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Zero And First Order Derivative Spectrophotometric Methods For Determination Of Dronedarone In Pharmaceutical Formulation

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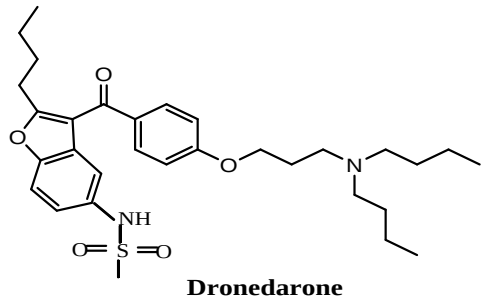
Abstract: Two Simple, fast and reliable derivative spectrophotometric methods were developed for determination of Dronedarone in bulk and pharmaceutical dosage forms. The solutions of standard and the sample were prepared in methanol. The quantitative determination of the drug was carried out using the zero order derivative values measured at 290 nm and the first order derivative values measured at 275 nm. Calibration graphs constructed at their wavelengths of determination were linear in the concentration range of Dronedarone using 4-20 µg.mL-1 (r^2 = 0.9997 and r^2 = 0.9996) for zero order and first order derivative spectrophotometric method. 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. These methods were successfully applied to pharmaceutical formulations because no interferences from tablet excipients were found. The proposed methods were found to be simple, sensitive, accurate, precise, rapid and economical for the routine quality control application of Dronedarone in pharmaceutical formulations.

Keywords: Dronedarone, Derivative spectrophotometry, Zero order derivative spectrum, first order derivative spectrum, validation.

INTRODUCTION

Chemically Dronedarone is a benzofuran derivative related to amiodarone, a popular antiarrhythmic[1]. Dronedarone is a drug by sanofi-aventis, mainly for the indication of cardiac arrhythmias. In Dronedarone, the iodine moieties are not present, reducing toxic effects on the thyroid and other organs. A methyl sulfonamide group is added to reduce solubility in fats and hepatic impairment. Dronedarone displays amiodarone like class III antiarrgythmic activity in vitro and in clinical trials. The drug also appears to exhibits activity in each of the four Vaughan-Williams antiarrhythmic classes. Synthetic name is N-{2-butyl – 3 – {p – {3-{dibutyl amino} propoxyl} benzoyl}-5-benzofuranyl} methane sulfonamide. Literature survey reveals a very few chromatographic methods[2] for the determination of Dronedarone in its pure form and tablet dosage form and a one method for Spectrophotometric[3] estimation of Dronedarone. So far, no derivative spectrophotometric method has been reported for the estimation of Dronedarone from pharmaceutical dosage form with. This paper deals with validation and development of a method by derivative spectrophotometry for the assay of Dronedarone from its bulk drug and in pharmaceutical dosage forms.



Dronedarone

EXPERIMENTAL

Instrumentation

A Lab India model 1885 double beam UV/Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV win system software (UV win version 3000). A Sartorius CP224S analytical balance (Gottingen, Germany), an ultrasonic bath (Frontline FS 4, Mumbai, India).

Materials and methods

Dronedarone was a gift sample by Pharmatrain Pvt. Ltd. Hyderabad, India and was used without further purification. All chemicals and reagents used were of analytical grade and were purchased from Merck Chemicals, India.

Preparation of standard and sample solutions

Stock solution of 100 µg.mL^{-1} of Dronedarone was prepared in methanol, for zero order and first order derivative spectrophotometric analysis. The standard solutions were prepared by accurately weigh and transfer 10 mg of Dronedarone working standard into a 100 mL volumetric flask add about 70mL of Methanol and sonicate to dissolve it completely and make volume up to the mark with the same solvent (Stock solution). Further pipette 1.2ml of the Dronedarone stock solution into a 10ml volumetric flask and dilute up to the mark with methanol. Methanol was used as a blank solution.

Assay procedure

Accurately weigh and transfer equivalent to 10 mg of tablet powder Dronedarone working standard into a100 mL volumetric flask add about 70 mL of methanol and the solutions were filtered through a 0.45 µm nylon filter and sonicated for about 15 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 and makes volume up to the mark with the same solvent (Stock solution). Appropriate dilutions were made with methanol from stock solution for both zero order and first order derivative spectrophotometric methods.

Development of the methods

Method A: Zero order spectroscopic method

The solutions were scanned in the range from 400-200 nm, and the peak was observed and gives maximum absorbance at 290 nm. So, the wavelength selected for the analysis of the drug was 290 nm. The drug followed the Beer's- Lamberts law in the range of 4-20 µg/ml.

Method B: First order derivative spectroscopic method

The standard drug solution was diluted so as to get the final concentration in the range of 4-20 µg/ml and scanned in the first order derivative spectra. The first order derivative spectra at showed a maxima and minima at 275 and 315 nm respectively. The amplitude of absorbance was measured at 275 nm (peak maxima) and at 315 nm (peak minima) and was plotted against concentration to give calibration curve, and regression equation was calculated. The amplitude was linear in the concentration range of 4-20 µg/ml.

VALIDATION OF THE PROPOSED METHODS

The proposed method is validated according to the International Conference on Harmonization (ICH) guidelines[4].

Linearity and Range

From stock solution 4-20 µg.mL^{-1} concentration range solutions are prepared in methanol solvent**.** Under the experimental conditions described, the graph obtained for zero order and first order 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 = 0.032x - 0.004 (r^2 = 0.998) at 290 nm for zero order derivative spectrophotometry and y = 0.00075x - 0.001 (r^2 =1.000) for first order derivative spectrophotometry. The range was found to be 4-20 µg.mL^{-1} for both zero order and first order derivative spectrophotometric methods. The calibration curves are showed in figures 1 and 2.

Precision

To determine the precision of the method, Dronedarone solutions at a concentration of 12 µg /L were analyzed each five times for both zero order and first order derivative spectrophotometric methods. Measure the absorbance and calculate the

%RSD. The %RSD for the five replicates absorbance was found to be within the specified limits.

Solutions for the standard curves were prepared fresh every day. The % RSD for the area of five standard injections results should not be more than 2%. The precision results are tabulated in table-1.

Sensitivity

The limit of detection (LOD) and limit of quantification (LOQ) were calculated by using the equations LOD = 3 σ / S and LOQ = 10 σ /S, where σ is the standard deviation of intercept, S is the slope. The LOD and LOQ were found to be 0.011µg/ml and 0.356µg/ml respectively for zero order derivative method and The LOD and LOQ were found to be 0.2411µg/ml and 0.730µg/ml for first order derivative methods respectively.

Recovery

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 Dronedarone to reanalyzed solutions of commercial tablets. Measure the Absorbance of the standard solution, Accuracy 50%, Accuracy 100% and Accuracy 150% solutions, Calculate the amount found and amount added for Dronedarone, calculate the individual recovery and mean recovery values. The results are shown in Table-2.

Analysis of the marketed formulation

There was no interference from the excipients commonly present in the tablets. The drug content was found to be 99.6% with a % R.S.D. of 0.179 and 99.3% with a % R.S.D. of 0.951 for zero order and first order derivative spectrophotometric methods respectively. It may therefore be inferred that degradation of Dronedarone 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 Dronedarone in pharmaceutical dosage form. The results are shown in Table-3.

The summary of the validation parameters is depicted in Table-4.

TABLE- 1: Intra and Inter day precision Results

Parameters	Intra day precision		Inter day precision	
	S.D	%RSD	S.D	%RSD
Zero derivative	0.00044	0.136	0.0011	0.351
First derivative	0.0000837	1.37	0.0000548	0.90

TABLE- 2: Accuracy Results

Zero order derivative method					
Accuracy level	Absorbance	Amount added(mg)	Amount found(mg)	% recovery	Mean recovery
50%	0.207	5.0	4.96	99.3%	99.1%
100%	0.415	10.0	9.96	99.6%	
150%	0.607	15.0	14.5	98.3%	
First order derivative method					
50%	0.004	5	4.99	99.8%	99.8%
100%	0.008	10	9.98	99.8%	
150%	0.11	15	14.9	99.8%	

TABLE- 3: Assay results for determination of Dronedarone in pharmaceutical Formulation

Parameters	Amount of Tablet label claim	Drug content %	%RSD
Zero order	400mg	99.6	0.179
First order	400mg	99.3	0.951

TABLE- 4: Regression analysis data and summary of validation parameters for the proposed methods

Parameter	Zero order	First order
Absorption maxima and minima (nm)	290	275
Beer's-Lamberts range (µg/ml)	4-20	4-20
Regression equation y=mx+c	Y= 0.032x-0.004	Y= 0.00075x-0.001
Slope(m)	0.032	0.00075
Intercept(c)	-0.004	-0.001
Correlation coefficient (r^2)	0.998	1.000
Mean Recovery %	99.1	99.8
Precision (% RSD)	0.136	1.37
Intermediate precision	0.351	0.9
LOD (µg/ml)	0.011	0.241
LOQ (µg/ml)	0.356	0.730

Figure-1

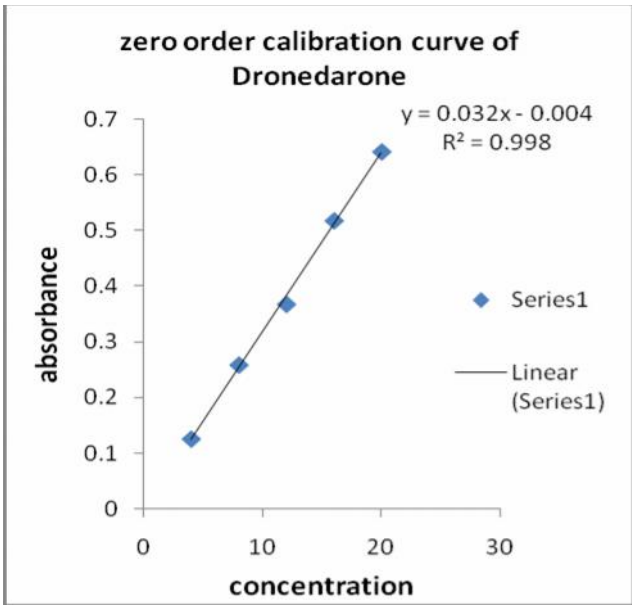
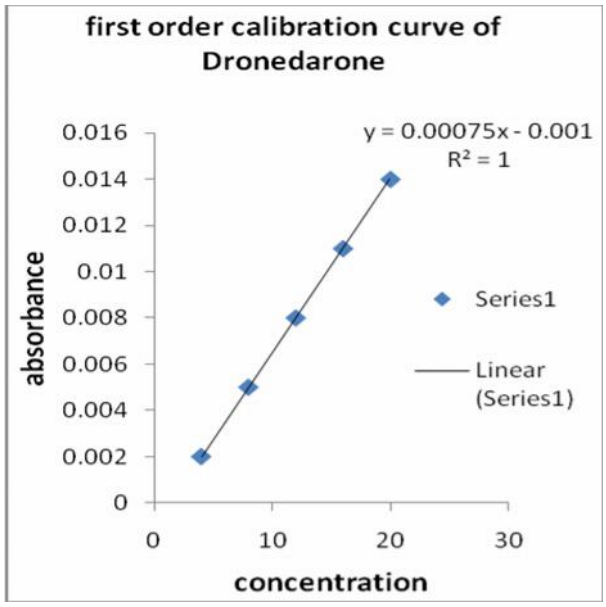


Figure -2



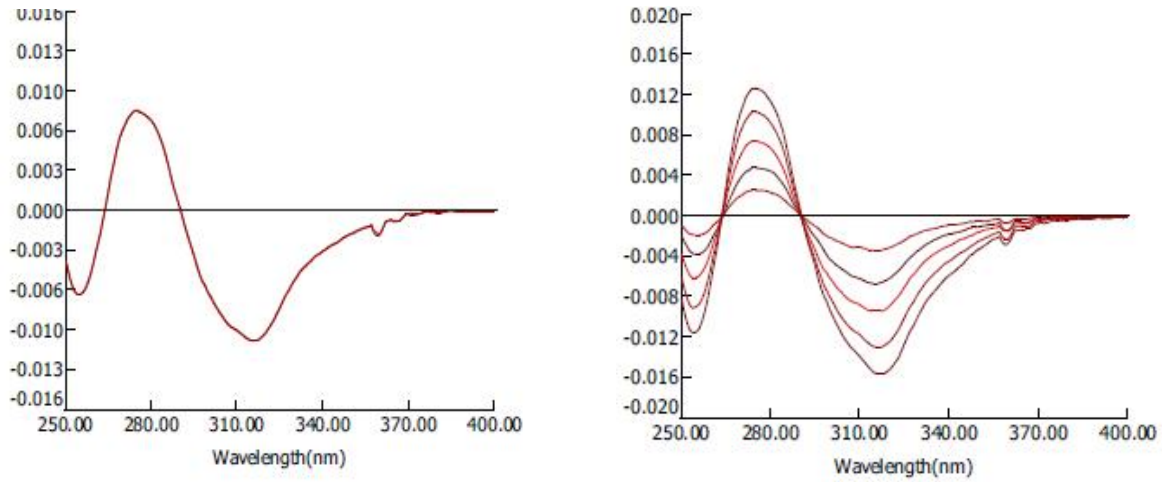


Figure-3: first order derivative spectrum

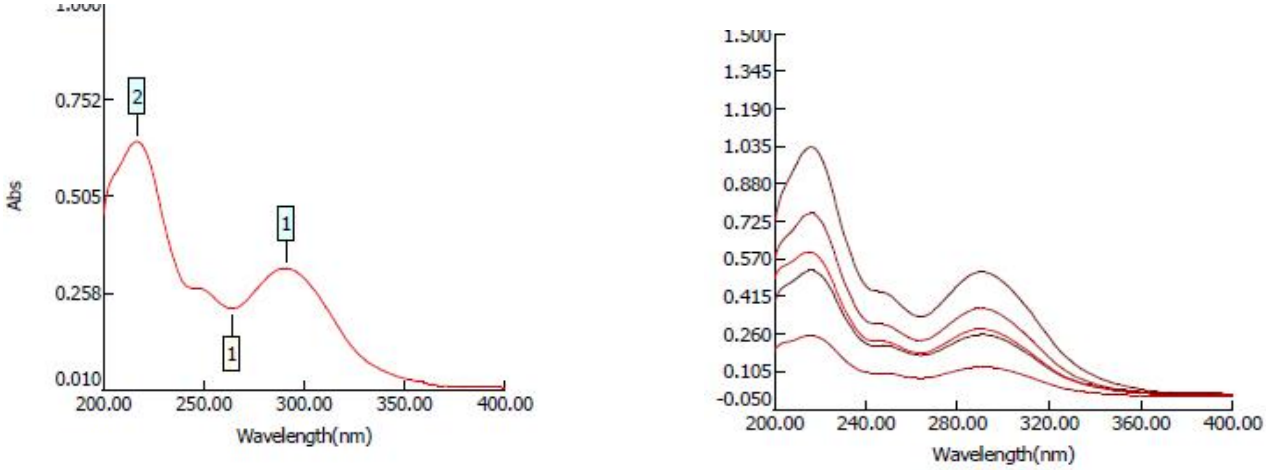


Figure-4: zero order derivative spectrum

CONCLUSION

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

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