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Spectrophotometric methods for the determination of darifenacin

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ABSTRACT

Three simple and sensitive spectrophotometric methods have been developed for the estimation of darifenacin in bulk and pharmaceutical dosage forms. Method A is based on oxidation followed by complex formation of the drug with 2, 5 dihydroxy 3, 6 dichloro 1, 4 benzoquinone (chloralinic acid λ_{max} 530 nm). The absorbance of the colored species is measured against the corresponding reagent blank at 530nm. Method B is based on complex formation of the drug with chloranil (λ_{max} 570nm). Method C is based on oxidation followed by complex formation of the drug with potassium permanganate ($KMnO_4$ λ_{max} 430nm). These methods have been statistically evaluated and found to be precise and accurate.

Keywords: spectrophotometric, darifenacin, determination

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INTRODUCTION

Darifenacin which is chemically (S)-2-{1-[2-(2, 3-dihydrobenzofuran-5-yl) ethyl]-3-pyrrolidinyl}-2, 2-diphenylacetamide is a selective muscarinic M3 receptor antagonist. A number of methods such as HPTLC, 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 drug and pharmaceutical formulations. In the present investigation three simple and sensitive spectrophotometric methods have been developed for the determination of darifenacin. The developed methods involve the formation of colored complexes with chloranilic acid, chloranil and potassium permanganate reagents. The colored chromogens showed absorption maximum at 530nm, 570nm, and 430nm respectively. Beers law is obeyed in the concentration ranges of 1-3µg/ml, 2-6µg/ml and 1-3µg/ml respectively. The results of analysis for the three methods have been validated statistically and by recovery studies [1-6].

EXPERIMENTAL

Preparation of reagents

1. Chloralinic acid (0.014M in acetone): 73mg of Chloralinic acid in 25ml acetone was prepared.
2. Chloranil (0.1%):100mg of chloranil dissolved in 100 ml of 1, 4- dioxane.
3. Potassium permanganate (0.019M): 0.015g in 50ml distilled water, from this 1ml was diluted to 25ml with distilled water.
4. Standard drug solution for Method A: About 25mg of darifenacin was accurately weighed and dissolved in 5ml of Dimethyl formamide, to this add 1drop of methyl red indicator titrate then with 0.1NHcl until yellow color appears and make up the volume with acetone to get 1mg/ml.This solution was further diluted to get working standard solution of 100µg/ml.
5. Standard drug solution for Method B: About 100mg of darifenacin was accurately weighed and dissolved in 25 ml of 10% of Na2Co3 and extract with 75ml of chloroform. Make up the chloroform extract to 100ml to get 1mg/ml.This solution was further diluted to get working standard solution of 100µg/ml.
6. Standard drug solution for Method C: About 100mg of darifenacin was accurately weighed and dissolved in 100 ml of Methanol to obtain a stock solution of 1mg/ml. This solution was further diluted to get working standard solution of 100µg/ml.

Assay procedures

Method A

Aliquots of working standard solution of darifenacin ranging from 0.1-0.3 ml were transferred into a series of 10 ml volumetric flasks. To this 1 ml of chloranilic acid was added. The total volume was made up to 10ml with acetone. The absorbance of the pink colored

chromogen was measured at 530 nm against reagent blank and 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 0.2-0.6 ml were transferred into a series of 10ml volumetric flasks. To this 1 ml of chloranil was added. The total volume was made up to 10ml with chloroform. The absorbance of the bluish violet colored chromogen was measured at 570nm against reagent blank. The amount of drug present in the sample solution was computed from its calibration curve.

Method C

Aliquots of working standard solution of darifenacin ranging from 0.1-0.3 ml were transferred into a series of 10ml volumetric flasks. To this 1 ml of potassium permanganate was added and allowed to stands for 20minutes. The total volume was made up to 10ml with water. The absorbance of the cherry red colored chromogen was measured at 430nm against reagent blank. The amount of drug present in the sample solution was computed from its calibration curve.

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 all 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 common excipients and other additives usually present in the Tablets did not interfere in the proposed methods.

CONCLUSION

The proposed methods are simple, selective and reproducible and can be used in the routine analysis of darifenacin in bulk and pharmaceutical formulations with reasonable accuracy and precision.

Table-1: Optical characteristics, precision and accuracy of the proposed method

Parameters	Method A	Method B	Method C
λ_{max} (nm)	530	570	430
Beer's law limit(µg/mL)	1-3	2-6	1-3
Sandell'sensitivity(µg/cm^2/0.001abs.unit)	0.326	0.719	0.0325
Molar absorptivity(litre.$mole^{-1}$.cm^{-1})	$0.1303x10^4$	$0.059x10^4$	$0.135x10^5$
Regression equation(Y*)			
Slope(b)	0.0024	0.0013	0.0241
Intercept(a)	0.072	0.006	0.0656
Correlation coefficient(r)	0.9986	0.9992	0.9992
%Relative standard deviation**	1.274	0.92	0.86
%Range of error			
0.05 significance level	0.861	0.769	0.685
0.01 significance level	1.274	1.138	1.014

*Y = a + bx, where 'Y' is the absorbance and x is the concentration of Darifenacin µg/mL

**For six replicates

Table-2: Estimation of Darifenacin in Pharmaceutical Formulations

Formulations (Tablets)	Label led amount(mg)	Amount found* by proposed method			% recovery** by proposed method		
		Method A	Method B	Method C	Method A	Method B	Method C
Tablet 1	7.5	7.47	7.46	7.48	99.6	99.46	99.7
Tablet 2	7.5	7.46	7.45	7.47	99.46	99.3	99.6
Tablet 3	15	14.97	14.96	14.98	99.8	99.7	99.26
Tablet 4	15	14.98	14.95	14.97	99.86	99.6	99.1

***** Average of six determinations

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

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