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Extractive spectrophotometric methods for the determination of darifenacin

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ABSTRACT

Two simple and sensitive extractive spectrophotometric methods have been developed for the estimation of Darifenacin in pure and pharmaceutical dosage forms. These methods are based on the formation of ion-pair complexes of the drug with acidic dyes Solochrome black T (SBT: λmax 520 nm) and Methyl Orange (MO: λmax 420 nm). The absorbance of the chloroform extracts is measured against the corresponding reagent blanks. These methods have been statistically evaluated and found to be precise and accurate.

Key words: Darifenacin, Spectrophotometric methods, pharmaceutical dosage forms.

INTRODUCTION

Darifenacin which is chemically (S)-2-{1-[2-(2,3-dihydrobenzofuran-5yl) ethyl]-3-pyrrolidinyl}-2, 2-diphenyl acetamide is a novel antimuscarinic agent, which has demonstrated clinical benefit in over-active bladder disease. Darifenacin is a selective muscarinic M3 receptor antagonist. A few number of methods such as HPLC, LC-MS were reported for the estimation of Darifenacin. Literature survey reveals that visible spectrophotometric methods have not been reported for its quantitative determination in its pure form and pharmaceutical formulations. In the present investigation two simple and sensitive extractive spectrophotometric methods have been developed for the determination of Darifenacin. The developed methods involve the formation of colored chloroform extractable complexes with SBT and MO. Extractable complexes showed absorption maximum at 520 and 420nm respectively. Beers law is obeyed in the concentration ranges of 10-30µg/ml and 5-15µg/ml respectively. The results of analysis for the two methods have been validated statistically and by recovery studies.

EXPERIMENTAL

Preparation of reagents

- Solochrome Black T Solution (0.5% w/v): 0.5 g of SBT dye was dissolved in 100 ml of distilled water.
- Methyl Orange Solution (0.1% w/v): 0.1 g of MO dye was dissolved in 100 ml of distilled water.
- Acid phthalate Buffer pH 2.4 (I.P)
- Standard drug solution: About 100mg of Darifenacin was accurately weighed and dissolved in 100 ml of water to obtain a stock solution of 1 mg/ml. This solution was further diluted with distilled water to get working standard solution of 100 µg/ml.

Assay procedures

Method A

Aliquots of working standard solution of Darifenacin ranging from 1 - 3 ml were transferred into a series of 125 ml separating funnels. To these 1 ml of 0.5% SBT dye was added. The total volume of aqueous phase was adjusted to 10 ml with distilled water and 10 ml of chloroform was added. The contents were shaken for 2 minutes. The two phases were allowed to separate and the absorbance of the separated organic layer (pink colored chromogen) was measured at 520 nm against reagent blank. The amount of Darifenacin present in the sample solution was computed from its calibration curve.

Method B

Aliquots of working standard solution of Darifenacin ranging from 0.5 - 1.5 ml were transferred into a series of 125 ml separating funnels. To these 1 ml of pH 2.4 Acid Phthalate buffer and 2 ml of 0.1% MO dye was added. The total volume of aqueous phase was adjusted to 10 ml with distilled water and 10 ml of chloroform was added. The contents were shaken for 2 minutes. The two phases were allowed to separate and the absorbance of the separated organic layer (yellow colored chromogen) was measured at 420 nm against reagent blank. The amount of Darifenacin present in the sample solution was computed from its calibration curve.

Table 1: Optical Characteristics, Accuracy and precision of the proposed methods

Parameters	Method A	Method B
λmax (nm)	520	420
Beers law limit (µg/ml)	10-30	5-15
Sandell's sensitivity(µg/cm^2/0.001 Absorbance unit)	0.0458	0.0217
Molar absorptivity(Litre/mole^{-1}cm^{-1})	9.5×10^3	2.02×10^4
Regression equation(Y*)		
Slope(b)	0.0195	0.0436
Intercept(a)	0.0302	0.0334
Correlation coefficient(r)	0.9991	0.999
% Relative Standard Deviation**	0.801	0.586
% Range of error		
0.05 Significance level	0.812	0.564
0.01 Significance level	1.264	0.828

* Y = a + bx, where 'Y' is absorbance and x is the concentration of Darifenacin in µg/ml
** For six replicates

Table 2: Estimation of Darifenacin in Pharmaceutical Formulations

Formulation	Labelled Amount (mg/Tab)	Amount found* by proposed method		% Recovery** by proposed method	
		Method A (mg)	Method B (mg)	Method A	Method B
Tablet 1	7.5	7.45	7.41	98.12	98.24
Tablet 2	7.5	7.38	7.45	98.8	98.04
Tablet 3	15	14.82	14.86	98.75	98.26
Tablet 4	15	14.89	14.82	98.46	98.62

* Average of six determinations
** Recovery of amount added to the pharmaceutical formulation (Average of three determinations)

RESULTS AND DISCUSSION

The optical characteristics such as beers law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation, percent range of error (0.05 and 0.01 confidence limits) were calculated for both the methods and results are summarized in Table 1. The values obtained for the determination of Darifenacin in Pharmaceutical formulations (Tablets) by the proposed methods are presented in Table 2. Studies reveal that the excipients and other additives usually present in the Tablets did not interfere with the results obtained in the proposed methods.

CONCLUSION

The proposed methods are applicable for the assay of drug Darifenacin and have an advantage of wider range under Beers law limits. The proposed methods are simple, selective and reproducible and can be used in the routine determination of Darifenacin in pure form and formulations with reasonable precision and accuracy.

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