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QUANTITATIVE ANALYSIS OF SOLIFENACIN SUCCINATE IN PHARMACEUTICAL DOSAGE FORM USING UV ABSORPTION SPECTROSCOPY

G. DIVYA TEJA*, CH. DEVA DASU, SRINIVASA BABU P, RAVISANKAR P

*[1]Department of Pharmaceutical Analysis and Quality Assurance, Vignan Pharmacy College, Vadlamudi, Guntur-522 213. Andhra Pradesh, India.

***Corresponding Author: Email: gadeteja.22@gmail.com, Mobile: +91-9177861313**

ABSTRACT

Simple, accurate, sensitive, precise and economical spectrophotometric method has been developed for the determination of Solifenacin succinate in tablet formulation. Measurement of ultraviolet absorption at 220 nm. The proposed method was validated statistically. The developed method obeyed Beer's law in the concentration range of 2-10 µg/mL. The limit of detection and limit of Quantitation for estimation of solifenacin succinate were 0.301786 µg/mL and 0.914505 µg/mL respectively. The recovery was in the range of 99.174 to 101.012 %. The developed method can be used for routine quality control analysis of solifenacin succinate in pharmaceutical tablet dosage form.

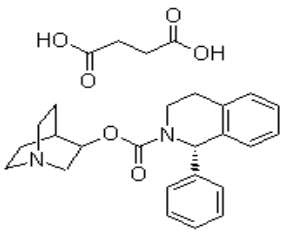
KEY WORDS - Solifenacin succinate, UV Spectroscopy, Validation, Assay.

1. INTRODUCTION

Solifenacin succinate is chemically 1-Azabicyclo[2.2.2]octan-8-yl(1S)-1-phenyl-3,4-dihydro-1H-isoquinoline-2-carboxylate butanedioic acid (Fig. 1). It is a competitive muscarinic acetylcholine receptor antagonist used for the treatment of overactive bladder with urge incontinence. Overactive bladder syndrome is a condition in which the bladder muscles contract uncontrollably and cause frequent urination, urgent need to urinate, and inability to control urination. Each tablet contains 5 or 10 mg of solifenacin succinate and is formulated for oral administration. It is manufactured by Astellas and co-marketed by Astellas and Glaxo Smith Kline under the brand name Vesicare. The binding of acetylcholine to these receptors, particularly the M_3 receptor subtype, plays a critical role in the contraction of smooth muscle. By preventing the binding of acetylcholine to these receptors, Solifenacin succinate reduces 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. After oral administration, peak plasma levels (Cmax) of Solifenacin succinate are reached within 3 to 8 hours and at steady state ranged from 32.3 to 62.9 ng/mL. The absolute bioavailability of Solifenacin succinate is approximately 90%. Solifenacin succinate is metabolized in the liver by CYP3A4 coenzyme through N-oxidation of the quinuclidin ring and 4R-hydroxylation of tetrahydro isoquinoline ring. The elimination half-life of Solifenacin succinate following chronic dosing is approximately 45-68 hours. Because of a long elimination half-life, a once-a-day dose can offer 24 hour control of the urinary bladder smooth muscle tone. Adverse events associated with the use of Solifenacin succinate may include fatigue, asthenia, constipation, urinary retention, dyspepsia, pruritus, blurred vision.

Literature review revealed that methods have been reported to determine Solifenacin succinate individually in formulations by, NP-HPLC (Shashikant, 2011), RP-HPLC (Krishna, 2010; Yanagihara, 2007; Nilesh Desai, 2011; V. Vijayasree, 2013), LC-MS (Jan Macek, 2010; Mistri HN, 2008), Visible spectroscopy (Lokesh Singh, 2011) techniques. However the reported methods are either poorly validated or uneconomical to be used for routine laboratory analysis. Hence the present study describes a simple and cost effective validated method for the determination of Solifenacin succinate in tablet dosage form.

Fig. 1: Solifenacin succinate molecular structure



2. MATERIALS AND METHODS

SHIMADZU double beam UV-VIS Spectophotometer model UV-1800 equipped with UV probe ver 2.3 software. UV-1800 UV-VIS spectrophotometer achieves a resolution of 1 nm with matched quartz cells of 10 mm path length. Solifenacin succinate working standard manufactured by Megafine pharma, Distilled water, Vesicare Tablets.

Preparation of standard drug solutions: 10 mg of Solifenacin succinate pure drug was accurately weighed, transferred into a 100 ml volumetric flask containing 30 ml of distilled water and sonicated for about 10 minutes.

The volume was made up to the mark with distilled water to get the stock solution (100 µg/ml). This solution was further diluted with the same to get the working standard solution.

Preparation of Calibration curve: Aliquots of standard drug (0.2 ml to 1.0 ml, 100 µg/ml) solution in distilled water was transferred into a series of 10 ml volumetric flasks and the solution was made up to 10 ml with distilled water. After setting the instrument for its spectral properties the solutions were scanned in the wavelength ranging from 190 nm - 400 nm. The wavelength of maximum absorption for solifenacin succinate was found at below 200 nm. So to eliminate solvent effect, absorbances of the solutions were recorded at the selected wavelength of 220 nm. Calibration curve was prepared by plotting concentration of solifenacin succinate on x-axis and their respective absorbances on y-axis.

Procedure for assay of pharmaceutical formulations: Ten tablets of solifenacin succinate were weighed and powdered. A quantity of tablet powder equivalent to 25 mg of solifenacin succinate was accurately weighed and transferred into a 100 ml volumetric flask containing 50 ml of distilled water. The solution was sonicated for extracting the drug for about 15 minutes, filtered through a cotton wool and the filtrate was made up to volume with triple distilled water. Transfer 2 ml of the filtered sample solution to 100 ml volumetric flask and made up to volume with distilled water. The amount of solifenacin succinate was computed from its calibration plot.

Validation of the developed method

Precision: Precision was determined by intra-day and inter-day study. Precision of the method was evaluated by carrying out the assay and analyzing corresponding responses 6 times on the same day and on different days for the sample solution. The percent relative standard deviation (% RSD) was calculated.

Accuracy (Recovery studies): Accuracy studies were performed at three different levels (80%, 100% and 120%) and the samples were analyzed in triplicate by the proposed method. Known amount of standard solifenacin succinate at 80%, 100% and 120% of predetermined sample was added to a pre quantified tablet sample.

LOD and LOQ: Limit of Detection and Limit of Quantitation were calculated using following formula LOD= 3.3(SD) / S and LOQ= 10 (SD) / S, where SD=standard deviation of response (absorbance) and S= slope of the calibration.

3. RESULTS AND DISCUSSION

The proposed method obeyed Beer's law in the concentration range of 2-10 µg/ml. The optical characteristics and the data concerning to the proposed method is represented in Table 1. The limit of detection and limit of quantitation for estimation of solifenacin succinate were 0.301786 µg/mL and 0.914505 µg/mL respectively. Precision study was performed and represented in Table 2. Recovery studies were carried out for the developed method by addition of known amount of standard drug solution of solifenacin succinate to pre-analysed tablet sample solution at three different concentration levels. The resulting solutions were analyzed by the proposed methods. The recovery (Table 3) was in the range of 99.174 to 101.012 %. The assay results were tabulated in Table 4.

4. CONCLUSION

The present method demonstrated the estimation of Solifenacin succinate available as tablet dosage forms using UV spectrophotometry. From the above experimental data results and parameters it was concluded that the developed method has the following advantages, the standard and sample preparation requires less time, hence suitable for the analysis of Solifenacin succinate raw material and its pharmaceutical dosage form. Infact the method developed for solifenacin succinate was found to be simple, precise, accurate and cost effective and it can be effectively applied for routine analysis.

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Fig. 2: UV spectrum of solifenacin succinate in distilled water

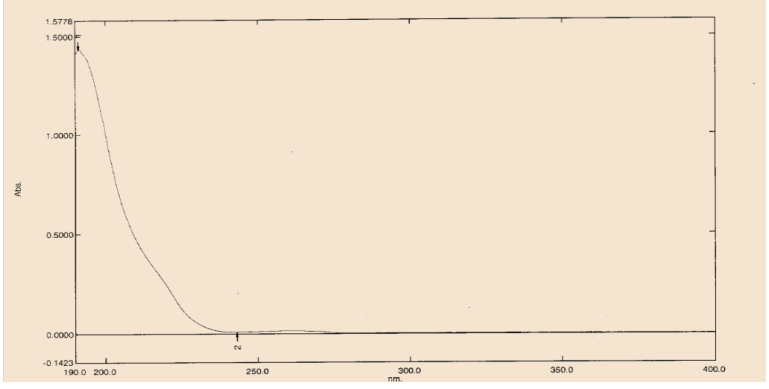

Fig. 3: Calibration curve of solifenacin succinate by UV method

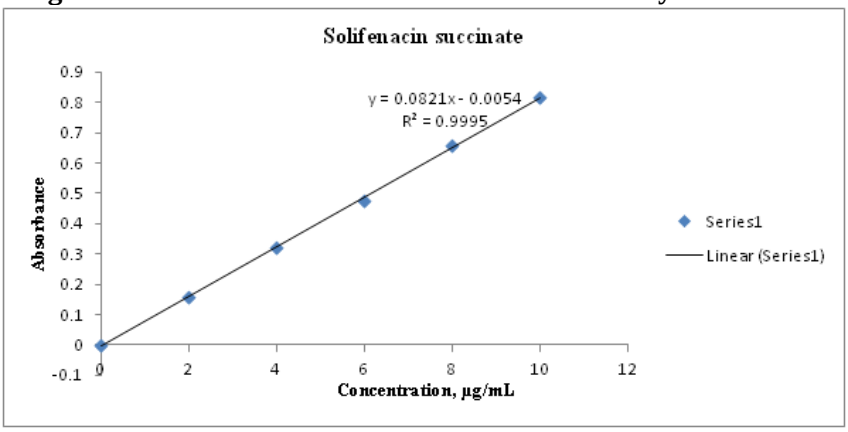

Table.1: Optical characteristics, regression data of the proposed method

Parameter	Result
λ_{max} (nm)	220
Beer's law limits (µg / ml)	2-10
Molar absorptivity (L. mole^{-1} cm^{-1})	3.9356 x10^4
Detection limits (µg / ml)	0.301786
Quantitation limits (µg / ml)	0.914505
Sandell's sensitivity (µg /cm ^{2}/0.001 absorbance unit)	0.012210
Regression equation (Y = a+ bc): Slope (b)	0.0821
Standard deviation of slope (S_b)	0.000897
Intercept (a)	-0.005428
Standard deviation of intercept (S_a)	0.005434
Standard error of estimation(S_e)	0.007508
Correlation coefficient (r)	0.9997
% Relative standard deviation*	1.3288

*Average of six determinations.

Table 2: Results of precision study

Precision*	Intra-day	Inter-day
Mean % recovery	100.0162404	99.772635
SD	1.329082503	1.779597869
%RSD	1.32886669	1.783653273

*average of 6 determinations

Table 3: Results of accuracy study

Accuracy*	Mean % recovery ± SD	%RSD
80%	99.71579 ± 0.541345	0.542888
100%	99.65083 ± 1.566163	1.571651
120%	100.3359 ± 0.67657	0.674305

*average of 3 determinations

Table 4: Assay results

S.No	Formulation	Labeled amount	Amount found	Mean % recovery ± SD	% RSD
1.	Vesicare Tablets (Astellas)	5 mg	5.096 mg	101.924± 1.282	1.288

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