

Spectrophotometric estimation of solifenacin succinate in tablet formulations

Abstract

Aim: The aim of this study is to develop a simple, sensitive, rapid, accurate, and precise spectrophotometric method for the estimation of solifenacin succinate in tablet dosage forms. **Materials and Methods:** For methods I and II, in a series of 10 ml volumetric flasks, aliquots of standard drug solution (100 µg/ml) in double distilled water were transferred and diluted with the same so as to give several dilutions in the concentration ranges of 10 – 60 µg/ml and 10 – 60 µg/ml, respectively, of solifenacin succinate. To 5 ml of each dilution taken in a separating funnel, (5 ml of bromo thymol blue for method I and 5 ml of bromo phenol blue for method II) reagent and 5 ml of chloroform were added. The reaction mixture was shaken gently for five minutes and allowed to stand so as to separate the aqueous and chloroform layers. The absorbance maxima were measured at 415.6 nm and 412 nm for methods I and II, respectively. **Results:** The recovery studies were found close to 100%, which indicates the accuracy and precision of the proposed methods. Statistical analysis was carried out, the results of which were found to be satisfactory. Standard deviation values were found to be low and that indicated the reproducibility of the proposed methods. **Conclusion:** The results indicated that both methods could be used for the routine estimation of solifenacin succinate from tablet formulations.

Key words: Bromo phenol blue, bromo thymol blue, solifenacin succinate, spectrophotometric

INTRODUCTION

Solifenacin succinate is an orally administered urinary antispasmodic anticholinergic drug. The chemical name of Solifenacin succinate is 1-azabicyclo [2.2.2] octan-8-yl (1s)-1-phenyl-3,4-dihydro-1h-isoquinoline-2-carboxylate butanedioic acid.^[1] Solifenacin is a competitive muscarinic acetylcholine receptor antagonist. The binding of acetylcholine to these receptors, particularly the M₃ receptor subtype, plays a critical role in the contraction of the smooth muscle. By preventing the binding of acetylcholine to these receptors, solifenacin reduces the smooth muscle tone in the bladder, allowing the bladder to retain larger volumes of urine and reducing the number of micturition, urgency, and incontinence episodes.^[2,3] A literature survey reveals one semi-micro high-performance liquid chromatography (HPLC) method^[4] and one simultaneous liquid chromatography electrospray ionization tandem mass spectrometry (LC-ESI-MS / MS) method^[5] for the determination of Solifenacin succinate in plasma. There are no spectrophotometric methods reported for the estimation of Solifenacin succinate in the pharmaceutical dosage form. Thus, efforts are being made to develop a fast, selective, and sensitive analytical method for the estimation of Solifenacin succinate in its tablet formulations. Solifenacin succinate is only available in the form of an oral tablet.

MATERIALS AND METHODS

Materials

Shimadzu UV 1700, a UV-Visible double beam spectrophotometer, with a

Lokesh Singh, Sanju Nanda¹

Department of Pharmaceutical Analysis, Swami Keshvanand Institute of Pharmacy, Bikaner, Rajasthan-334 001, India.

¹Department of Pharmaceutics, Maharishi Dayanand University, Rohtak, Haryana, India

Address for correspondence:

Mr. Lokesh Singh Swami, Keshvanand Institute of Pharmacy, NH-11, Raisar, Bikaner, Rajasthan-334 001, India. E-mail: lokeshshekhawat@in.com

Access this article online

Website: www.phmethods.org

DOI: 10.4103/2229-4708.81086

Quick response code



spectral band width of 1 nm, wavelength accuracy of ± 0.3 nm, and 1.0 cm matched quartz cells, was used for development of the analytical method. All the chemicals and reagents used were of analytical grade. Solifenacin succinate supplied by BePharm, Ltd. (China), was used as such, without further purification. Bromo thymol blue and Bromo phenol blue (Loba Chemie, Mumbai) reagents were prepared in double distilled water. All the reagents were extracted several times with chloroform so as to remove the chloroform-soluble impurities. The tablets of Solifenacin succinate were procured from a local pharmacy. BISPEC tab® 10 mg [Dr. Reddy's] and SOLITEN film-coated tab® 10 mg [Ranbaxy], were procured. A standard solution of Solifenacin succinate was prepared by dissolving 10 mg in 100 ml of double distilled water, to give a stock solution of concentration 100 $\mu\text{g/ml}$ of the drug.

Methods

Procedure for preparation of the calibration curve

For method I, in a series of 10 ml volumetric flasks, aliquots of the standard drug solution (100 $\mu\text{g/ml}$) in double distilled water were transferred and diluted with the same, so as to give several dilutions in the concentration range of 10 – 60 $\mu\text{g/ml}$ of Solifenacin succinate. To 5 ml of each dilution, taken in a separating funnel, 5 ml of bromo thymol blue (0.3% w/v) reagent and 5 ml of chloroform were added. The reaction mixture was shaken gently for five minutes and allowed to stand, so as to separate the aqueous and chloroform layers. The chloroform layer was separated out and an absorbance maximum was measured against a reagent blank. The calibration curve was plotted [Figure 1] between the concentrations of Solifenacin succinate and the measured absorbance.

For method II, in a series of 10 ml volumetric flasks, aliquots of the standard drug solution (100 $\mu\text{g/ml}$) in double distilled water were transferred and diluted with the same, so as to give several dilutions, in the concentration range of 10 – 60 $\mu\text{g/ml}$ of Solifenacin succinate. To 5 ml of each dilution, taken in a separating funnel, 5 ml of bromo phenol blue reagent (0.3% w/v) and 5 ml of chloroform were added. The reaction mixture was shaken gently for five minutes and allowed to stand, so as to separate the aqueous and chloroform layers. The chloroform layer was separated out and an absorbance maximum was measured against a reagent blank. The calibration curve was plotted [Figure 2] between the concentrations of Solifenacin succinate and the measured absorbance. The spectral characteristics of Solifenacin succinate for method I and method II are given in Table 1.

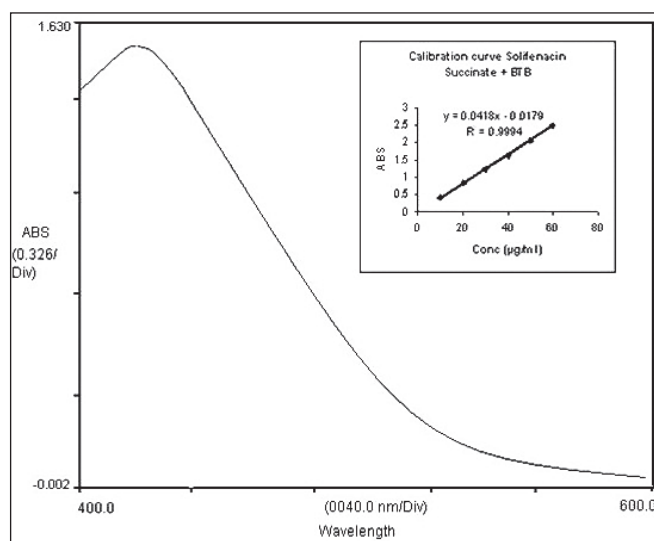


Figure 1: UV spectrum of Solifenacin succinate with bromo thymol blue reagent

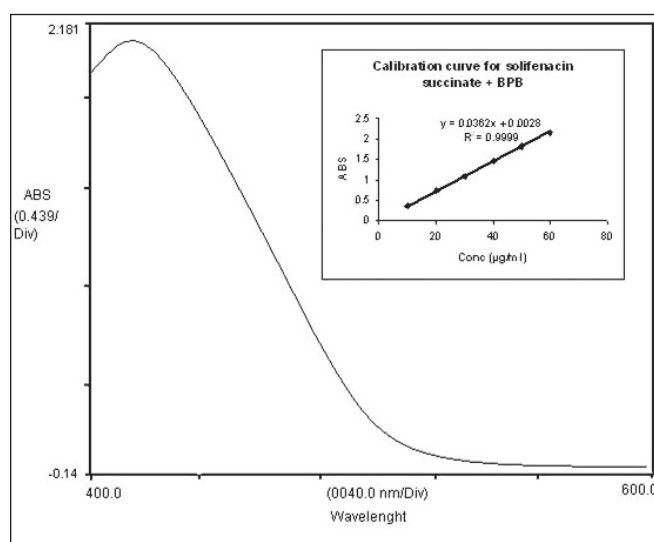


Figure 2: UV spectrum of Solifenacin succinate with bromo phenol blue reagent

Table 1: Spectral characteristics of Solifenacin succinate

| Parameters | Method I | Method II |
|-------------------------------------------|--------------------------|--------------------------|
| λ max | 415.6 nm | 412 nm |
| Beer's law limit ($\mu\text{g/ml}$) | 10 – 60 $\mu\text{g/ml}$ | 10 – 60 $\mu\text{g/ml}$ |
| Regression equation *A + bc | $y = 0.0418x - 0.0179$ | $y = 0.0362x + 0.0028$ |
| Slope (b) | 0.0418 | 0.0362 |
| Intercept (a) | -0.0179 | +0.0028 |
| Correlation coefficient (r) | 0.9994 | 0.9999 |
| Molar Absorptivity* (L/mol/cm) | 1.98×10^{10} | 1.73×10^{10} |

$y = a + bc$, where c is the concentration in $\mu\text{g/ml}$, y is the absorbance unit of six replicate samples, and b is the slope of the line equation; *Average of nine determinations

Table 2: Summary of validation parameters for the proposed methods and analysis of the marketed formulations

| Method | Formulation | Label claim (mg/tab) | % Label claim* estimated | % Recovery** (Accuracy) | SD | %RSD repeatability |
|--------|--------------------------|----------------------|--------------------------|-------------------------|-------|--------------------|
| I | BISPEC tab [®] | 10 mg | 99.95 | 99.64 | 0.298 | 0.2981 |
| | SOLITEN tab [®] | 10 mg | 99.91 | 99.86 | 0.346 | 0.3463 |
| II | BISPEC tab [®] | 10mg | 99.91 | 99.97 | 0.287 | 0.2872 |
| | SOLITEN tab [®] | 10 mg | 99.84 | 99.82 | 0.429 | 0.4296 |

*Average of six determinations; **Average of determinations at three different concentration levels; SD - Standard Deviation

Method validation

Calibration curve (linearity of the method)

The calibration curves were constructed by plotting the absorbance versus concentrations of Solifenacin succinate, after which the regression equations were calculated. The calibration curves were plotted over six different concentrations in the range of 10 – 60 µg/ml for method I and 10 – 60 µg/ml for method II.

Accuracy (% recovery)

The accuracy of the methods was determined by calculating the recoveries of Solifenacin succinate by the standard addition method. Known amounts of the mixed standard solution of Solifenacin succinate were added to prequantified sample solutions of the tablet dosage forms. The amounts of Solifenacin succinate were estimated by applying the values of absorbance to the regression equations of the calibration curve and the results of the recovery studies are reported in Table 2.

Method precision (Repeatability)

The precision was checked by repeatedly scanning (n = 6) the standard solutions of Solifenacin succinate (10 µg/ml) and the low value of standard deviation, as well as the relative standard deviation, which showed good method precision. Intermediate precision (Reproducibility): The intermediate precision for the proposed method was determined by estimating a standard solution of Solifenacin succinate for three different concentrations, thrice. The results were reported in terms of relative standard deviation (RSD).

Specificity

The excipients were spiked into a pre-weighed quantity of drugs, to assess the specificity of the methods. The comparison of the standard spectra and the spectra from the tablet solution showed that the wavelengths of maximum absorbance and maxima / minima did not change. It was concluded that the excipients did not interfere with the quantization of Solifenacin succinate in the tablet, by developed methods.

Robustness

The stability of the drug solution and the drug dye complex was studied at an ambient temperature. The robustness of the proposed methods was also tested by changing the wavelength range and scanning speed. The results were unaffected by these minor changes, which assured its reliability during normal usage.^[6]

Procedure for analysis of tablet formulation

For analysis of tablet formulation, 20 tablets (10 mg) of Solifenacin succinate were weighed accurately and finely powdered. An accurately weighed, powdered sample, equivalent to 10 mg of Solifenacin succinate, was taken in a 100 ml volumetric flask containing 40 ml of double distilled water, and sonicated for 10 minutes. The resultant was filtered through Whatman filter paper No. 41 into another 100 ml volumetric flask. The filter paper was washed several times with double distilled water. The washings were added to the filtrate and the final volume was brought up to the mark with double distilled water.

For method I, 3 ml of the filtrate from the sample solution was diluted to 10 ml with double distilled water. This was treated as per the procedure used in the preparation of the calibration curve, and the amount of drug present in the sample was computed from the respective calibration curve.

For method II, 3 ml of filtrate from the sample solution was diluted to 10 ml with double distilled water. This was treated as per the procedure used in the preparation of the calibration curve and the amount of drug present in sample was computed from the respective calibration curve. The procedure of analysis from the tablet formulations for all the methods were repeated five times with two different tablet formulations and the results are reported in Table 2.

Recovery studies

Recovery studies were carried out for both the developed methods by the addition of a known

amount of standard drug solution of Solifenacin succinate to a pre-analyzed tablet sample solution, at three different concentration levels. The resulting solutions were analyzed by the proposed methods. The results of the recovery studies are reported in Table 2.

RESULT AND DISCUSSION

The developed analytical methods were found to be specific, accurate, and precise, and played a vital role in many of the essential features required for an analytical system. They were adopted in a wide range of pharmaceutical analysis. Taking into account the above-mentioned characteristics, two accurate, simple, precise, economical, and rapid, visible spectrophotometric assay methods were developed, for the quantitative estimation of Solifenacin succinate in tablet dosage forms.

The optimum reaction conditions for the quantitative determination of ion pair complexes were established via a number of preliminary experiments. To test the accuracy and reproducibility of the proposed methods, the recovery experiments were carried out by adding a known amount of drug to the pre-analyzed formulation and reanalyzing the mixture by using the proposed methods.

Stability studies of chromogen were carried out by measuring the absorbance values at a time interval of 10 minutes, for four hours, and it was found to be 90 minutes for Method I and 120 minutes for Method II. The optical characteristics such as absorption maxima, Beer's law limits, correlation coefficient (r), slope (m),

y -intercept (c), and molar absorptivity calculated from nine replicate readings are incorporated in Table 1. The reproducibility, repeatability, and accuracy of these methods were found to be good, which was evident by the low standard deviation values. The average percentage of recovery values obtained were 99.75 for I and 99.89 for II, which indicated no interference from the excipients used in the formulation. Hence, these developed methods could be used for the routine estimation of Solifenacin succinate in tablet formulations.

REFERENCES

1. Budavari S, editor. The Merck Index. 14th ed. Whitehouse Station, NJ: Merck and Co Inc; 1996. p. 1494.
2. Cardozo L, Lisek M, Millard R. Randomized, double-blind placebo controlled trial of the once daily antimuscarinic agent solifenacin succinate in patients with overactive bladder. *J Urol* 2004;172:1919-24.
3. Garely AD, Kaufman JM, Sand PK. Symptom bother and health - related quality of life outcomes following solifenacin treatment for overactive bladder: The VESiCare Open-Label Trial (VOLT). *Clin Ther* 2006;28:1935-46.
4. Yanagihara T, Aoki T, Soeishi Y, Iwatsubo T, Kamimura H. Determination of solifenacin succinate, a novel muscarinic receptor antagonist, and its major metabolite in rat plasma by semi-micro high performance liquid chromatography. *J Chromatogr B Analyt Technol Biomed Life Sci* 2007;859:241-5.
5. Mistri HN, Jangid AG, Pudage A, Rathod DM, Shrivastav PS. Highly sensitive and rapid LC-ESI-MS/MS method for the simultaneous quantification of uroselective alpha1-blocker, alfuzosin and an antimuscarinic agent, solifenacin in human plasma. *J Chromatogr B Analyt Technol Biomed Life Sci* 2008;876:236-44.
6. CPMP/ICH/281/95, Note for Guidance on Validation of Analytical Procedures: Methodology, ICH Topic Q2B Validation of Analytical Procedures: Methodology, Step 4 (CPMP Adopted Dec 96).

Source of Support: Nil, Conflict of Interest: None declared.

Staying in touch with the journal

1) Table of Contents (TOC) email alert

Receive an email alert containing the TOC when a new complete issue of the journal is made available online. To register for TOC alerts go to www.phmethods.org/signup.asp.

2) RSS feeds

Really Simple Syndication (RSS) helps you to get alerts on new publication right on your desktop without going to the journal's website. You need a software (e.g. RSSReader, Feed Demon, FeedReader, My Yahoo!, NewsGator and NewzCrawler) to get advantage of this tool. RSS feeds can also be read through FireFox or Microsoft Outlook 2007. Once any of these small (and mostly free) software is installed, add www.phmethods.org/rssfeed.asp as one of the feeds.