ISSN 2231-0541

PHARMANEST

An International Journal of Advances in Pharmaceutical Sciences

Volume 4 | Issue 2 | March-April 2013 | Pages 206-212

Original Research Article

VALIDATED RP-HPLC METHOD FOR THE ESTIMATION OF SOLIFENACIN SUCCINATE IN TABLET DOSAGE FORMS

[a] V. VIJAYASREE, [a] D. ANANTHA KUMAR, [b] J.V.L.N. SESHAGIRI RAO*

[a]College of Pharmaceutical Sciences, Andhra University, Visakhapatnam-530003.

[b]Yalamarty College of Pharmacy, Visakhapatnam-530052.

Author for Correspondence: jvlnsrao@rediffmail.com

Received: 11-04-2013 Revised: 14-04-2013

Accepted: 18-04-2013 Available online: 01-05-2013

ABSTRACT

A rapid and reproducible reverse phase high performance liquid chromatographic method has been proposed for the estimation of Solifenacin. HPLC separation was carried out on a Symmetry C_{18} Xterra column (150 x 4.6mm; 5µ) using a mobile phase composed of methanol and potassium dihydrogen phosphate buffer (65:35 v/v), which was pumped at a flow rate of 0.6 mL/min. The drug in the eluate was monitored at 210 nm. Under optimized conditions, the retention time obtained for the drug was 2.7 min. The method showed linear responses in the concentration range of 30 to 70 µg/mL of Solifenacin succinate. The method was found to be giving reproducible recoveries of the drug from its tablet dosage forms.

Key words: Solifenacin succinate, Tablets, Estimation, HPLC.

INTRODUCTION

Solifenacin [1, 2] is a urinary antispasmodic drug belonging to the antimuscarinic class. It is a competitive muscarinic acetylcholine receptor antagonist. By preventing the binding of acetylcholine to these receptors, particularly the M_3 subtype, the drug reduces smooth muscle tone in the bladder allowing the bladder to retain larger volumes of urine. The drug thus, is used for symptomatic treatment of overactive bladder with or without urge incontinence. Chemically, Solifenacin is 1-azabicyclo [2.2.2] oct-8-yl (1*S*)-1-phenyl-3,4- dihydro-1*H*-isoquinoline-2-carboxylate (Fig. 1). The succinate salt of Solifenacin is employed for the treatment. Very few HPTLC and HPLC methods [3-9] were reported earlier for the analysis of Solifenacin along with its degradation products and other drugs. In the present investigation, we have developed and validated [10] a rapid HPLC method for the assay of Solifenacin, which is applicable for estimation of the drug in its tablet dosage forms.

MATERIALS AND METHODS

Chemicals and Drugs

The reference sample of Solifenacin succinate was procured from Ranbaxy Laboratories, Gurgoan. HPLC grade methanol and GR grade potassium dihydrogen phosphate and *ortho*- phosphoric acid were purchased from Qualigens, India. High purity water was prepared by using Millipore MilliQ plus water purification system. Commercial tablets of Solifenacin succinate (Soliten; 10 mg; Ranbaxy Laboratories) were used in the study.

Instrumentation and chromatographic conditions

A Shimadzu Prominence HPLC instrument equipped with a Symmetry C_{18} Xterra analytical column (150 x 4.6 mm; 5µ), an LC-20AT pump, a CTO-20A column oven, a Rheodyne 7725 sample injector with a 20 µL loop and an SPD-20A UV-Vis detector was employed for this analysis. Empower2 software was used for the data acquisition, analysis and quantification of peaks.

A freshly prepared 65:35 v/v mixture of methanol and phosphate buffer (pH 3.3) was used as the mobile phase. The mixture was filtered through a 0.45 µ membrane filter and sonicated before use. The flow rate of the mobile phase was maintained at 0.6 mL/min. The column temperature was maintained at 25 ± 1^0 C.

A DGU-20A degasser was used to enhance the solubility of the drug and to remove entrapped air in the solution. The detection of the analyte was done at 210 nm.

Preparation of phosphate buffer (pH 3.3)

7.0 g of potassium dihydrogen phosphate was weighed into a 1000 mL beaker and dissolved in 1000 mL of HPLC grade water. The pH of the solution was adjusted to 3.3 with *ortho*-phosphoric acid.

Preparation of standard solution of the drug

About 10 mg of Solifenacin succinate was weighed accurately and transferred into a 10 mL volumetric flask and dissolved in 7 mL of the mobile phase. The solution was sonicated for 20 min and then the volume made up with a further quantity of the mobile phase to get a 1 mg/mL solution. From the above solution, a 0.5 mL aliquot was taken into a separate 10 mL volumetric flask and the volume was made up with the mobile phase to get a 50 µg/mL of the solution which was used as the working standard solution. Calibration standard dilutions ranging from 30-70 µg/mL were prepared in 10 mL volumetric flasks

using the stock solution. A 20 µL volume of each dilution was injected five times into the column and the corresponding chromatograms were obtained. From these chromatograms, the average area under the peak of the drug for each concentration was calculated. A graph of the peak areas over the drug concentrations was plotted and its regression was computed. This regression equation was subsequently used to estimate the amount of Solifenacin succinate in its tablet dosage forms.

Solifenacin succinate in tablet dosage form

Five tablets of Solifenacin succinate (Soliten; 10 mg) were weighed and powdered uniformly in a mortar. An accurately weighed portion of this powder equivalent to 10 mg of Solifenacin succinate was transferred into a 10 mL volumetric flask containing 7 mL of the mobile phase. The contents of the flask were sonicated for about 20 min for complete solubility of the drug and the volume was made up with the mobile phase. The mixture was then filtered through a 0.45 µ membrane filter. From the above solution, a 0.5 mL aliquot was taken into a 10 mL volumetric flask and the volume was made up with the mobile phase to get a dilution of 50 µg/mL of the drug. This solution was then injected (20 µL) five times into the column. The mean peak area of the drug was calculated from the chromatograms and the drug content in the formulation was computed by using the regression equation of the calibration plot.

RESULTS AND DISCUSSION

The present study was carried out to develop a sensitive, precise and accurate HPLC method for the analysis of Solifenacin succinate in tablet dosage forms. In order to achieve efficient separation of the component peak under isocratic conditions, mixtures of methanol and phosphate buffer (3.3 pH) in different proportions were tested as the mobile phase on a C_{18} stationary phase. A binary mixture of methanol and phosphate buffer in a 65:35 v/v proportion was proved to be the most suitable for the purpose since the chromatographic peaks obtained were better defined and resolved and almost free from tailing. The retention time obtained for Solifenacin succinate was 2.7 min. A model chromatogram showing the separation of the drug is shown in Fig.2. For the linearity study, each of the dilutions in the range of 30-70 µg/mL was injected five times. The average peak areas of Solifenacin succinate at different concentration levels were calculated (Table 1). In the relevant plot, a good linear relationship (r=0.9990) was observed between the concentration of Solifenacin succinate and the respective peak areas. The regression equation computed for the plot was y=46545x+85903 (where, y is the peak area of the drug and x is the concentration of Solifenacin succinate). Method precision was studied in terms of repeatability and intermediate precision. To study the repeatability of the test, a 50 µg/mL of the working standard solution was injected six times in the system and areas under the curve were noted. The % RSD of the areas obtained for the above six injections was 0.32 which indicates that the method is quite precise (Table 2). The intermediate precision was assessed by injecting the drug solution in triplicate at three different concentration levels (40, 50 and 60 µg/mL) on three different days. The % RSD of the area obtained for the above injections was 1.1.

The accuracy of the method was determined by adding known amounts of the drug (50, 100 and 150%) to the working standard

solution (50 µg/mL) and analyzing the samples for recovery. A mean recovery of 99.4% of Solifenacin succinate was obtained from the pre-analyzed samples indicating high accuracy of the proposed method. (Table 3). To determine the robustness of the method, the chromatographic conditions were deliberately altered slightly. The flow rate (±10%) and the organic content in the mobile phase (±2%) were altered and the influence of these changes on the plate count and tailing factor were evaluated. The method was found to be robust enough as the selected factors were affected by these changes within the allowed limits. (Tables 4a and 4b). Limit of detection and limit of quantification were calculated basing on the signal to noise ratios. The LOD and LOQ were found to be 2.98 and 9.98 µg/ml respectively.

The drug content in the commercial tablet sample was quantified by using the proposed analytical method. A recovery of 99.90% of the labeled claim of the drug was obtained.

The low coefficient of variation indicates the reproducibility of the method for estimation of Solifenacin succinate in tablet dosage forms (Table 5). The chromatograms obtained for the formulation solutions did not show any interfering peaks at the retention time of the drug showing that the method is specific.

CONCLUSION

The proposed RP-HPLC method for quantitative determination of Solifenacin succinate is precise, accurate and selective and was duly validated. This method can also be used for the estimation of Solifenacin succinate in its tablet dosage forms with satisfactory results.

ACKNOWLEDGEMENT

The authors are thankful to Ranbaxy Laboratories, Gurgoan, for providing a reference sample of Solifenacin succinate.

Table.1. Linearity range

Concentration (µg/ml)	Average Area
30	2258896
40	2719216
50	3176180
60	3662682
70	4114402

Regression equation y=46545x+85903 (r=0.9990)

Table.2. Precision of the method (Repeatability)

Injection replicate	Area
1	3203717
2	3186236
3	3184066
4	3172206
5	3185143
6	3182456
Average	**3185637.3**
Standard deviation	**10202.6**
% RSD	**0.32**

Table.3. Accuracy of the proposed method

%concentration (at specification level)	Area (n=3)	Amount added (mg)	Amount recovered (mg)	% Recovery	Mean recovery
50%	2433886	5.0	4.90	98.1	99.4
100%	4948405	10.0	9.98	99.80	
150%	7471111	15.0	15.0	100.4	

Table.4a. Robustness data

S. No.	Flow rate (mL/min.)	System suitability results	
		USP Plate count	USP Tailing
1	0.5	3879.6	1.6
2	0.6	3394.2	1.8
3	0.7	3088.2	1.7

Table.4b. Robustness data

S. No.	Percentage of methanol in the mobile phase	System suitability results	
		USP Plate count	USP Tailing
1	63	3615.8	1.6
2	65	3394.2	1.6
3	67	3098.2	1.7

Table.5. Estimation of Solifenacin succinate from its tablets

Sample	Labeled amount(mg)	Amount found* ± S.D.	%Recovery ± R.S.D.
Soliten	10 mg	9.99 ± 0.23	99.88 ± 2.9

*Average ± standard deviation of five determinations

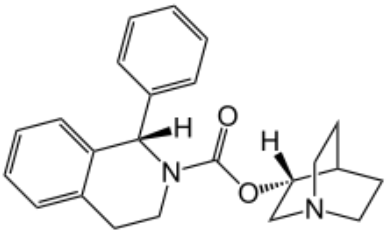

Fig.1.Structure of Solifenacin

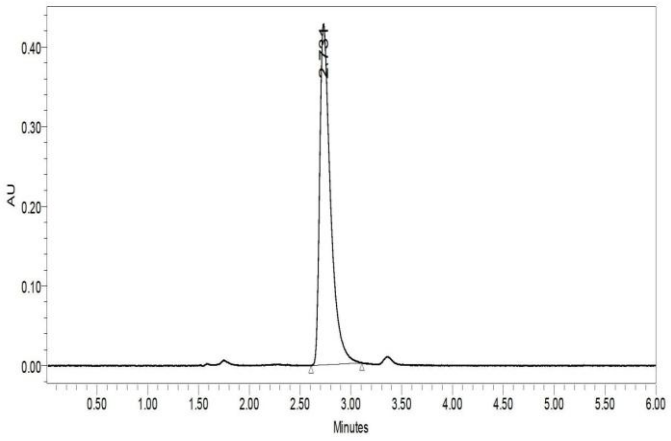

Fig.2. Typical Chromatogram showing the separation of Solifenacin succinate

REFERENCES

1. http://www.drugbank.ca/drugs/DB01591
2. http://www.drugs.com/monograph/vesicare.html
3. Desai D, Mehta G, Ruikar D, Jain R, Rajput S. Development and Validation of Stability-Indicating HPTLC Method of Solifenacin Succinate, Asian Journal of Pharmaceutical and Biological Research, 2011, 1 (3), 310-316.
4. Wankhede SB, Somani K, Chitlange SS. Stability indicating normal phase HPTLC method for estimation of Alfuzosin and Solifenacin in pharmaceutical dosage Form, International Journal of Chem Tech Research, 2011, 3(4), 2003-2010.
5. Desai N, Hussen SS, Vasanthraju SG, Karthik A, Udupa N. Development and validation of stability indicating RP-HPLC method for determination of Solifenacin in bulk formulations, Int. J. Pharm. Pharm. Sci., 2011, 3, 70-74.
6. Saroj Kumar R, Ravi Kumar BVV, Ajaya Kumar P. A RP-HPLC method Development and validation for the estimation of Solifenacin in bulk and pharmaceutical dosage forms, Int. J. Bioassays, 2012, 1, 210-13.
7. Desai D, Patel G, Shukla N, Rajput S, Development and validation of stability-indicating HPLC method for Solifenacin succinate: isolation and identification of major base degradation product, Acta Chromatographica, 2012, 24 (3), 399-418.
8. Nageswara rao K, Ganapaty S, Lakshmana rao A, Development and validation of RP-HPLC method for estimation of Solifenacin in bulk and tablet dosage form, Pharmanest, 2012, 3 (5), 366-374.
9. Rami Reddy BV, Srinivasa Reddy B, Raman NVVSS, Subhash Reddy K, Rambabu C. Development and validation of specific stability indicating RP-HPLC methods for related compounds and assay of Solifenacin succinate, J. Chem., 2013, Article ID 412353.
10. ICH Harmonized Tripartite Guideline, Q2 (R1), Validation of Analytical Procedures, Text and Methodology, International Conference on Harmonization, Geneva, 2005, 1-13.