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A Simple Analytical Method Development and Validation for the Quantification of Darifenacin Hydrobromide in Pure and Its Tablet Dosage Form using UV-Spectrophotometry

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A B S T R A C T

A simple, accurate and precise Zero order spectroscopy method was developed and validated for the estimation of Darifenacin Hbr bulk and pharmaceutical dosage forms. Distilled water was used as a diluent to dissolve Darifenacin Hbr. The drug mixture was sonicated for 5 mins for the enhanced solubility. The maximum absorption was found to be at 234.0 nm, which was selected for the further analysis of Darifenacin Hbr bulk and its tablet dosage forms. The proposed method was validated according to ICH guidelines. The method showed high sensitivity with linearity range from 10 to 60µg/mL (r^2=0.999). The limit of detection and limit of quantitation for estimation of Darifenacin Hbr was found to be 1.17µg/ml and 3.98957µg/ml, respectively. % Recovery was found to be in the range of 99.09% – 100.89 %. The reports expressed that the proposed method was found to be simple, precise, accurate and rapid for the estimation of Darifenacin Hbr bulk and tablet dosage form using UV spectroscopy.

Keywords: Darifenacin Hbr, Distilled Water, UV Spectroscopy, ICH Guidelines

A R T I C L E I N F O

CONTENTS

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1. Introduction

Darifenacin hydrobromide is a chemically 2-[(3S)-1-[2-(2,3-dihydro-1-benzofuran-5-yl)ethyl]pyrrolidin-3-yl]-2,2-diphenylacetamide.Darifenacin hydrobromide is a M3 muscarinic acetylcholine receptor, which is primarily responsible for bladder muscle contractions. It there by decreases the urgency to urinate. It should not be used in people with urinary retention. It is not known whether this selectivity for the M3 receptor translates into any clinical advantage when treating symptoms of overactive bladder syndrome. Darifenacin selectively antagonizes the muscarinic M3 receptor. M3 receptors are involved in contraction of human bladder and gastrointestinal smooth muscle, saliva production, and iris sphincter function. The chemical structure was shown in the following Figure-1. From the extensive literature survey very few methods have been reported for the estimation of Darifenacin Hbr in single and in its combined dosage form Literature survey revealed that Darifenacin Hbr was determined by liquid chromatographic methods in LC-MS2-3, GC4-5, GC-MS UV-Visible spectroscopy6-7 and HPTLC-LC8. However, in the present study the authors have developed three simple validated spectro photometric methods for the determination of Darifenacin Hydrobromide in pharmaceutical dosage forms.

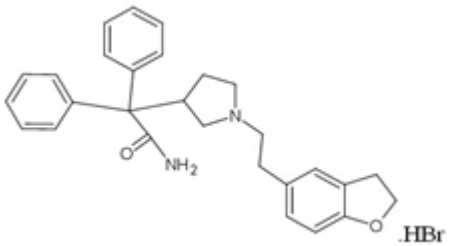


Figure 1: Darifenacin hydrobromide

2. Materials and Methods

Materials:

An analytically pure sample of Darifenacin hydrobromide was procured as gift sample from MSN laboratories (Hyderabad, India). Tablet formulation [Dariten, Acme Formulation Pvt. Ltd. India] was procured from a local pharmacy with labelled amount 5 mg per tablet. Distilled water is used as solvent for dilution of Darifenacin. Distilled water was prepared by distillation unit in Lab. Spectral measurement is carried out using Spectrophotometer, ELICO SL-244 UV/VIS double beam spectrophotometer with 'spectratreats' software using 1 cm matched quartz cell. Ultra Sonicator –Model: 2200 MH Soltech, Spincotech Pvt. Ltd.ko Denshi Digital Electronic balance - Model: HT 220T, VIBRA Shinko Denshi, ESSAE Co. Ltd., Capacity: 220g, Sens: 0.0001g All the above instruments are available in department of Pharmaceutical analysis, JNTUA-OTPRI, Ananthapuramu.

Methods:

Preparation of stock solutions:

Darifenacin pure 100 mg was weighed and transferred to a 100 ml volumetric flask and dissolved in distilled water. It was dissolved properly and diluted up to the mark with diluent to obtain final concentration of 1000 µg/ml. 50µg/ml solution was prepared from the stock solution was prepared using distilled water, which was used as working standard.

Selection of analytical concentration ranges and calibration curve: From the standard stock solution of Darifenacin, appropriate aliquots were pipetted out in to 10 ml volumetric flasks and dilutions were made with distilled water to obtain working standard solutions of concentrations from 10-60 µg/ml. Absorbance for these solutions were measured at 233 nm. The standard solution analytical concentration range was found to be 10-60 µg/ml and those values were reported. The regression equation and correlation coefficient was determined and are presented.

Analysis of marketed formulations:

For the estimation of Darifenacin in tablets formulations, 20 tablets were weighed and triturate to fine powder. Tablet powder equivalent to 25 mg of Darifenacin was weighed and transfer into 25 ml volumetric flask than dissolved in diluent. It was kept for sonication for 3 min and this was filtered through 0.45 micron Whatman filter paper No. 41 and then final dilution was made with diluent to get the final stock solution of 1000 µg/ml. From this stock solution, various dilutions of the sample solution were prepared and analyzed.

3. Results and Discussion

Darifenacin Hydrobromide has the zero order absorbance overlay spectra maxima (figure 2) at 234.0 nm. The polynomial regression data for the calibration plots showed good linear relationship in the concentration range of 10-60 µg/ml with correlation coefficient (r^2) was found to be higher than 0.999 and the linearity curve was shown in figure 3. Validation was performed in terms of specificity and selectivity, precision and accuracy, linearity, LOD &LOQ.

Linearity and range: Calibration standards of Darifenacin Hydrobromide, covering the range 10-60µg/mL were prepared with the suitable dilution made from Darifenacin Hydrobromide stock solution. The calibration curves were obtained by plotting the intensity of absorbance against of concentration of Darifenacin Hydrobromide. The slope and intercept of the calibration line were determined by linear regression using the least squares method.

Specificity and selectivity

The interference from endogenous compounds was investigated by the analysis of tablets of various concentrations.

Precision: The intra & inter-day precision was evaluated by analyzing six sample solutions (n = 6), at the final concentration of analysis (50µg/ml) of Darifenacin Hydrobromide. The Darifenacin Hbr concentrations were determined and the relative standard deviations (RSD) were calculated.

Accuracy

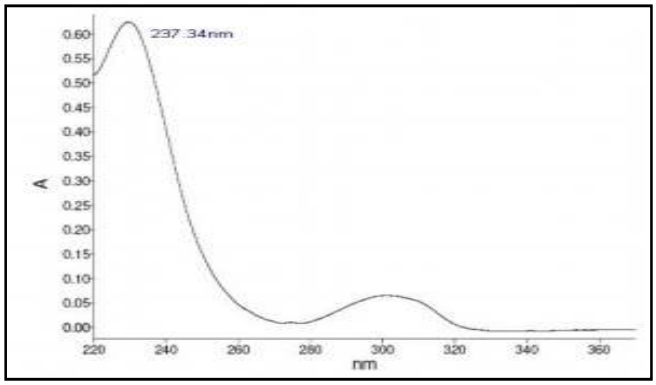
Darifenacin Hydrobromide reference standards were accurately weighed and added to a mixture of the tablets

excipients, at three different concentration levels (50,100 and 150 µg/ml of Darifenacin Hbr.) At each level, samples were prepared in triplicate and the recovery percentage was determined.

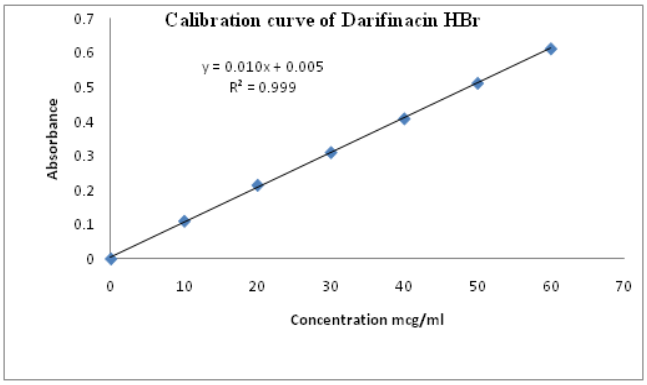
Detection and quantitation limits

Limit of detection LOD and limit of quantification LOQ were calculated by using the standard deviation from the precision and the slope of linearity were carried out at three different levels i.e. 50 %, 100 %and 150 % by adding the pure drug to the previously analysed tablet powder sample. Percentage recovery for Darifenacin Hydrobromide was determined by all the methods and they were found to be under acceptance criteria which are 99.20% to 100.69 % according to ICH guidelines [9]. The results of accuracy were in table 2.

The percentage recovery value indicates non interference from excipients used in formulation. The precision was carried out as described in method and the results were presented in table 1. The values obtained in the repeatability (precision) shows that there is no significant difference in the precision values; hence the developed method can be used to analyze the Darifenacin Hydrobromide in tablet formulation. The mean assay of the precision value is 100.29. The LOD determined as the amount drug was found to be 1.17µg/mL and LOQ was determined as the lowest concentration was found to be3.9895µg/mL in formulation. The summary of all the optical characterizes were shown in table 2.



Method A: Zero Order Derivative Spectroscopy



Results of calibration curve at 237 nm for Darifenacin hydrobromide

Table 1: Results of Precision

Sample No.	Intra Day	Assay
1.	0.509	99.80
2.	0.519	101.76
3.	0.514	100.78
4.	0.509	99.80
5.	0.507	99.41
6.	0.511	100.29
Mean	0.511	100.29
Std Dev	0.0039	0.7822
% RSD	0.779	0.779

Table 2: Summary of Optical characteristics and Other Parameters

S No.	Parameters	Results
1	Absorption Maxima (nm)	237
2	Beer's-Lambert's range (µg/ml)	10-60
3	Regression equation (y)*	Y = 0.010x+0.005
4	Slope (b)	0.010
5	Intercept (a)	0.005
6	Correlation coefficient (r^2)	0.999
7	Intraday precision (% RSD)**	0.07
8	Interday precision (% RSD)**	0.96

9	Accuracy (% mean recovery)	99.06-100.26
10	Limit of detection (µg / ml)	1.17
11	Limit of quantification (µg / ml)	3.9895
12	Assay of tablets (%Purity)	100.29

*y = a + bx; when x is the concentration in mg/ml and y is absorbance unit, **Average of six determinations

4. Conclusion

A novel, simple and cost effective spectrophotometric method for the quantitative estimation of Darifenacin Hybromide in bulk drug and pharmaceutical formulations have been developed. From the recovery studies non interference of excipients was observed. Hence the method was found to be precise, robust and accurate. The developed method can be successfully used for routine analysis of Darifenacin Hydrobromide in its pure and pharmaceutical formulation.

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