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Research

Development of UV Validated Analytical Methods for Dronedarone Hydrochloride in Tablet Dosage Form and its Application

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Abstract:
An efficient, accurate, and cost-effective UV-spectrophotometric approach has been established for the quantification of Dronedarone hydrochloride in pharmaceutical formulations. The method employed was the area under the curve (AUC), wherein the area was integrated over the wavelength range of 270 nm to 300 nm. Calibration curves were constructed for the procedure utilizing instrumental responses at designated wavelengths and analyte concentrations in the solution. The detector response exhibited linearity within the concentration range of 2-6 µg/ml for the procedure. The tablet formulation was examined, revealing a drug percentage of in the assays. Studies on accuracy and precision were conducted, yielding satisfactory results. The analysis results were statistically validated. The method's limit of detection and limit of quantitation were established. The approach was validated by adhering to the analytical performance parameters recommended by the International Conference on Harmonization. All validation parameters fell within the permissible range. The devised approach was effectively utilized to quantify the concentration of Dronedarone hydrochloride in pharmaceutical formulations.

Keywords: Dronedarone hydrochloride, UV-spectrophotometric, assays, International Conference on Harmonization.

1. Introduction

Dronedarone hydrochloride is a synthetic antiarrhythmic drug belonging to the benzofuran class, chemically related to amiodarone but developed to overcome the latter's limitations in terms of long half-life and organ toxicity. It is primarily prescribed for the management of atrial fibrillation (AF) and atrial flutter (AFL), aiming to reduce hospitalization and recurrence of arrhythmic events. Dronedarone exerts its pharmacological effects by blocking multiple cardiac ion channels—namely sodium (Na^+), potassium (K^+), and calcium (Ca^{2+}) channels—and by antagonizing adrenergic receptors, classifying it as a multichannel blocker with properties of all four Vaughan-Williams classes. Compared to amiodarone, it lacks iodine, thereby significantly minimizing thyroid and pulmonary adverse effects.

In recent years, with increasing use of dronedarone in clinical settings, it has become imperative to establish reliable and efficient analytical methods to ensure the quality, efficacy, and safety of its formulations. Analytical method development and validation play a pivotal role in pharmaceutical quality control, aiding in the identification, quantification, and purity assessment of active pharmaceutical ingredients (APIs) in various dosage forms.

Among various analytical techniques available, ultraviolet-visible (UV-Vis) spectrophotometry is widely recognized for its simplicity, sensitivity, low operational cost, and rapid throughput. Although

sophisticated techniques such as high-performance liquid chromatography (HPLC) and liquid chromatography–mass spectrometry (LC-MS) are often employed for assay and stability studies, they are relatively time-consuming and resource-intensive. In contrast, UV spectrophotometry offers a practical alternative for routine quality control analysis, particularly when applied with validated protocols conforming to International Council for Harmonisation (ICH) guidelines.

The objective of the present study is to develop a robust, simple, accurate, and cost-effective UV spectrophotometric method for the quantitative estimation of dronedarone hydrochloride in tablet dosage form. The method involves determining the drug's maximum absorbance wavelength (λmax), followed by the construction of a calibration curve over a suitable concentration range. The developed method is validated according to ICH Q2(R1) guidelines for analytical procedure validation, covering parameters such as linearity, accuracy, precision, specificity, robustness, limit of detection (LOD), and limit of quantification (LOQ).

Furthermore, the validated method is successfully applied to commercially available tablet formulations of dronedarone hydrochloride to demonstrate its applicability in routine pharmaceutical analysis. The proposed method is expected to be suitable for regular use in quality control laboratories, offering a rapid, economical, and reliable tool for drug estimation in the absence of sophisticated instrumentation.

2. Materials and Methods

Chemicals and Reagents

Dronedarone hydrochloride pure working standard was obtained as a gift sample from a certified pharmaceutical source.

Marketed tablet formulation containing dronedarone hydrochloride (label claim: 400 mg per tablet) was procured from a local pharmacy.

Solvents and reagents: Analytical grade methanol and distilled water were used throughout the study. All chemicals used were of analytical reagent (AR) grade unless otherwise stated.

Instrumentation

A UV-visible double beam spectrophotometer (e.g., Shimadzu UV-1800 or equivalent) equipped with 1 cm matched quartz cuvettes was used for all absorbance measurements.

Digital analytical balance (±0.1 mg accuracy), ultrasonicator, and Whatman filter paper No. 41 were employed for sample preparation.

Preparation of Standard Stock Solution

A standard stock solution of dronedarone hydrochloride was prepared by accurately weighing 10 mg of the pure drug and dissolving it in 10 mL of methanol. The solution was then sonicated for 10 minutes and volume was made up to 100 mL with distilled water to obtain a final concentration of 100 µg/mL.

Selection of Wavelength (λmax)

The standard solution (100 µg/mL) was scanned in the UV range of 200–400 nm against methanol as blank using the spectrophotometer. The wavelength corresponding to maximum absorbance (λmax) was found to be approximately 289 nm and was selected for further analysis.

Preparation of Calibration Curve

From the standard stock solution, serial dilutions were prepared to obtain concentrations ranging from 5 to 30 µg/mL. The absorbance of each solution was measured at the selected λmax (289 nm). A calibration curve was constructed by plotting absorbance versus concentration. Linear regression analysis was used to determine the slope, intercept, and correlation coefficient (R^2) of the curve.

Sample Preparation from Tablet Formulation

Twenty tablets were accurately weighed, and the average weight was calculated. Tablets were crushed into a fine powder. An amount of powder equivalent to 10 mg of dronedarone hydrochloride was transferred to a 100 mL volumetric flask containing 10 mL of methanol. The mixture was sonicated for 15 minutes and filtered. The volume was then made up to 100 mL with distilled water to obtain a concentration of 100 µg/mL. Appropriate dilutions were made to obtain a working concentration within the calibration range.

Method Validation

The method was validated according to ICH Q2(R1) guidelines for the following parameters:

Linearity: Determined over the concentration range of 5–30 µg/mL. The calibration curve was evaluated for correlation coefficient (R^2), slope, and intercept.

Accuracy (Recovery Studies): Accuracy was assessed by standard addition method at three levels: 80%, 100%, and 120% of the target concentration. Percent recovery and relative standard deviation (RSD) were calculated.

Precision:

Repeatability (intra-day precision): Analyzed six replicates of a fixed concentration on the same day.

Intermediate precision (inter-day precision): Analyzed the same concentration over three different days.

Specificity: Assessed by analyzing the standard solution in the presence of common tablet excipients to check for interference.

LOD and LOQ: Calculated based on the standard deviation of the response (σ) and the slope (S) of the calibration curve using the formulas:

LOD = 3.3 × (σ/S)

LOQ = 10 × (σ/S)

Robustness: Evaluated by making slight variations in analytical parameters such as wavelength (±2 nm) and solvent composition.

3. RESULTS AND DISCUSSION

Method Development

The selection of the solvent for the study method was based on the solubility of dronedarone hydrochloride. It was found that dronedarone hydrochloride was completely soluble in methanol and it was selected for stock preparation. The scanning of appropriately diluted solution in entire range of UV region was performed. The zero order, first order and second order derivative spectra are shown in Fig1-3. The zero order spectrums were converted into first and second order derivative using software. The highest absorption of second order derivative spectrum was found at 292 nm and it was used to analyze dronedarone hydrochloride. There were no interferences observed and spectra were smooth and hence selected conditions were utilized for further analysis of drug.

Method Validation

The newly developed UV spectrophotometric method has been validated as per ICH guideline. The validation parameters include linearity, specificity, accuracy, precision, LOD and LOQ.

Linearity:

The UV absorbance of dronedarone hydrochloride in second derivative spectrawas linear in the concentration range of 2 to 6 µg/ml. The overlay derivative spectra of hydrochloride are given in Fig. 4. The UV absorbance of linear concentration of dronedarone hydrochloride by the proposed method is given in table-

Calibration graph was obtained by plotting absorbance versus concentration of dronedarone hydrochloride (Fig.5). The regression equation obtained reveal slope of 0.0827 and intercept of 0.006. The correlation coefficient (r^2) was found to be 0.9954.

Specificity: The specificity of the method was proven by comparing the derivative spectra of additives (placebo) with that of standard derivative spectra.

There was no interference from the additives of placebo and assay sample, therefore the method is found to be specific

Accuracy: The recovery studies resulted in >99% percentage recovery of drug shown in table-2. The excellent recoveries of dronedarone hydrochloride by the proposed method fulfilled the limits stated in guideline.

Precision: The precision of the method was evaluated by intra-day and inter- day precision studies. The results of intra-day and inter-day studies are given in table 3.

The % RSD values were less than 2 as recommended by guideline, and thus the method was found to be precise.

LOD and LOQ: On the basis of slope value, theoretically LOD and LOQ were calculated. The LOD was found to be 0.0318µg/ml and the LOQ was found to be 0.0964µg/ml which reveals the method is sensitive for identification of dronedarone hydrochloride.

Stability of solution: The results of stock solution stability reveal that it is stable up to 48hrs at room temperature without light protection and stable up to 5 days at refrigerated condition table 4-5.

Optical characteristics: Optical characteristics of dronedarone hydrochloride such as $A^{1\%}$ molar absorptivity and Sandell's sensitivity were calculated and the 1cm results are given in table 6.

Application of the UV spectrophotometric method for the assay of Dronedarone hydrochloride in tablet dosage form

The assay of dronedarone hydrochloride tablets was performed by the proposed method. The second order derivative spectrum of dronedarone hydrochloride tablet is shown in Fig 6. The assay results are given in the table 7. It was found that the percentage label claim of dronedarone hydrochloride tablets was 99.92 and the % RSD obtained was found to of <2.

Fig. 1: Zero order spectrum of dronedarone hydrochloride

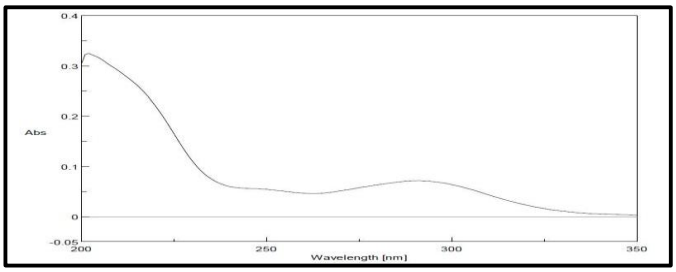


Fig. 2: First order derivative spectrum of dronedarone hydrochloride

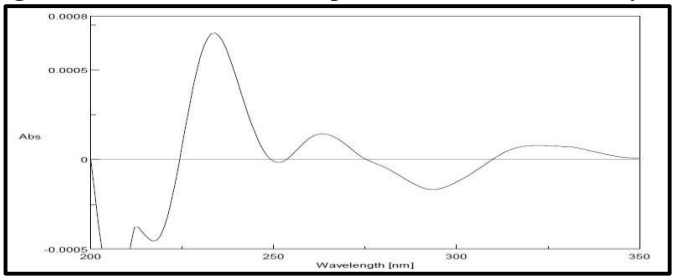


Fig. 3: Second order derivative spectra of dronedarone hydrochloride

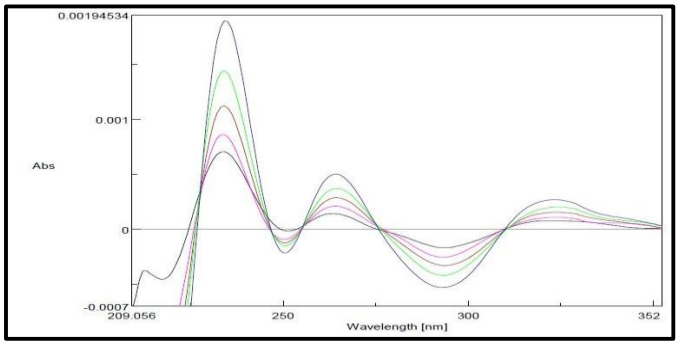


Fig. 4: Second order derivative overlay spectra of dronedarone hydrochloride

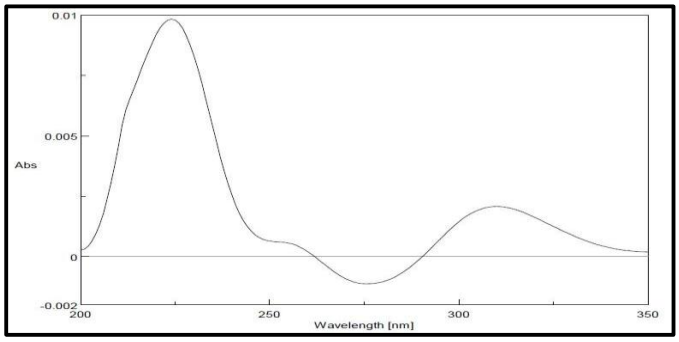


Table 1: Calibration data for dronedarone hydrochloride by second derivative UV spectrophotometric method

S. No	Concentration (µg/ml)	Absorbance
1	2	0.1809
2	3	0.2533
3	4	0.3252
4	5	0.4065

5	6	0.5177

Fig. 5: Calibration graph of dronedarone hydrochloride

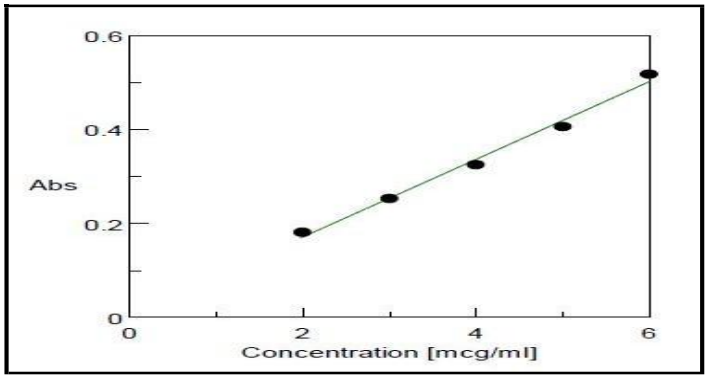


Table 2: Recovery data of dronedarone hydrochloride

Conc. of drug taken (µg/ml)	Conc. of standard added (µg/ml)	Mean Conc. found ± SD*	Mean Recovery (%)	% RSD*
5	2.5 (50%)	7.490±0.0273	99.87	0.3644
5	5 (100%)	10.020±0.0204	100.20	0.2036
5	7.5 (150%)	12.512±0.0394	100.10	0.3148

*n=6

Table 3: Precision data of dronedarone hydrochloride

Conc. (µg/ml)	Intra-day		Inter-day	
	Mean Conc. ± SD*	% RSD*	Mean Conc. ± SD*	% RSD*
3	2.9870±0.0204	0.6829	3.098±0.0118	0.3809
4	4.0172±0.0174	0.4331	4.0204±0.0168	0.4179
5	4.9904±0.0362	0.7254	4.9880±0.0240	0.4812

*n=6

Table 4: Stability data of Dronedarone Hydrochloride (bench top)

Time (hrs)	Conc. of drug (µg/ml)	Absorbance	% amount remaining	%RSD (n=6)
0	4	0.3251	100	0. 5942
4		0.3237	99.57	0. 7331
8		0.3198	98.37	0. 9251
12		0.3132	96.34	1.0926
24		0.3086	94.93	0.4874
48		0.2944	90.55	1.1263

Table 5: Stability data of Dronedarone Hydrochloride (refrigerated)

Time (Days)	Conc. of drug (µg/ml)	Absorbance	% amount remaining	%RSD (n=6)
0	4	0.3251	100	0. 5942
1		0.3229	99.32	0. 9429
2		0.3201	98.46	0. 2814
3		0.3175	97.66	0. 8391
4		0.3142	96.64	0.6482
5		0. 3109	95.63	1.0043

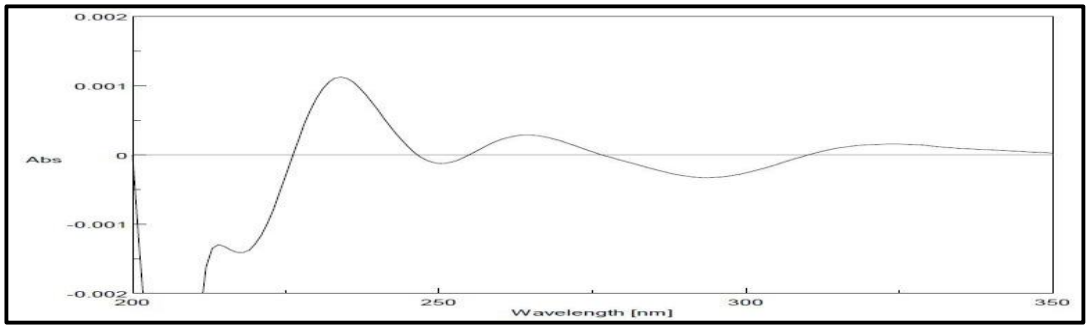
Table 6: Optical characteristics of dronedarone hydrochloride

Parameters	Values
A 1% 1cm	84.72
Molar absorptivity (ε)	5025.75
Sandell's sensitivity (gm x 10^{-3}/cm^2x 0.001 absorbance unit)	0.01105

Table 7: Assay of dronedarone hydrochloride tablets

Brand name of tablets	Labeled amount of Drug (mg)	Mean Assay ±SD	% Label Claim	%RSD (n = 6)
Maltaq®	400	399.68 ±1.8568	99.92	0.4646

Fig. 6: Second order derivative of dronedarone hydrochloride tablets



4. Conclusion

A UV spectrophotometric method was developed for the estimation of dronedarone hydrochloride in tablet dosage form. The normal spectrum of dronedarone hydrochloride was obtained by scanning an appropriately diluted standard solution in methanol. The resulting zero-order spectrum was converted to first and second-order derivative spectra to enhance resolution. Among these, the second-order derivative spectrum was smooth, devoid of interference from tablet excipients, and was therefore selected for quantitative analysis.

The maximum absorbance in the second-order derivative spectrum was observed at 292 nm. The method exhibited linearity within the Beer's law range of 2–6 µg/ml, with a high correlation coefficient from regression analysis, indicating excellent linearity. The calculated optical characteristics confirmed the strong UV absorbance of the drug.

Recovery studies demonstrated the high accuracy of the method, and specificity was confirmed by the absence of interference from excipients in both placebo and sample solutions. Repeatability studies confirmed the precision of the method. Stability studies indicated that the stock solution of the drug remained stable under specified conditions during the analysis period.

The limits of detection (LOD) and quantification (LOQ) values indicated that the method is sufficiently sensitive for determining and quantifying dronedarone hydrochloride. The assay of the marketed tablet formulation showed results consistent with the labeled claim, confirming the successful application of the developed second-order derivative UV spectrophotometric method for routine quality control of dronedarone hydrochloride in pharmaceutical dosage forms.

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