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SECOND DERIVATIVE UV SPECTROPHOTOMETRIC QUANTIFICATION OF SOLIFENACIN SUCCINATE IN PHARMACEUTICALS EMPLOYING MULTIVARIATE CALIBRATION TECHNIQUE: ASSESSMENT OF GREENNESS PROFILE

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ABSTRACT

The present work proposes to provide a UV spectrophotometric technique for the determination of solifenacin succinate in pharmaceutical tablets, a multivariate calibration method is used. The multivariate calibration method measures the sample absorbance at various wavelengths for more precise measurements. The UV spectrophotometric method was created, and method validation was completed. According to the obtained test findings for the current method, there was no statistically significant difference and all validation parameters complied with ICH standards. The current study targets on the development of UV spectrophotometric method in second derivative mode for solifenacin succinate in bulk and pharmaceutical formulation employing multivariate calibration technique. Multivariate calibration technique utilizes the linear regression equations to correlate the relationship between concentration and amplitude at five different wavelengths, the multivariate calibration technique increases the correlation and reduces instrumental variations. solifenacin succinate showed absorption amplitude at 228nm in ethanol as solvent. The results were treated statistically. The analytical Eco scale, Agree metrics, and Green analytical procedure index was used to assess the method's greenness scores.

Keywords: Solifenacin succinate, Second derivative mode, Multivariate calibration technique, Pharmaceutical formulations, ICH guidelines, Validation

INTRODUCTION

The anti-cholinergic drug class that includes the well-known muscaranic receptor antagonist solifenacin succinate (SFS) is used to treat overactive bladder **[1]**. [(3R)-1-azabicyclo[2.2.2]octan-3-yl] (1S)-1-phenyl-3,4-dihydro-1H-isoquinoline-2-carboxylate;butanedioic acid is the chemical name for solifenacin succinate. The molecular formula is $C_{27}H_{32}N_2O_6$ and has molecular mass 480.6 g/mol **[2]**.

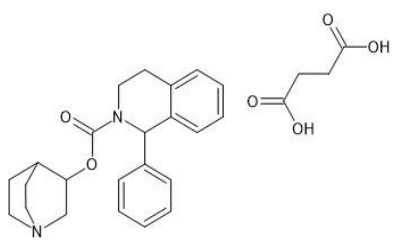

Figure 1: Chemical structure of Solifenacin succinate

All antimuscarinic medications, however, have the potential to impair salivary production and impair vision by inhibiting the ciliary muscle of the lens, resulting in dry mouth and impaired vision, respectively. These medications may also result in tachycardia, constipation due to reduction of gut motility, and other adverse effects (AEs) of the central nervous system, such as sleepiness and diminished cognitive function **[3]**. A competitive muscarinic-receptor antagonist called solifenacin succinate (SOL) was approved by the US Food and Drug Administration in late 2004 to treat overactive bladder (GAB) with symptoms like urgency, urge incontinence, and frequent urination **[4]**. Currently, a variety of antimuscarinic medications are available, and the development of extended release (ER) formulations has enhanced the effectiveness and tolerance of these medications **[5]**. Antimuscarinic medications may be equally helpful for people who simply experienced frequent urination without urgency as they are for patients who experience urgency **[6]**. The review of literature indicates that various techniques have been published for determining Solifenacin succinate in pharmaceutical formulations or biological fluids. For Solifenacin succinate, a few chromatographic techniques such as HPLC **[7, 8]** , RP-HPLC **[9–11]** spectrophotometric techniques like UV **[12–14]**, HPLC **[15]**, HPTLC **[16]**, NP-LC **[17]**. The literature review referred to the Multivariate calibration (MVC) technique using UV spectrophotometry, which haven't reported. Hence, the present method deals with the development of the MVC technique for the estimation of Solifenacin succinate. The MVC approach was used to decrease instrumental error and increase efficiency. The method is easy, inexpensive and applied to pharmaceutical dosage forms. For exact findings, MVC employs straight regression algorithms ranging between the wavelengths of 5-10nm **[18]**. In this study, we discussed the use of a UV spectrophotometric MVC approach with minimal mathematical content for estimating Solifenacin succinate in pharmaceutical dosage forms. As a result, to ensure the sensitivity in comparison to the traditional ultraviolet (UV) approach, five distinct wavelengths were chosen. The algorithm techniques of MVC's statistics multivariate data are converted into univariate data using the following equations **[19]**:

If the absorbance of a sample(x) is measured at five different wavelengths (λ), that is, at 221, 224, 227, 230, and 233nm, the following equation can be produced for each selected wavelength:

$A_{\lambda 221} = a \times C_x + k_1$ …………………. (1)

$A_{\lambda 224} = b \times C_x + k_2$ …………………. (2)

$A_{\lambda 227} = c \times C_x + k_3$ …………….…... (3)

$A_{\lambda 230} = d \times C_x + k_4$ …………….…… (4)

$A_{\lambda 233} = e \times C_x + k_5$ ……….……..…. (5)

Whereas,

- A_λ = Absorbance of the sample;
- a, b, c, d, e = Slope of the straight regression functions of a sample;
- k_1, k_2, k_3, k_4, k_5 = Intercept of the straight regression;
- C_x = Concentration of the sample

The above five equations can be rearranged as:

$A_T = a \times C_x + b \times C_x + c \times C_x + d \times C_x + e \times C_x + K_T$………. (6)

Equation (6) can be re- arranged as:

$A_T = C_x (a + b + c + d + e) + K_T$ ……………………. (7)

Whereas,

- A_T = Sum of the absorbances acquired
- K_T = Sum of intercepts of regression equation

The concentration of the sample (X) in a solution can be calculated by using the equation

$$Cx = \frac{A_T - K_T}{(a+Ab+c+d+\ )} \quad ……………\ (8)$$

Greenness evaluation techniques

The analytical eco scale **[20]** is constructed on allocating penalty points determined by the number of pictograms with associated signal words as established by "The Globally Harmonized System of Classification and Labelling of Chemicals (GHS)", as well as the quantity. Every reagent, its type and quantity, potential occupational exposure, and energy depletion, including waste, are all part of the analytical eco scale approach. Penalty points are deducted from a starting score of 100.

Analytical eco-scale = 100 - total penalty points…………… (9)

The Green Analytical Procedure Index **[21]** (GAPI) is also a pictorial representation that constitutes five pentagrams which unique color coding. The color coding in the pictogram involves three levels of assessment at each stage of an analytical procedure. A sample pictorial representation of the agree metrics output is shown in Fig. 3. The colour coding used by GAPI to assess greenness ranges from green to yellow to red, signifying the low, medium, and high environmental impact associated with the analytical procedure, respectively. A brief description of GAPI was well described and reported by J. Płotka-Wasylka in the year 2018 **[21]**. AGREE metrics, **[22]** unique software for quantifying the greenness profile, are used in the second assessment methodology. The software's output is a circular diagram containing numbers on the edges ranging from 1 to 12 in a clockwise orientation. These numbers depict the 12 ideologies of green analytical chemistry. The outcomes of all these 12 principles are given a rating of 0 to 1 based on the inputs and their weightage. This aggregate scale is colour coded as red, yellow, and green, with red denoting zero, dark green denoting one or near to one, and yellow denoting a number between red and dark green. The sum of the 12 principles and the core generates a score that reflects the extent of greenness.

MATERIALS AND METHODS

Materials

Analytical grade materials were used for all "chemicals and reagents" in this experiment. Each film-coated tablet in a marketed formulation contains 50mg of Solifenacin succinate from various brands that were selected and purchased from a retail pharmacy.

Instrumentation

- UV- Visible double beam spectrophotometer (LABINDIA UV 3092 model)
- Soniclean Sonicator (model 106 T, Thebarton, Australia)
- Analytical balance (AS 245, Mettler Toledo, India)

Method development

Solubility

In ethanol, solifenacin succinate was completely soluble. So, ethanol was employed as the study's solvent throughout the research.

Preparation of standard solution

The standard solution of Solifenacin succinate reference standard were prepared by dissolving 50 mg of the drug in 50 ml of the solvent to obtain 1 µg mL^{-1} with the use of sonicator. The solution is diluted to get concentrations in the range of 7-13 µg mL^{-1}

Preparation of sample solution:

Solifenacin succinate tablets were weighed, added to a mortar, ground into a powder, and thoroughly combined. 50 mg of Solifenacin succinate, correctly measured from the tablet powder, was dissolved in 50 mL of ethanol using a sonicator, filtered, and diluted for additional studies.

METHOD VALIDATION

The prepared method were validated per ICH guidelines **[23]** for linearity, accuracy, precision.

Linearity

Solifenacin succinate stock solution was dissolved in the solvent to produce concentrations between 7 and 13 µg mL^{-1}. The amplitudes of these solutions were measured around 228 nm, i.e., 222, 225, 228, 231, and 234 nm, in the derivative mode, to reduce instrumental fluctuations and increase correlation.

Precision

The intra-day and inter-day precisions were measured three times daily (intra-day precision) and three different days (inter-day precision) accordingly, using replicate measurements on homogeneous solutions containing 10 µg mL^{-1}. **Tables 3** and **4** list the amplitude measurements made at the chosen wavelength sets. At the chosen wavelengths, the SD and % RSD values were also determined and are shown in **Tables 5** and **6**. **Figures 9** and **10**, respectively, depict the overlay UV spectra for the intraday precision and interday precision.

Accuracy

Using the usual addition approach, the development method's correctness was evaluated at three different levels: 80%, 100%, and 120% and the recovery percentage was determined.

Assay

At 228 nm, the extracted sample solution's amplitude was captured. The estimated amount of the medication in the formulation is shown in **Table 5**.

RESULTS AND DISCUSSION

The maximum amplitude was recorded at 228 nm using ethanol as the solvent **(Figure 2)**.

Linearity

As demonstrated in **Figure 3**, the linearity was measured at 222, 225, 228, 231 and 234 nm for various concentrations between 0.7 to 13 µg mL^{-1}. **Table 1** presents the observed results in tabular form. In the chosen concentration range, it was discovered that all of the standard curve were linear. **Figures 4-8** and **Table 2** provide the calibration graphs, related residual plots, and regression analysis, respectively.

Precision:

The system precision spectra for Solifenacin succinate are represented in **Figure 9**. The interday precision spectra for Solifenacin succinate are represented in **Figure 11**. The intraday precision spectra were represented in **Figure 10** for Solifenacin succinate. The % RSD of system precision, interday and intraday precision, was determined for Solifenacin succinate. It was found to be less than 2%, which shows that the approach method is precise. The outcomes are represented in for Solifenacin succinate. The proposed method shows good precision compared to the values obtained from various precision methods.

Accuracy

Solifenacin succinate's accuracy was tested at 80, 100, and 120%. **Figure 12** shows the overlay spectra for Solifenacin succinate. The results for accuracy are shown in **Table 4**, and the obtained results were found to be within limits.

Assay of marketed formulations

The recommended spectrophotometric method was used to investigate the quantity of Solifenacin succinate in tablet formulation. The UV absorption spectrum of a commercial tablet was obtained for three replicates. After extraction and filtration, there was no appreciable decrease in the pharmaceutical formulation's excellent analytical recovery values. The results are provided in the **Table 5** for Solifenacin succinate, which demonstrates that the new strategy out performs the earlier ones.

Evaluation of Greenness Profile

The results of greenness profile for the proposed methods were evaluated. The results of analytical scale is shown in **Table 6**, while the results for GAPI and agree metrics is depicted in **Figure 14** and **Figure 15**.

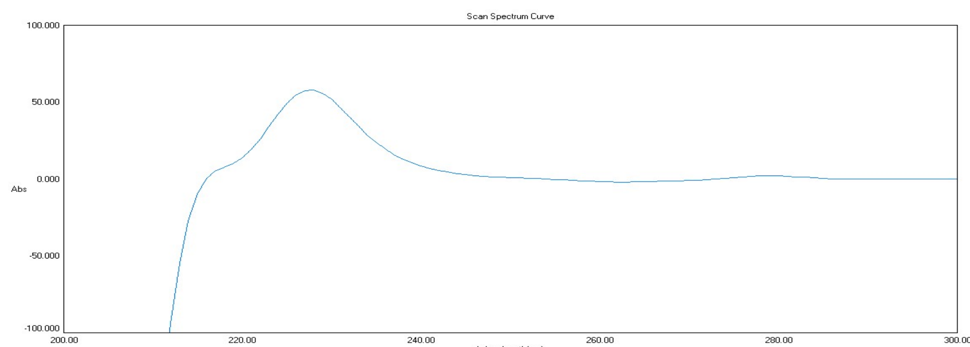

Figure 2: UV spectrum of Solifenacin succinate in second derivative mode

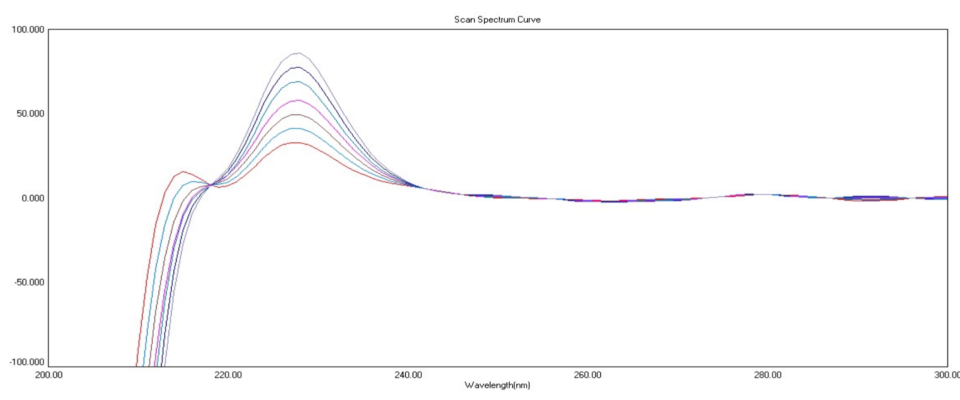

Figure 3: Overlay spectrum linearity of Solifenacin succinate in Second derivative mode

Table 1: Multivariate UV calibration data at five selected wavelengths

Concentration ($\mu g\ mL^{-1}$)	222nm	225nm	228nm	231nm	234nm
7	13.870	28.135	32.937	25.865	16.396
8	17.957	35.299	41.460	32.760	20.487
9	22.096	42.274	49.614	39.569	24.661
10	26.183	49.438	58.137	46.465	28.753
11	29.151	58.454	69.005	53.812	32.215
12	33.239	65.618	77.528	60.707	36.306
13	37.326	72.782	86.051	67.603	40.398

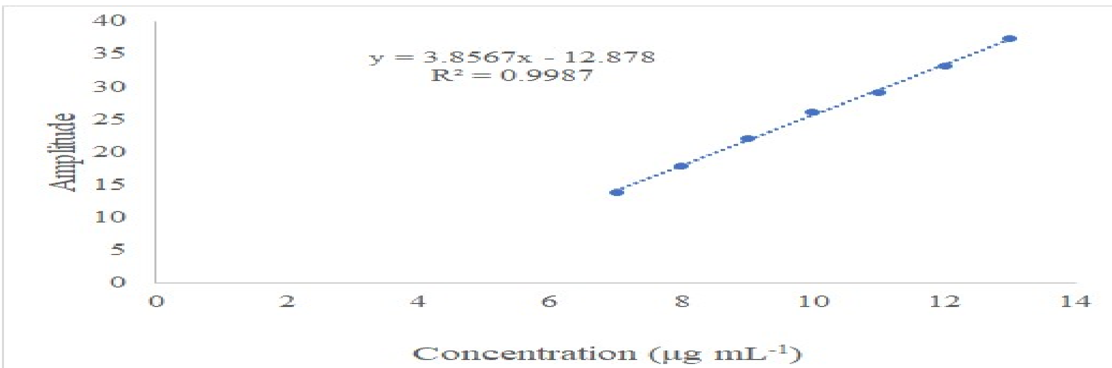

Figure 4: Calibration curve at 222 nm

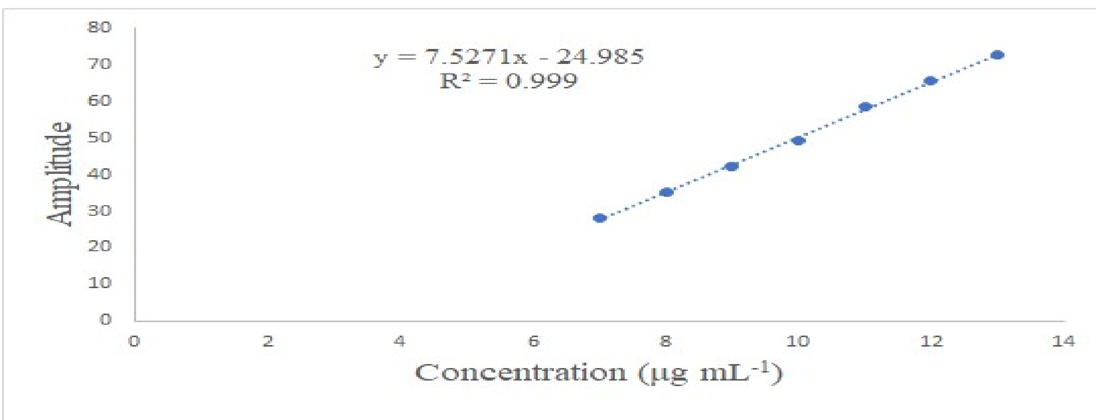

Figure 5: Calibration curve at 225 nm

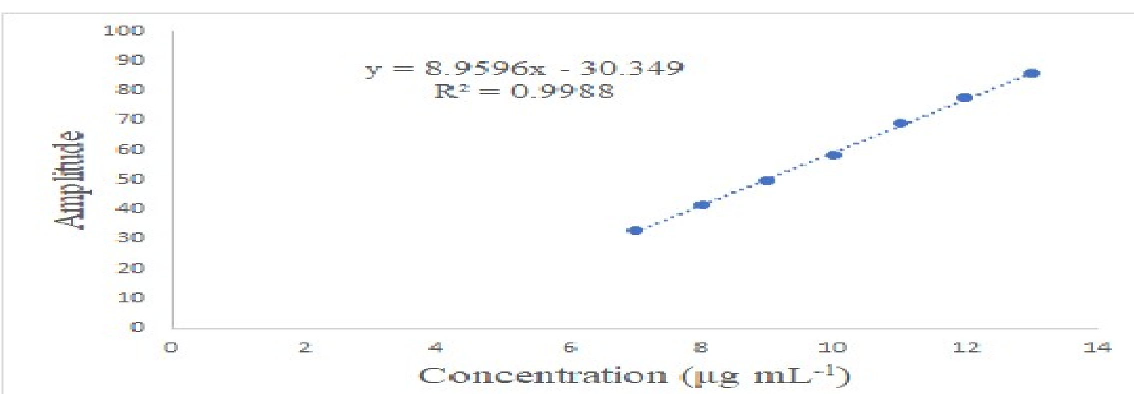

Figure 6: Calibration curve at 228 nm

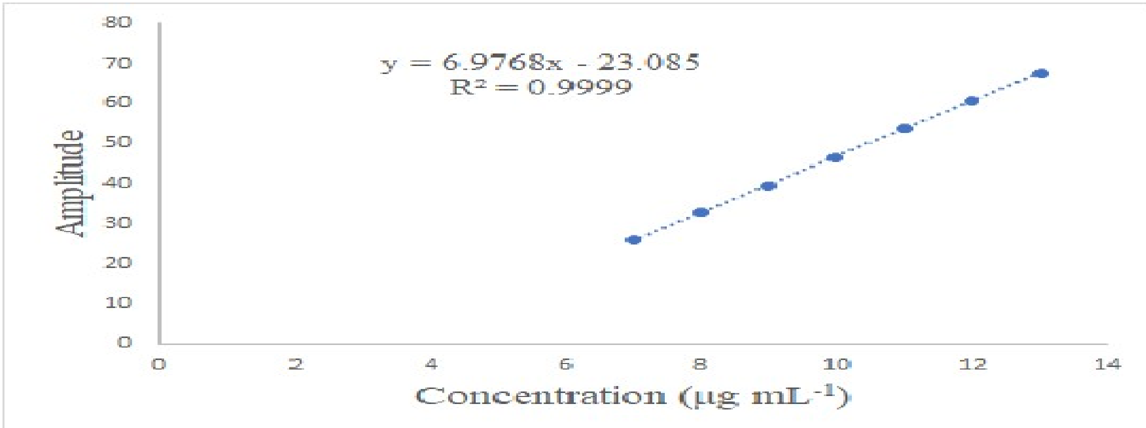

Figure 7: Calibration curve 231 nm

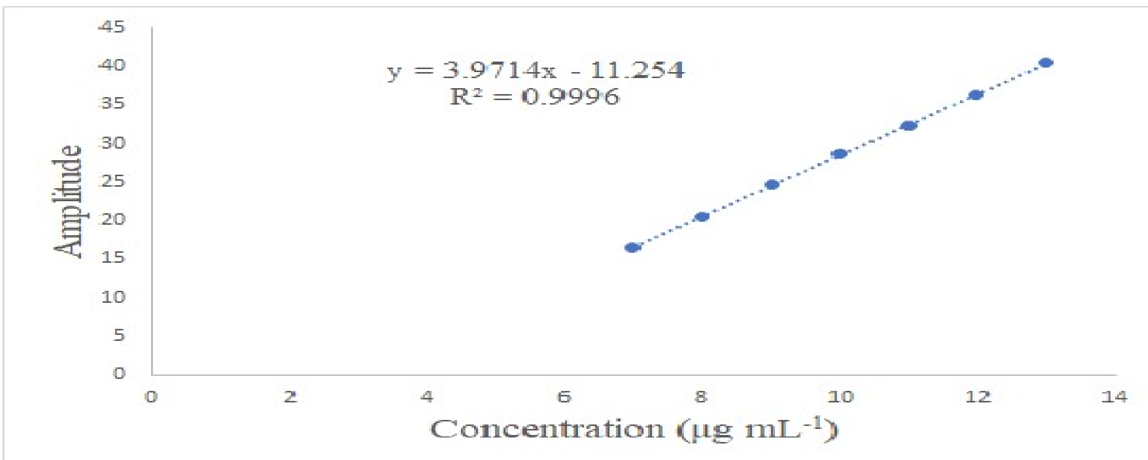

Figure 8: Calibration curve 234 nm

Table 2: Linearity data shows statistical parameters at the selected wavelengths

Wavelength(nm)	Regression equation	Slope	Intercept	R^2	LOD (µg mL^{-1})	LOQ (µg mL^{-1})
222	Y= 3.8567x - 12.878	0.2589	-12.878	0.9987	1.46	4.43
225	Y = 7.5271x - 24.985	0.1327	-24.985	0.999	1.27	3.87
228	Y = 8.9596x - 30.349	0.1114	-30.349	0.9988	1.40	4.25
231	Y = 6.9768x - 23.085	0.1433	-23.085	0.9999	0.35	1.074
234	Y = 3.9714x - 11.254	0.2516	-11.254	0.9996	0.83	2.54

Table 3: System precision, Intraday and Interday precision data for the prepared method of Solifenacin succinate

	System precision	Interday and Intraday precision		
	Absorbance of standard for 10 µg mL^{-1}	% Recovery of sample equivalent to 10 µg/ml of sample		
		Day 1	Day 2	Day 3
1	414.732	99.12	98.01	98.3
2	413.543	98.85	99.2	99.49
3	416.243	99.32	99.1	99.32
4	415.729	99.25	99.47	99.5
5	414.754	99.35	99.11	98.48
6	415.871	99.29	98.16	99.5
Mean	415.145	99.20	98.84	99.10
SD	0.996	0.19	0.60	0.56
%RSD	0.24	0.19	0.61	0.56

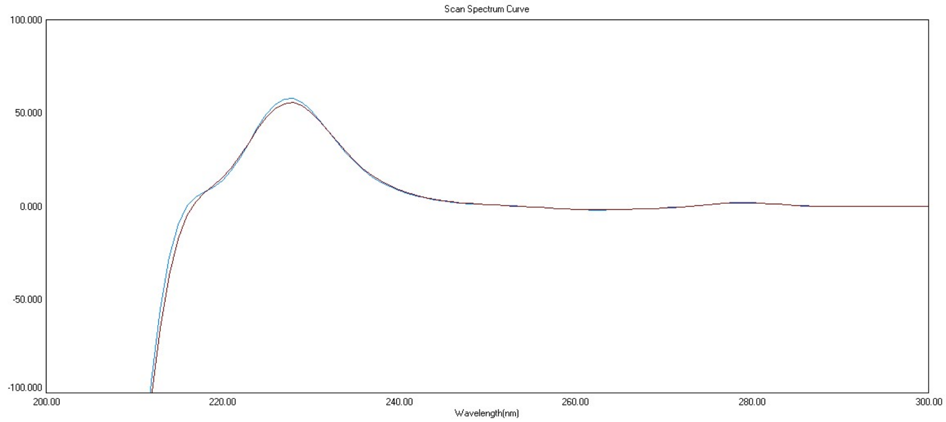

Figure 9: Overlay UV spectrum showing precision

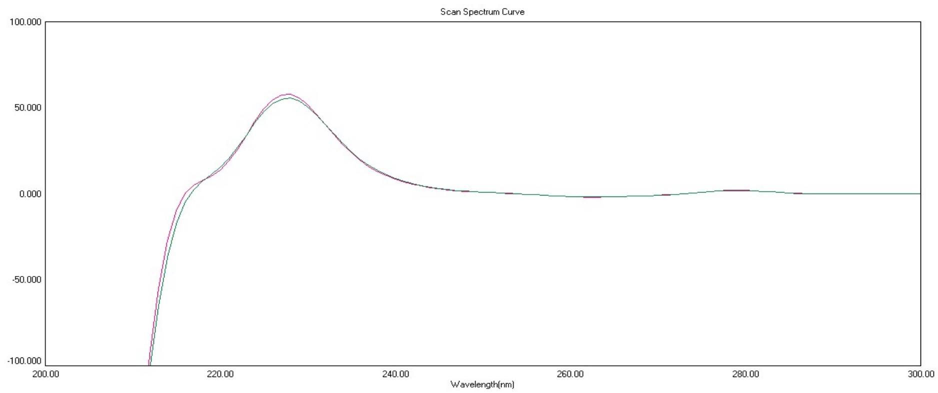

Figure 10: Overlay UV spectrum showing Intraday precision

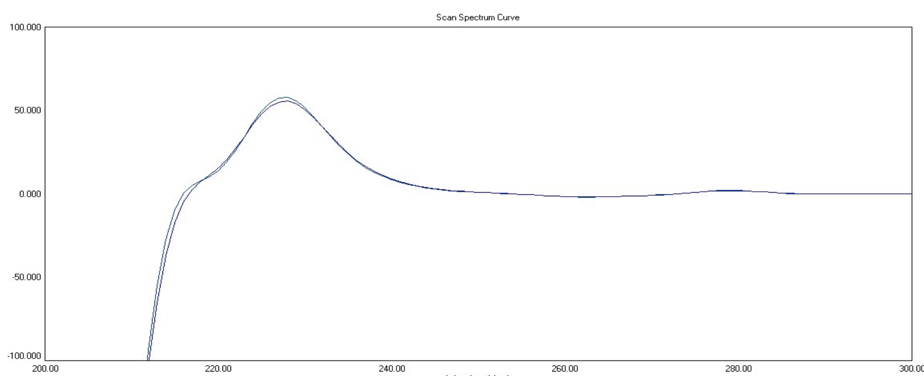

Figure 11: Overlay UV spectrum showing Interday precision

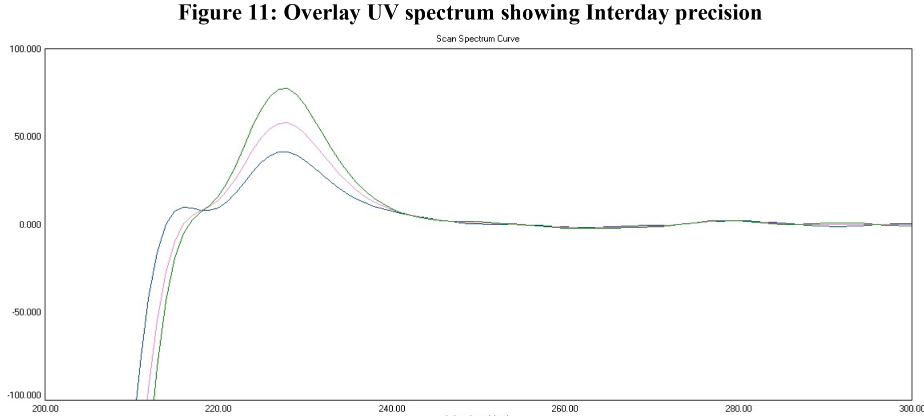

Figure 12: Overlay spectra of accuracy of Solifenacin succinate at 80, 100, 120 % spiking

Table 4: Accuracy data for prepared method of Solifenacin succinate

Concentration levels (%)	Amount present	Amount added (μg mL^{-1})	Amount recovered (μg mL^{-1})	Mean % Recovery	SD
80	5	3	7.94	98.79	0.5051
100	5	5	9.89	98.87	0.1528
120	5	7	11.91	99.11	0.1734

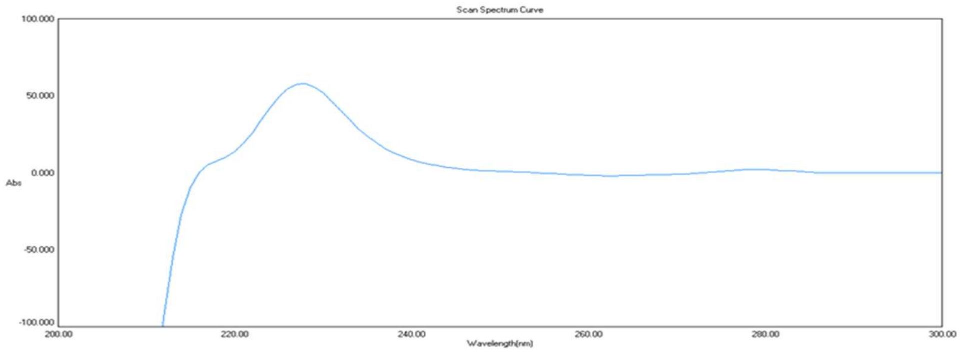

Figure 13: UV spectrum of standard Solifenacin succinate (10μg mL^{-1}) using ethanol as a blank

Table 5: Assay results for marketed formulation of Solifenacin succinate

Marketed formulation	Label claim (mg)	Mean ± SD (n=3)	% RSD
Batch - 1	50	4.91±0.04	0.4748
Batch - 2	50	4.89±0.04	0.7186

Table 6: Summary of Eco scale penalty points for the proposed method

Description	Penalty points	Total Penalty Points	Score
Ethanol	4	4	96
Instrument	0		
Occupational hazard	0		
Waste	0		

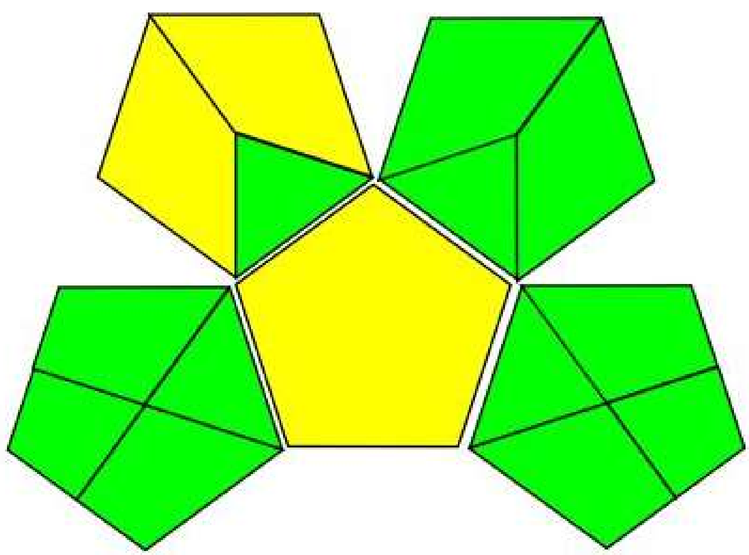

Figure 14: GAPI Pictogram for the proposed method

Figure 15: Agree metrics output for the proposed method

CONCLUSION

By assessing several validation parameters in accordance with ICH recommendations, the newly developed spectrophotometric multivariate analytical technique for the evaluation of Solifenacin succinate was validated and determined to be within the allowed ranges. The proposed method for determining Solifenacin succinate in its tablet formulation was shown to be sensitive, accurate, precise, and repeatable. We strongly advise using the developed approach for a routine analysis of Solifenacin succinate in pharmaceutical formulations because it is more useful and dependable than the other UV spectrophotometric methods. The proposed method possess an ideal greenness profile assessed by analytical ecoscale, GAPI and agree metrics shall be used for routine simultaneous determination of solifenacin succinate as an alternative to time-consuming and expensive separation techniques.

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CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article exists.

REFERENCES

[1] Morales-Olivas FJ, Estañ L. Solifenacin pharmacology. Arch Esp Urol Spain 2010; 63(1):43–52.

[2] Corp MS& D. THE MERCK INDEX: An Encyclopedia of chemicals,Drugs,and Biologicals,. 2013[Online] 15th editi The Royal Society of Chemistry: UK 2013.

[3] Smulders RA, Krauwinkel WJ, Swart PJ, *et al*. Pharmacokinetics and safety of solifenacin succinate in healthy young men. J Clin

Pharmacol 2004; 44(9):1023–33.

[4] Maniscalco M, Singh-Franco D, Wolowich WR, *et al*. Solifenacin succinate for the treatment of symptoms of overactive bladder. Clin Ther 2006; 28(9):1247–72.

[5] Chapple CR, Martinez-Garcia R, Selvaggi L, *et al*. A comparison of the efficacy and tolerability of solifenacin succinate and extended release tolterodine at treating overactive bladder syndrome: Results of the STAR trial. Eur Urol 2005; 48(3):464–70.

[6] Han JY, Lee KS, Park WH, *et al*. A comparative study on the efficacy of solifenacin succinate in patients with urinary frequency with or without urgency. PLoS One 2014; 9(11):7–12.

[7] Desai D, Patel G, Shukla N, *et al*. Development and validation of stability-indicating HPLC method for solifenacin succinate: Isolation and identification of major base degradation product. Acta Chromatogr 2012; 24(3):399–418.

[8] Desai N, Hussen SS, Vasanthraju SG, *et al*. Development & validation of stability indicating HPLC method for determination of Solifenacin in bulk formulations. Int J Pharm Pharm Sci 2011; 3(1):70–74.

[9] Jadhav RA, Sanil YM, Shankarwar SG, *et al*. Development and Validation of Rapid Stability-Indicating RP-HPLC Method for Assay and Related Substances of Solifenacin Succinate. Chromatographia Springer Berlin Heidelberg 2020; 83(9):1107–19.

[10] Rihana Parveen SK, Srinivasa Babu P, Chandrasekar KB, *et al*. Analytical method development and validation of tolterodine in pharmaceutical dosage forms by RP-HPLC. Der Pharm Lett 2014; 6(3):246–54.

[11] Reddy RSR, Sherikar A V, Nadre1 M. Development and Validation of a Stability Indicating Analytical Method for the Determination of Related Substances By Rphplc for Solifenacin Succinate in Solifenacin Succinate Tablets. Pharmacophore 2017; 8(2):11–23.

[12] Alia Afra S, Rameeja S, Madhavi R, *et al*. A new spectrophotometric method for the determination of solifenacin in pure form and in pharmaceutical formulations. Int J Res Pharm Sci 2013; 4(2):221–25.

[13] Teja GD, Deva Dasu C, Babu SP, *et al*. Quantitative analysis of solifenacin succinate in pharmaceutical dosage form using UV absorption spectroscopy. J Chem Pharm Sci 2013; 6(3):195–98.

[14] Papanna RK, Kanakapura B, Gowda SBS, *et al*. Determination of Solifenacin Succinate in Pure and Pharmaceutical Dosage forms by Spectrophotometry. J Anal Chem 2021; 76(11):1262–70.

[15] Reddy BVR, Reddy BS, Raman NVVSS, *et al*. Development and validation of a specific stability indicating high performance liquid chromatographic methods for related compounds and assay of solifenacin succinate. J Chem 2013; 2013.

[16] Tantawy MA, Weshahy SA, Wadie M, *et al*. Stability-indicating HPTLC method for the simultaneous detection and quantification of alfuzosin hydrochloride, solifenacin succinate along with four of their official impurities. Microchem J Elsevier 2020; 157(May):104905.

[17] Landge SB, Jadhav SA, Dahale SB, *et al*. Development and Validation of New Chromatographic Method for the Determination of Enantiomeric and Diastereomeric Purity of Solifenacin Succinate: An Antimuscarinic Agent. Chromatogr Res Int 2011; 2011:1–7.

[18] Nayabaniya A, Seetharaman R, Lakshmi K. Spectrophotometric Determination of Carvedilol in Bulk drug and its Formulation by Multivariate Calibration Technique. Res J Pharm Technol 2020; 13(2):915.

[19] Kokilambigai, K. S, seetharaman R., Lakshmi KS. Multivariate calibration technique for the spectrophotometric quantification of rasagiline in bulk drug and pharmaceutical formulations. Res J Pharm Technol 2020; 13(2):843–49.

[20] Gałuszka A, Migaszewski ZM, Konieczka P, *et al*. Analytical Eco-Scale for assessing the greenness of analytical procedures. TrAC Trends Anal Chem 2012; 37:61–72.

[21] Płotka-Wasylka J. A new tool for the evaluation of the analytical procedure: Green Analytical Procedure Index. Talanta 2018; 181:204–09.

[22] Pena-Pereira F, Wojnowski W, Tobiszewski M. AGREE - Analytical GREEnness Metric Approach and Software. Anal Chem 2020; 92(14):10076–82.

[23] ICH. Validation of Analytical Procedures: Text and Methodology Q2(R1). 2005[Online] 2005.