra day	Inter-day
Sample sol conc.µg/ml	10	10
AUC (mean)	0.0069	0.0074
%RSD	0.9871	0.9573

Table 4: Summary of validation parameters

Parameter	Result
λ range	289-307
Regression Equation (y=mx+c)	Y=0.001x + 0.000
Linearity range	5-25µg/ml
Slope	0.001
Intercept	0.000
Correlation coefficient (R^2)	0.999
Limit of Detection (LOD) µg/ml	0.84
Limit of Quantitation (LOQ) µg/ml	2.58
Accuracy (Mean % Recovery)	100.70
Precission (%RSD)	0.0441

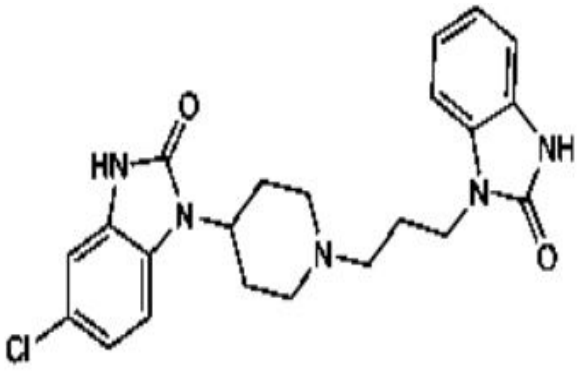

Fig. 1: Structure of Domperidone.

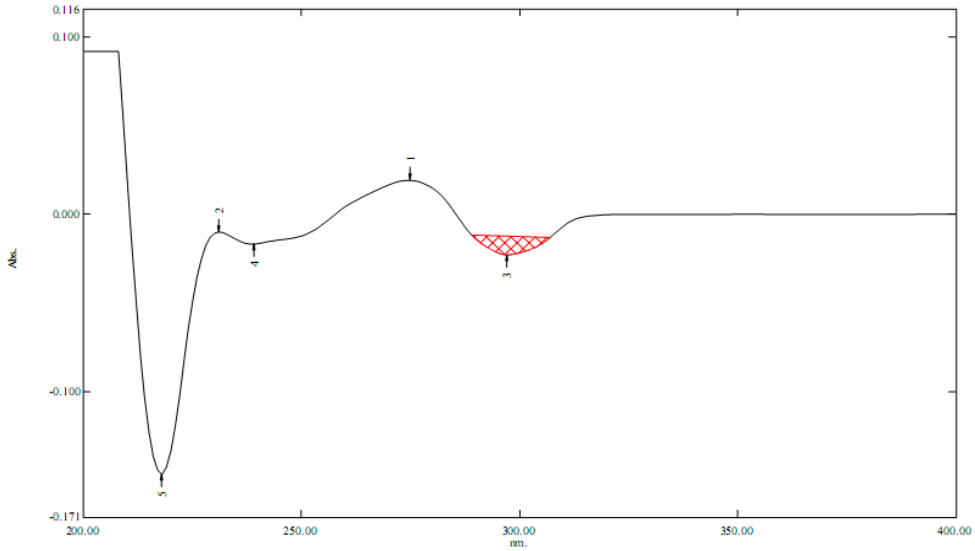

Fig. 2: First order derivative Area under Curve spectrum of Domperidone in Methanol (25µg/ml).

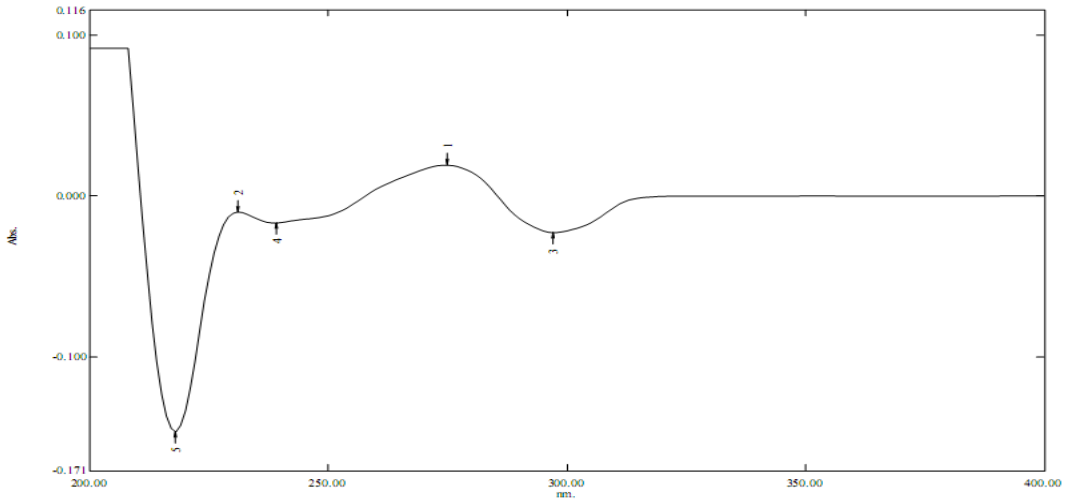

Fig. 3: first order derivative spectrum of Domperidone in Methanol (25µg/ml).

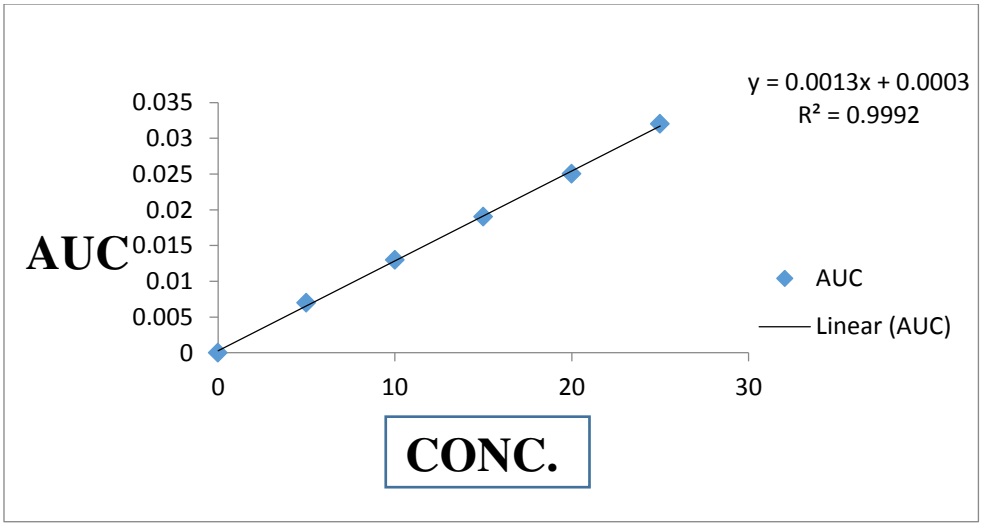

Fig. 4: Linearity of Domperidone.

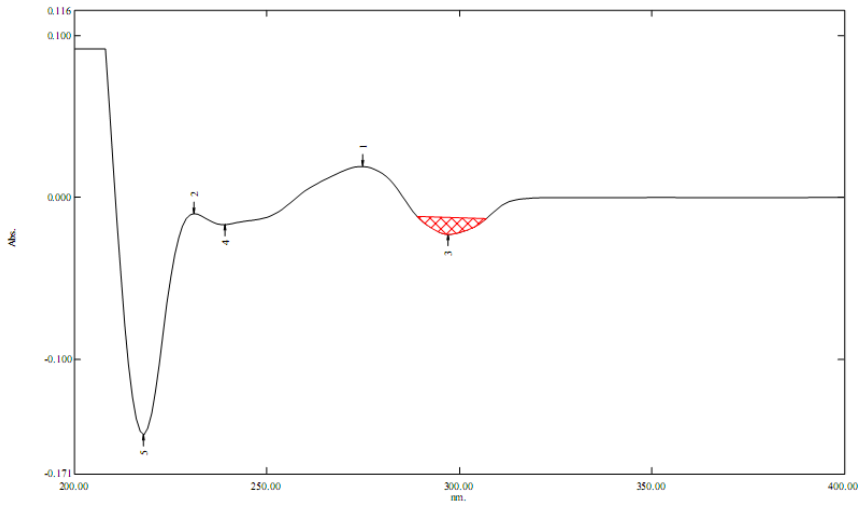

Fig. 5: First order derivative Area under Curve spectrum of Domperidone of dosage form in Methanol (25µg/ml).

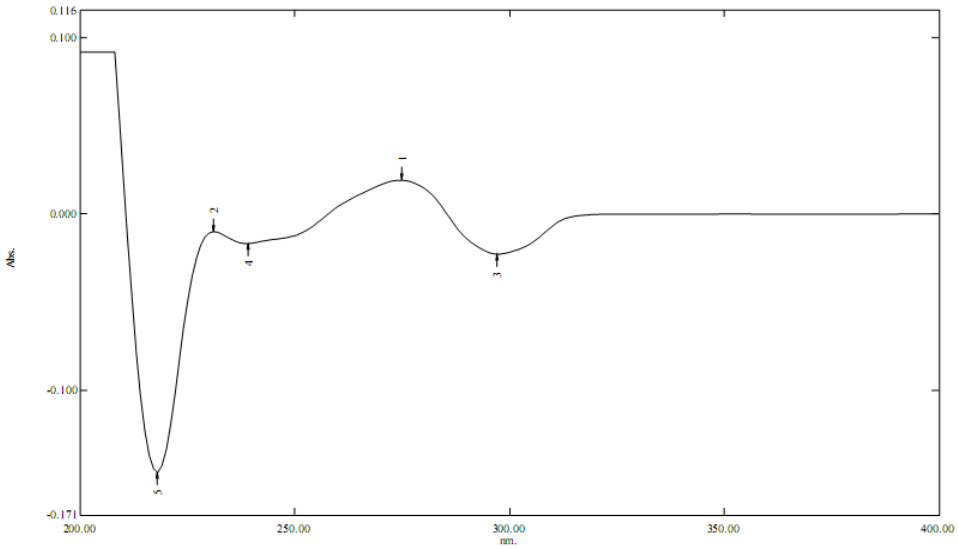

Fig. 6: First order derivative spectrum of Domperidone of dosage form in Methanol (25 µg/ml).

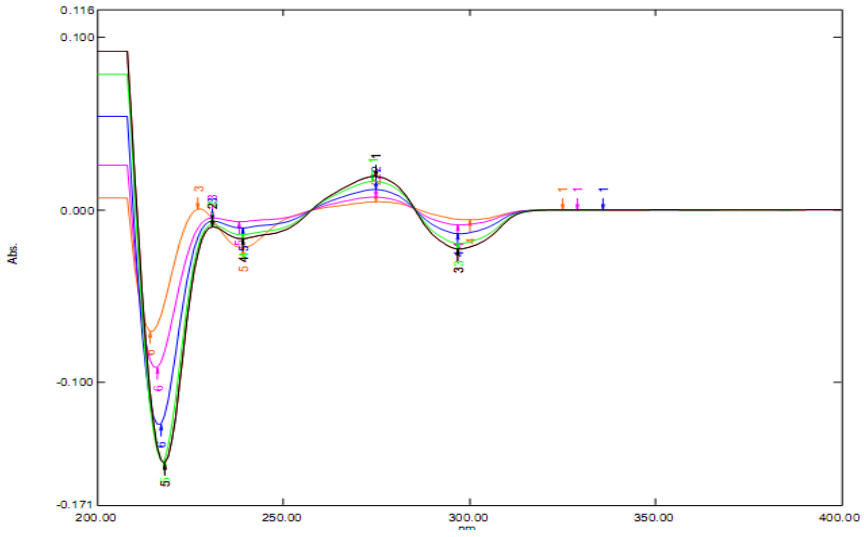

Fig. 7: First order derivative overlay of Domperidone at diff. Concentration.

Conclusion

The UV spectroscopic AUC method for the analysis of Domperidone by First order derivative Area under Curvewas found to be simple, precise, and accurate; can be used for assay of bulk drug and pharmaceutical dosage formulations.

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