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Short Communication

Spectrophotometric Estimation of Dronedarone Hydrochloride in Pharmaceutical Dosage Forms by using Multivariate Technique

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ABSTRACT

An accurate and precise UV spectrophotometric method with multivariate calibration technique for the determination of dronedarone hydrochloride in pharmaceutical dosage forms has been described. The term multivariate calibration refers to the process of constructing a mathematical model that relates a property such as content or identity to the absorbance of a set of known reference samples at more than one wavelength. Dronedarone shows maximum wavelength at 288 nm using methanol as a solvent and obeyed Beer's law in the linear range of 10-35µg/ml. The present method was found to be accurate, precise, and can be successfully used for quantitative estimation of dronedarone in drug and tablet dosage form compare to other complex techniques.

Keywords: Dronedarone, UV-Spectrophotometer, Multivariate Calibration Technique.

INTRODUCTION

Dronedarone is a drug discovered by Sanofi-Aventis, mainly for the indication of cardiac arrhythmias. Chemically, dronedarone is a benzofuran derivative with IUPAC name N-(2-Butyl-3-(p-(3-(dibutylamino)propoxyl)benzoyl)-5-benzofuranyl)methanesulfonamide [1]. Dronedarone is related to amiodarone, a popular antiarrhythmic. The use of amiodarone is limited by toxicity due its high iodine content (pulmonary fibrosis, thyroid disease) as well as by liver disease. In dronedarone, the iodine moieties are not present, reducing toxic effects on the thyroid and other organs. Dronedarone displays amiodarone – like class III antiarrhythmic activity in vitro and in clinical trials. The drug also appears to exhibit activity in each of the 4 Vaughan-Williams antiarrhythmic disease [2]. A survey of pertinent literature indicates that few analytical methods reported on quantification of dronedarone in pharmaceutical dosage forms and biological samples include HPLC, HPTLC and spectrophotometric methods [3-13].

However till date no multivariate spectrophotometric method for the quantification of dronedarone is reported. Therefore attempt was made to develop and validate spectrophotometric multivariate calibration method for quantification of dronedarone. Multivariate calibration refers to the process of constructing a mathematical model which relates a property such as content or identity to the absorbance of a set of known reference samples at more than one wavelength [14].

MATERIALS AND METHODS

Chemicals: Dronedarone hydrochloride pure drug was obtained from MSN Pharma Limited (Hyderabad) as a gift sample with 99.59% (w/w) assay value and was used without further purification. All chemicals and reagents used were of analytical grade (Rankem, India). Dronedarone hydrochloride tablets were purchased from local market and used with in self-life period.

Instrumentation: The multivariate technique was performed in 1.0cm quartz cells using T60U UV Visible spectrophotometer (PG Instruments Ltd., England) with a fixed 2nm spectral band width and UV-Win5 software v5.1.1 was used for all absorbances.

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Selection of solvent: The ideal property of a solvent should be that the drug must be completely soluble in the solvent used. The methanol is selected as a solvent based on literature survey and practical experience.

Preparation of stock solutions: Standard stock solution of dronedarone hydrochloride was prepared by dissolving 100mg in 100 mL volumetric flask and ultra-sonicated for 10 min to get a clear solution and then volume was made up to the mark with methanol to get a stock solution of 1000µg/mL concentration. From 1000µg/mL, 10mL of solution was pipette out in 100ml volumetric flask and made up with methanol to the mark to get a standard stock solution of 100µg/mL. From standard stock solution 1-3.5mL serial dilutions were pipette out in to 10mL volumetric flask and volume was made up to the mark with methanol to get a concentration of 10, 15, 20, 25, 30 and 35µg/mL.

Construction of calibration curve: Aliquots of the working standard solution of dronedarone hydrochloride was transferred into a series of 10mL volumetric flask and suitably diluted with methanol to get a concentration of 10, 15, 20, 25, 30 and 35µg/mL. These solutions were scanned in spectrum mode between 400-200nm to determine the λ_{max}. The λ_{max} of dronedarone was found to be 288nm. The absorbance of resulting solutions was measured at 282, 284, 286, 288, 290, 292 and 294nm and calibration curves were plotted.

Preparation of sample solution: For analysis of drug in tablet dosage form, 20 tablets were weighed accurately and triturated in the mortar to get a fine powder. The tablet powder equivalent to 100mg was weighed and transferred to 100mL volumetric flask and dissolved with methanol. The solution was ultra-sonicated for 10min and filtered using Whatmann filter paper no.41. The tablet solution was diluted to get a final concentration of 10µg/mL. All determinations were conducted with six replicates.

Method Validation: The method was validated according to International Conference on Harmonisation (ICH) Q2B guidelines 1996 [15] for validation of analytical procedure in order to determine the linearity, limit of detection, limit of quantitation, accuracy and precision.

RESULTS AND DISCUSSIONS

The multivariate UV spectrophotometric method was used to quantify the dronedarone hydrochloride in tablet dosage forms. The UV spectrum (Fig. 1) shows absorption maxima at 288 nm. The calibration curve showed linearity over a concentration range from 10-35 µg/mL, which follows the Beer and Lambert's law. In order to improve this correlation and minimize instrumental error, absorbances of these solutions were measured over a range surrounding 288nm i.e., 282, 284, 286, 288, 290, 292 and 294nm (Table 1).

The evaluation of linearity is done by linear regression analysis. The linearity response was found to be linear in the concentration range of 10-35µg/ml with coefficient of correlation (r^2) greater than 0.999. The LOD and LOQ values were shown in Table 1. The accuracy of the method was evaluated by the recovery studies. Recovery studies were carried out by spiking different concentrations of pure drug solution to pre-analyzed sample solution at different concentration level (50,100 and 150%).

The percentage recovery values were found to be 99.27-100.33 with %RSD of <2% (Table 2) which indicates that the proposed method was accurate. Precision was determined as intra-assay and inter day-assay, in accordance with ICH guidelines. By analyzing the samples of dronedarone hydrochloride at a concentration of 10, 20 and 30 µg/ml, the intra-day and inter-day precision were determined. The results of inter-day and intra-day precision studies are shown in Table 3. The low %RSD values obtained from the analysis of tablet indicated that the method was highly precise.

The developed method was applied to the quantification of dronedarone hydrochloride in tablets available in local market. The results were tabulated in Table 4. It can be seen that, the results obtained by proposed method was very much similar to that of established methods.

CONCLUSION

The proposed multivariate spectrophotometric method for quantification of dronedarone hydrochloride pharmaceutical dosage forms has been developed and validated. The method was selective, precise, accurate, reproducible and linear over the concentration range. The method is simple and suitable for the determination of dronedarone hydrochloride in formulations without interference of excipients or other common degradation products.

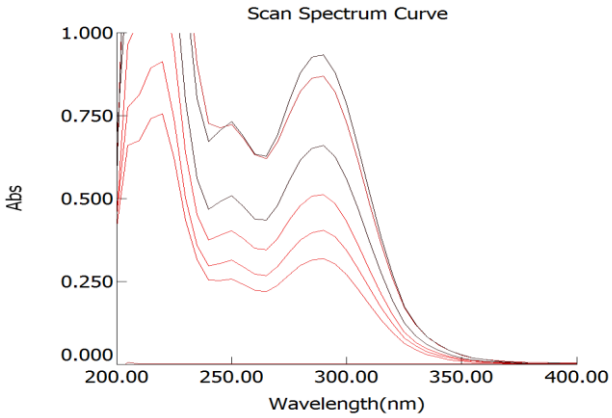

Figure 1: Absorbance spectrum of Dronedarone hydrochloride

Table 1: Calibration data of proposed method

Parameters	Results						
	At 282	At 284	At 286	At 288	At 290	At 292	At 294
Beers law range (µg/mL)	10-35	10-35	10-35	10-35	10-35	10-35	10-35
Molar extinction coefficient (1/mol/cm)	0.0261	0.0263	0.0269	0.0271	0.027	0.0265	0.0262
Sandell's sensitivity (µg/cm²)	0.0383	0.038	0.0372	0.0369	0.037	0.0377	0.0382
Limit of detection (µg/mL)	0.62	0.22	0.29	0.19	0.29	0.4	0.51
Limit of quantification (µg/mL)	1.88	0.68	0.89	0.58	0.89	1.22	1.55
Regression equation							
Intercept (a)	0.0018	0.0004	0.0043	0.0051	0.0056	0.0011	0.0016
Slope (b)	0.0262	0.0263	0.0265	0.0267	0.0266	0.0264	0.0263
Correlation Coefficient (r^2)	0.9999	0.9999	0.9998	0.9997	0.9998	0.9998	0.9999

Table 2: Accuracy data of proposed method (standard addition method)

Amount of % drug added to the analyte	**Theoretical content (µg/mL)**	**Conc. Found (Mean± SD)***	**%RSD**	**Mean % Recovery**
50	5	4.96±0.0451	0.91	99.27
100	10	9.97±0.0451	0.45	99.68
150	15	15.05±0.04	0.27	100.33

Table 3: Precision data of proposed method

Analyte Conc. (µg/mL)	**Intra-assay precision**		**Inter-assay precision**	
	***Mean ±SD**	**%RSD**	***Mean ±SD**	**%RSD**
10	99.73±0.3215	0.32	99.81±0.2762	0.28
20	99.37±0.3215	0.32	100.33±0.9802	0.98
30	99.57±0.6486	0.65	99.28±0.9302	0.94

Table 4: Assay results of dronedarone hydrochloride

Brand name	Label claim (mg)	Assay value	%RSD
MULTAQ	400	99.85±0.2677	0.27

REFERENCES

1. The Merck Index, 14th ed. 2007. P-3449.
2. Gerald V. Naccarelli, *et al*. Safety and efficacy of dronedarone in the treatment of atrial fibrillation/flutter. Clin Med Insight Cardiol 2011; 5: 103-19.
3. V.K. Ahirao, *et al*. Stress degradation studies of dronedarone in pharmaceutical dosage form by a validated stability indicating method. J Chil Chem Soc 2012; 57(3): 1272-6.
4. Disha Patel, Avijit Chowdhury. Development and validation of Dronedarone HCl in plasma by RP-HPLC method coupled with UV detector. Iventi Impact: Biomedical analysis 2012; Vol 2012.
5. Tondepu Naresh, Sait, Shakil S, Surendranath KV, Kiran Kaja, Ravi Kumar, Suresh A. Stability indicating HPLC method for Dronedarone in bulk drugs and pharmaceutical dosage forms. Amer J Anal Chem 2012; 3(8): 544-7.
6. Arpan Patel, Jawed Akhtar, Chirag Sharma. Spectrophotometric estimation of Dronedarone in pure drug and pharmaceutical formulation. Asian J Biomed Pharm Res 2012; 2(1): 266-71.
7. Batuk Dabhi, Yashwantsinh Jadeja, Madhavi Patel, Hetal Jehaliya, Dinish Karia, Anamik Shah. Method development and validation of a stability indicating RP-HPLC method for the quantitative analysis of Dronedarone hydrochloride in pharmaceutical tablets. Scipharm 2013; 81: 115-122.
8. Rajyalakshmi Ch, Benjamin T. Forced degradation study on dronedarone and application of validated stability indicating HPLC-UV method in stability testing of dronedarone tablets. Der Pharm Chem 2013; 5(1): 189-195.
9. Arpan Patel, Javed Akhtar. RP-HPLC Method development and validation of Dronedarone HCL in its pure form and tablet dosage form. J Chem Pharm Res 2012; 4(4): 2173-2179.
10. Batuk Dobhi, Hetal Jehaliya, Madhavi Patel, Yashwantsinh Jadeja, Denish Karia, Anamik Shah. HPTLC method for estimation of dronedarone hydrochloride in both bulk drug and pharmaceutical dosage form. Int J Pharm Sci Rev Res 2012; 17(1): 48-51.
11. Boldeman R. W, Hermans J. J, Maessen JG. Determination of the class iii antiarrhythmic drugs Dronedarone and Amiodarone, and their principal metabolite in plasma and myocardium by high performance liquid chromatography and UV detection. J Chromatogr B; Anal Tech Biomed Life Sci 2009; 877: 1727-31.
12. Dinesh Sahu, Ghazal khan. RP-HPLC method development and validation of Dronedarone HCl in its pure form and tablet dosage form. Asian J Biomed Pharm Res 2011, 1(2), 352.
13. Cen xie, Shilei Yang, Dafang Zhong. Simultaneous determination of dronedarone and its active metabolite debutyldronedarone in active plasma by liquid chromatography- tandem mass chromatography: application to a pharmacokinetic study. J Chromatogr B; Analyt Technol Biomed Life Sci 2011; 879(28): 3071-5.
14. M. Saeed Arayne, Najma Sultana, Saima Sher Bahadur. Multivariate calibration in UV Spectrophotometric analysis. Pak J Pharm Sci 2007; 20(2): 163-74.
15. International Conference on Harmonization [ICH] of technical requirements for registration of pharmaceuticals for human use guideline on validation of analytical procedure – Methodology ICH, Geneva, Switzerland 1996.