Asian Journal of Chemistry; Vol. 23, No. 4 (2011), 1752-1754

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Spectrophotometric Determination of Solifenacin Succinate through Ion Association Complex Formation in Bulk Sample and Pharmaceutical Formulations

M. VENKATARAO, UMAMAHESWARI, G.S. RAO, D. SURESH and C.S.P. SASTRY*

Department of Pharmaceutical Analysis, Institute of Science, Technology & Research Academy, Sastra University, Thanjavur-613 402, India

*Corresponding author: Email: mvrao_82@yahoo.co.in

(*Received*: 17 July 2010; *Accepted*: 18 December 2010) AJC-9405

Simple, sensitive and reproducible spectrophotometric methods (method M_1 and method M_2) for the assay of solifenacin succinate are proposed. These methods are based on the formation of ion-association complex involving tertiary nitrogen of solifenacin and the acidic dye, tropaeolin OOO (TP OOO, λ_{max} 500 nm) (M_1), naphthol blue black (NBB, λ_{max} 624 nm) (M_2). Regression analysis of Beer's law plot showed good correlation in the concentration range of 6-21 µg/mL for method M_1 and M_2, respectively. The molar absorptivities fell with in range of 1.31×10^4-1.74×10^4 mol^{-1} cm^{-1}. The recoveries range from 99.02-100.16 %.

Key Words: Solifenacin, Assay, Spectrophotometric.

INTRODUCTION

Solifenacin succinate is a muscarinic receptor antagonist. Chemically, solifenacin succinate is butanedioic acid, compounded with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl-3,4-dihydro-1-phenyl-2(1*H*)-iso-quinolinecarboxylate (1:1) having an empirical formula of $C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$ and a molecular weight of 480.55. The structural formula of solifenacin succinate is shown in Fig. 1.

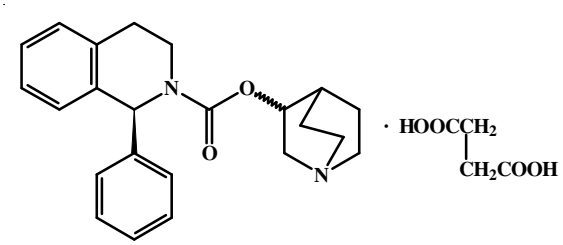

Fig. 1. Structure of solifenacin succinate

During the course of our efforts to develop sensitive visible spectrophotometric methods, it was observed that the analytically useful tertiary amino group in solifenacin has not been properly exploited[1-3]. Hence, there is a need to develop some new methods with either sensitivity or selectivity by exploiting the tertiary amino group in solifenacin. As the extraction spectrophotometric procedures are popular for their sensitivity and selectivity in the determination of drugs, the technique was therefore utilized in the present work for the assay of solifenacin. Solifenacin being basic in nature forms an ion-association complex with the acidic dye, namely naphthol blue black (NBB)[4], tropaeolin OOO (TP OOO)[4] which is extractable in chloroform. The protonated aliphatic tertiary nitrogen (positive charge) of the solifenacin in acid medium is expected to attract the oppositely charged part (negative charge) of the dye (SO_3^-) behave as single unit being held together by electrostatic attraction.

EXPERIMENTAL

A single-beam Varian-Cary (50 Conc) spectrophotometer with 1 cm quartz cells were used for the absorbance measurements in reference and proposed methods, respectively.

All reagents used were analytical grade and all solutions were prepared with double distilled water. Freshly prepared solutions were always used. Solifenacin succinate working standards were received from Analytical Development division of Orchid Health Care, Chennai, India. Solefenacin succinate 10 mg tablets (manufactured by Astellas) are purchased from market. Tropaeolin OOO (TP OOO), naphthol blue black (NBB) are purchased from sigma-aldrich chemicals.

Preparation of solutions

Preparation of tropaeolin OOO (TP OOO): Aqueous solution of TP OOO (Fluka, 0.2 % 5.70×10^{-3} M) was prepared by dissolving 200 mg of TP OOO in 100 mL of triply distilled water.

Preparation of naphthol blue black (NBB): Aqueous solution of NBB (Fluka, 0.2 %, 3.2×10^{-3} M) was prepared by dissolving 200 mg of NBB in 100 mL of triply distilled water.

Preparation of 0.1 M HCl: Prepared by diluting 8.6 mL of concentrated hydrochloric acid to 1000 mL with distilled water and standardized.

Preparation of pH 1.5 (glycine-HCl) buffer: pH 1.5 glycine buffer was prepared by mixing 338 mL of 0.1 M glycine solution (0.1 M, 7.507 g of glycine + 5.85 g of NaCl in 1 L of distilled water) and 662 mL of 0.1 M HCl and the pH of the solution was adjusted to 1.5 with 0.1 M HCl.

Preparation of standard solution: A 1 mg/mL solution was freshly prepared by dissolving 100 mg pure solifenacin succinate in 100 mL of distilled water and this stock solution was diluted stepwise with distilled water to obtain the working standard solutions of concentrations of 60 µg/mL.

Recommended procedures

For pure form (method M_1 and M_2): Into a series of 125 mL separating funnels containing aliquots of standard solifenacin succinate solution (1.0-3.0 mL, 60 µg/mL for method M_1 and M_2) 6.0 mL of buffer solution (0.1 M HCl for M_1 or pH 1.5 buffer for M_2) and 2.0 mL of TP OOO (M_1), NBB (M_2) were added. The total volume of aqueous phase in each separating funnel was adjusted to 15.0 mL with distilled water. To each separating funnel 10.0 mL of chloroform was added and the contents were shaken for 2 min. The phases were allowed to separate and the absorbance of the separated chloroform layer was measured at 500 nm (M_1) or 624 nm (M_2) against a similar reagent blank.

For pharmaceutical formulations: Twenty weighed tablets of solafenacin succinate (each tablet contains 10 mg of solifenacin succinate) were ground to a fine powder. The amount of powder equivalent to 12 mg of solifenacin succinate was extracted with methanol and filtered through 0.45 µm nylon membrane filter. The combined filtrate was evaporated to dryness and the residue was dissolved in 100 mL of distilled water and the solution was further diluted stepwise with distilled water to get working standard solutions and analyzed under procedures described for bulk samples.

The HPLC method was chosen as the reference method for ascertaining the accuracy of the proposed methods.

RESULTS AND DISCUSSION

Parameters fixation: The optimum conditions for the development of M_1 and M_2 methods were established by varying the parameters one at a time and keeping the others fixed and observing the effect produced on the absorbance of the coloured species.

Optimum condition fixation for method M_1 and M_2: The optimum conditions for the colour development of the methods were established by varying the parameters one at a time keeping the others fixed and observing the effect produced on the absorbance of coloured species. The following experiments were conducted for this purpose and the conditions so obtained were incorporated in the recommended procedure.

In the preliminary investigations, the two acidic dyes (TP OOO, NBB) were tested with different pH ranges or volumes of 0.1 M HCl. The comparative λ_{max} and ε_{max} values of the acidic dyes tested with solifenacin. The effect of pH (or acidity) was studied by extracting the coloured complex formed in the presence of various acidic buffers (or volumes of HCl). Of the various buffers (or acids) tried, 0.1 M HCl and pH 1.5 buffer were found to be more suitable for method M_1 and M_2, respectively. Six mL of buffer or acid was found to be optimal. Decrease in absorbance of the complex was observed when either the pH values or volumes of buffer (or acid) was decreased. The optimum volume of the dye used was also studied. Optimizations experiments revealed that an increase in absorbance reading with the icrease of the volume dye upto 2.0 mL (5.70×10^{-3} M for M_1 and 3.2×10^{-3} M for M_2). However, a significant increase in the absorbance value of the blank (more the 0.05 absorbance unit) was observed at volumes larger than 2.0 mL. From the organic solvents tested (benzene, toluene, nitrobenzene, carbon tetrachloride, 1,2-dichloromethane and chloroform), the chloroform was found to be most suitable because of the lowest extractability of free dyes and ease of extractablity of ion-association in it. A ratio of 3:2 of aqueous to chloroform phases was required for efficient extraction of the coloured species. Shaking times of 0.5-5.0 min produced a constant absorbance and hence a shaking time of 2 min was used throughout. The stoichiometric ratio of the Solifenacin to dye was found as 1:1 with TP OOO and NBB through slope analysis method.

Interference studies: The effect of various substances that often accompany in various pharmaceutical formulations were studied. To and aliquot containing 60 µg of solifenacin succinate, different amounts of various ingredients and additives were added individually until a solution showed the same absorbance (± 0.01) as that of pure solifenacin succinate solution under experimental conditions as described under the procedure. The commonly used ingredients and additives in the preparation of formulation such as talc (upto 200-fold excess, w/v). starch (150-fold, magnesium stearate (50-fold), lactose monohydrate (100-fold), hypromellose 2910 (60-fold), polyethylene glycol 8000 (30-fold) and titanium dioxide with red ferric oxide (20-fold), did not interfere with the assay of solifenacin succinate by proposed methods.

Analytical data: In order to test whether the coloured species formed in above methods adhere to Beer's law, the absorbances at appropriate lengths of a set of solutions containing varying amounts of solifenacin succinate and specified amount of reagents (as given in the recommended procedures for each method) were recorded against the corresponding reagent blanks. Beer's law limits, molar absorptivity, Sandell's sensitivity and optimum photometric range for solifenacin succinate in each method developed with mentioned reagents were calculated. Least-square regression analysis was carried out for getting the slope, intercept and the correlation coefficient values. The precision of the proposed methods was ascertained from the absorbance values obtained by actual determinations of six replicates of a fixed amount of solifenacin succinate in total solution (12 µg/mL for method M_1 and 14 µg/mL for method M_2). The per cent relative standard deviation and per cent range of error (95 % confidence limits) were calculated for the proposed methods (Table-1).

Analytical formulations: The analytical utility of each method was verified by means of replicate assays of commercial

TABLE-1
OPTICAL CHARACTERISTICS, PRECISION AND ACCURACY OF THE PROPOSED METHODS FOR SOLIFENACIN SUCCINATE

Parameters	Method M_1	Method M_2
λ_{max} (nm)	500	624
Beer's law limits (μg mL^{-1})	6-21	6-21
Molar absorptivity (1 mol^{-1} cm^{-1})	1.74×10^4	1.31×10^4
Detection limit (μg mL^{-1})	0.658	1.212
Sandell's sensitivity (μg cm^{-2}/0.001 absorbance unit)	0.021	0.028
Optimum photometric range (μg mL^{-1})	6-18	9-21
Regression equation (y)[a]		
Slope (b)	4.73×10^{-2}	3.63×10^{-2}
Intercept (a)	7.81×10^{-3}	2.04×10^{-3}
Correlation coefficient (r)	0.9995	0.9998
Relative standard deviation (%)[b]	0.516	0.624
Percentage range of error (95 % confidence limits)	0.998	2.281

[a]y = a + bc, where c = concentration in μg mL^{-1} and y is the absorbance unit. [b]Six replicate injections.

TABLE 2
ASSAY OF SOLIFENACIN SUCCINATE IN PHARMACEUTICAL FORMULATIONS

Pharmaceutical formulations[a] (tablets)	Labelled amount (mg)	Recovery (%) by proposed methods (mg)[b]		HPLC reference method (mg)
		Method M_1	Method M_2	
C1	10	99.67 ± 0.30	99.66 ± 0.36	99.86 ± 0.30
		t = 1.15	t = 1.37	
		F = 1.00	F = 1.44	
C2	10	99.02 ± 0.13	99.08 ± 0.23	99.87 ± 0.18
		t = 1.06	t =1.05	
		F = 1.91	F = 1.63	
C3	10	99.64 ± 0.30	100.16 ± 0.33	99.72 ± 0.26
		t = 1.00	t = 0.56	
		F = 1.33	F = 1.61	
C4	10	99.37 ± 0.22	99.82 ± 0.23	99.91 ± 0.17
		t = 1.00	t = 1.01	
		F = 1.67	F = 1.83	

[a]Four different batches of tablets from a pharmaceutical company. [b]Average (± RSD) of six determinations: the t- and F-values refer to comparison of the proposed method with the reference method.

formulations (tablets) containing solifenacin succinate. The values obtained by the proposed and reference methods for formulations were compared statistically with t- and F-tests and found not differ significantly. The results are summarized in Table-2.

Stability studies: The stability of solifenacin succinate in aqueous solution is up to 12 h, while during actual analysis the stability of coloured species after maximum colour development remains stable 15 min in all two methods. Hence these mehods can be used for the stability studies.

For method M_1 and M_2: The chemistry of these methods are based on formation of ion-issociation complex involving tertiary nitrogen of solifenacin and the acidic dye, (TP OOO, NBB). Due to the basic nature of solifenacin forms an ion-association complex with the acidy dye, namely TP OOO, NBB, which is extractable into chloroform. The protonated aliphatic tertiary nitrogen (positive charge) of the solifenacin in acid medium is expected to attract the oppositely charged part (negative charge) of the dye (SO^{3-}) and behave as a single unit being held together by electrostatic attration.

Conclusion

The proposed methods exploit the applications of formation of ion-association complex formation with acidic dye due to the presence of tertiary nitrogen atom in solifenacin succinate. The differences between proposed and reported methods depends on the nature of reagents, type of reactions and coloured species formed. Thus all the proposed methods are simple and sensitive with good precision and accuracy and can be used as alternatives for the assay of solifenacin succinate in bulk and pharmaceutical formulations.

ACKNOWLEDGEMENTS

The authors thank Laboratorios Orchid (India) for assistance and providing the drugs as gift samples.

REFERENCES

1. Remington's, The Science and Practice of Pharmacy, edn. 19, pp. 1186, 1322 (1995).
2. British Pharmacopoeia, HMSO, London, pp. 934, 1143 (1999).
3. United States Pharmacopoeia, USP Convention Inc., Rockville, Vol. 24, pp. 1335, 1336 (2000).
4. Analytical Profiles of Drug Substance, New York Academic Press, Vol. 14, pp. 157-180 (1985).
5. H. Seno, H. Hattori, A. Ishi and O. Suziki, *J. Chromatogr. B Biomed. Sci. Appl.*, **746**, 3 (2000).
6. G. Aymard, M. Legrand, N. Tricheren and B. Diquet, *J. Chromatogr. B Biomed. Sci. Appl.*, **744**, 227 (2000).
7. Y.Q. Li, W.X. Mo and Y. Zhang, *Huaxue Fence*, **29**, 329 (1993).
8. W. Baeyens, *Talanta*, **24**, 579 (1977).
9. S.A. Adelus and A.O. Onyekweli, *Pak. J. Sci. Ind. Res.*, **39**, 22 (1996).
10. D.L. Massart, B.G.M. Vandeginste, S.N. Demung, Y. Michoue and I. Kauffman, Chemometrics Textbook, Elsevier, Amsterdom (1998).