

Simultaneous Estimation of Solifenacin Succinate and Tamsulosin Hydrochloride in Combined Dosage Form by Using First Order Derivative Spectrophotometric Method

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Srinivasarao et al.: Derivative Spectrophotometric Method for Solifenacin Succinate and Tamsulosin Hydrochloride

Using first-order derivative techniques, a simple accurate and precise Ultraviolet spectrophotometric method was developed for the determination of solifenacin succinate and tamsulosin hydrochloride in combined dosage form. Every solifenacin succinate and tamsulosin hydrochloride was scanned in the wavelength region of 200–400 nm for determination of sampling wavelengths and selected sampling wavelengths were selected. Sampling wavelengths were chosen at 265 nm (zero crossing of solifenacin succinate) where the absorbance of tamsulosin hydrochloride was important and at 250 nm (zero crossing of tamsulosin hydrochloride) where the absorbance of solifenacin succinate was significant. For solifenacin succinate, linearity ranged from 10 to 100 µg/ml with a correlation coefficient of 0.998 and 2 to 10 µg/ml for the correlation coefficient of tamsulosin hydrochloride is 0.9988. The median recovery was considered to be satisfactory. For the routine study of solifenacin succinate and tamsulosin hydrochloride in combined dosage forms, the approach proposed can be applied.

Key words: Solifenacin succinate, tamsulosin hydrochloride, first order derivative spectroscopy

Chemically tamsulosin hydrochloride is 5-[(2R)-2-{2-(2-ethoxyphenoxy)ethyl} amino}propyl]-2-methoxybenzene-1-sulfonamide, fig. 1 and used as selective antagonist of α -1A-adrenergic receptors^[1]. Chemically solifenacin succinate (SFS) is butanedioic acid (3R)-1-azabicyclo[2.2.2]octan-3-yl (1S)-1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate, fig. 2 and used as competitive muscarinic acetylcholine receptor (M3) antagonist^[2]. Solifenacin Succinate and tamsulosin hydrochloride is available with the brand name of “VESOMNI” in the form of modified-release tablets with the dosage strength 6 mg/0.4 mg. Therapeutic indication of this brand is to treat moderate to severe storage symptoms like urgency, increased micturition frequency and voiding symptoms associated with benign prostatic hyperplasia (BPH) in men who are not adequately responding to treatment with monotherapy^[3]. Literature survey reveals spectrophotometric methods^[4-8], High Performance Liquid Chromatography (HPLC)^[9-11] and Liquid Chromatography-Electrospray Ionization-Mass Spectrometry (LC-ESI-MS/MS)^[11-12]

methods were available for tamsulosin hydrochloride and Ultraviolet^[13-14], HPLC^[15-16], Ultra-Performance Liquid Chromatography (UPLC)^[17], high-performance thin layer chromatography (HPTLC)^[18] and Liquid Chromatography with tandem mass spectrometry (LC-MS/MS)^[19-20] methods were available for estimation of solifenacin succinate. Only few reverse phase high performance liquid chromatography (RP-HPLC)^[21-22] method and spectrofluorimetric^[23] methods were reported for the estimation of solifenacin succinate & tamsulosin hydrochloride in combination dosage forms. However no UV spectrophotometric method is reported yet for the estimation of solifenacin succinate & tamsulosin hydrochloride in combination dosage forms. However chromatographic methods are complex

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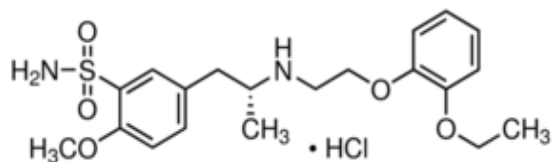


Fig. 1: Structure of Tamsulosin Hydrochloride

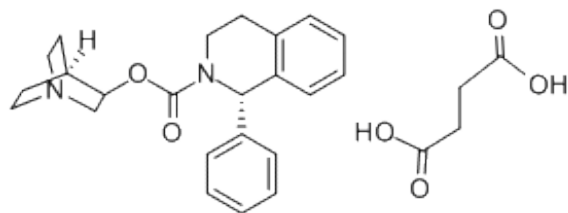


Fig. 2: Structure of Solifenacin Succinate

with costly instrument set up, skilled operators and expensive solvents limit the application of simultaneous quantification of above drugs. The derivative spectrophotometric^[24-25] method have the advantage of separation of unresolved signals, reduction of spectral background interferences and quantification of one component in presence of other. The present work described first order derivative spectrophotometric method for the estimation of solifenacin succinate and tamsulosin hydrochloride in tablet formulation.

MATERIALS AND METHODS

A double beam UV-visible spectrophotometer (LABINDIA) having two matched quartz cells with 1 cm light path and loaded with Microwave software (version 2.4.1) was used for recording of spectra and measuring absorbance. An electronic analytical weighing balance (APEX Ind Ltd) was used for all weighings and a Ultrasonicator (IBACO Services) used for sonication of all analytical solutions. Pure samples of solifenacin succinate, tamsulosin hydrochloride were obtained as gifted samples from pharma industry. Tablet formulation VESOMNI containing 6 mg solifenacin succinate and 0.4 mg tamsulosin hydrochloride was purchased from the local market and a Whatman filter paper no. 41 (Whatman International Ltd., England) was used. Double distilled water was used for all studies.

Preparation of Standard stock Solutions (100 µg/ml)

A standard stock solution (1 mg/ml) each of solifenacin succinate and tamsulosin hydrochloride were separately prepared in double distilled water and these stock solutions were further diluted with double distilled water to get a concentration of 100 µg/ml. These

solutions were used as working standard solutions for further analysis.

Preparation of Sample Solution

Twenty tablets were weighed and powdered. The quantity of the powder equivalent to 60 mg of solifenacin succinate was transferred to 100 ml volumetric flask. The content was mixed with distilled water (70 ml) and sonicated for 20 min to dissolve the drug as completely as possible. The solution was then filtered through a Whatman filter paper no. 41 and volume was adjusted up to the mark with distilled water. An aliquot of 1 ml was transferred to a 10 ml volumetric flask and the volume was adjusted up to the mark with distilled water to obtain required concentration of solifenacin succinate (60 µg/ml) and tamsulosin hydrochloride (4 µg/ml). These solutions were analysed by first order derivative spectroscopic method and absorbances were noted at 250 nm and 265 nm.

RESULTS AND DISCUSSION

From the appropriate dilution of working standard stock solution 10 µg/ml of solifenacin succinate and 10 µg/ml of tamsulosin hydrochloride were separately prepared and scanned in UV range of 200-400 nm. The zero order spectra were obtained and converted to first order derivation spectra in the instrument derivative mode. From the first order derivative spectra of standard, solifenacin succinate and tamsulosin hydrochloride, zero crossing point of solifenacin succinate was found at 265 nm as shown in fig. 3 and zero crossing point of tamsulosin hydrochloride was found at 250 nm as shown in fig. 4 and wavelength selected for their estimation was 250 nm for solifenacin succinate and 265 nm for Tamsulosin hydrochloride.

For each drug linearity was observed by diluting appropriate aliquots of working standard solution into a series of 10 ml volumetric flask with double distilled



Fig. 3: First order derivative overlain spectra of Solifenacin succinate

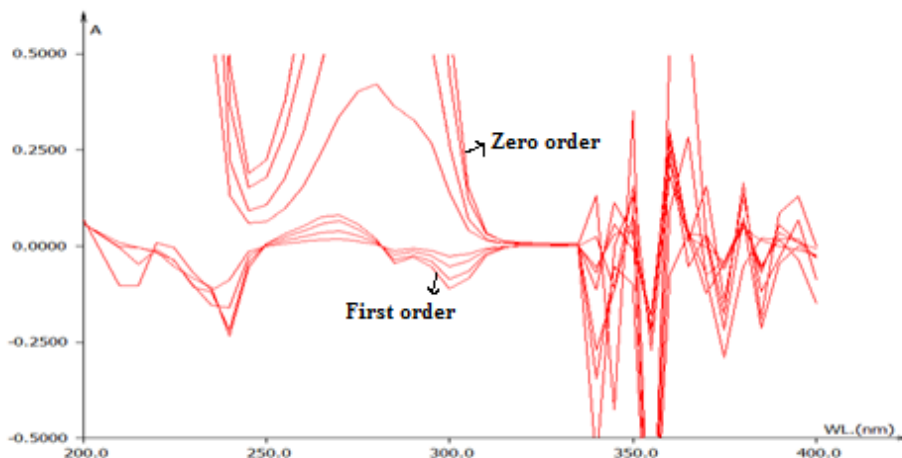


Fig. 4: First order derivative overlain spectra of Tamsulosin hydrochloride

water to get a concentration range of 10-100 $\mu\text{g/ml}$ for both solifenacin succinate and 2-10 $\mu\text{g/ml}$ for tamsulosin hydrochloride. The samples were scanned in 200-400 nm range and first order derivative spectra was obtained. The $dA/d\lambda$ of each of the solution measured at selected wavelength and plotted against concentration to obtain calibration curve. The calibration curve of solifenacin succinate and tamsulosin hydrochloride were shown in fig. 5 and fig. 6 respectively. The statistical parameters of the calibration curve for both drugs was shown in Table 1.

The precision was measured in terms of method precision and intermediate precision. The precision of the method was checked by repeated measurement of absorbances of solutions of solifenacin succinate (60 $\mu\text{g/ml}$) at 250 nm and tamsulosin hydrochloride (4 $\mu\text{g/ml}$) at 265 nm by proposed method without changing any parameter. The results were reported in terms of percentage Relative standard deviation (RSD). The intraday and interday precision of the proposed method was determined by analyzing the corresponding responses 3 times on the same day and on 3 different days for different concentrations of standard solutions of solifenacin succinate (40, 60, 80 $\mu\text{g/ml}$) and tamsulosin hydrochloride (2, 4, 6 $\mu\text{g/ml}$). The results were reported in terms of percentage RSD. The percentage RSD values for Solifenacin succinate and Tamsulosin hydrochloride were found to be 1.7 % and 1.07 % respectively. The low percentage RSD values (<2 %) indicates that proposed method is repeatable. The results of intraday and interday precision of solifenacin succinate and tamsulosin hydrochloride are shown in Table 2. The percentage RSD values of intraday precision for solifenacin succinate and tamsulosin hydrochloride were found to be 0.19 -0.87 and 1.09-1.47 % respectively and percentage RSD

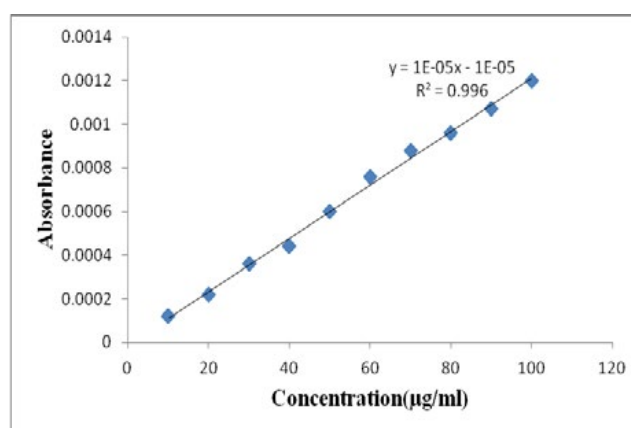


Fig. 5: Calibration curve for Solifenacin succinate at 250 nm

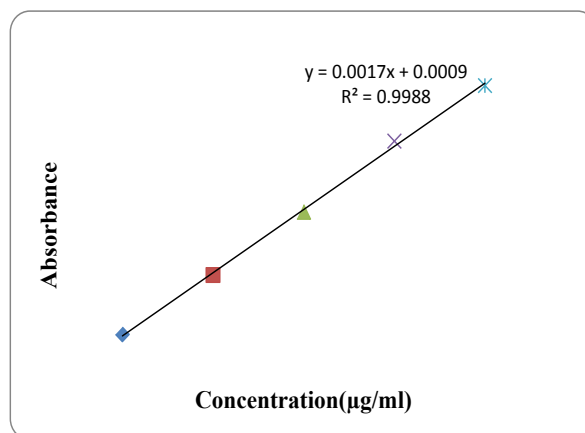


Fig. 6: Calibration curve for Tamsulosin hydrochloride at 265 nm

values of interday precision for solifenacin succinate and tamsulosin hydrochloride were found to be 0.27-0.63 and 0.84-1.70 % respectively. The low percentage RSD values (<2 %) reveals that the proposed method is precise.

The accuracy of the method was determined by calculating recovery of solifenacin succinate and tamsulosin hydrochloride by the standard addition

TABLE 1: OPTICAL CHARACTERISTICS AND REGRESSION ANALYSIS DATA

Parameter	Solifenacin succinate	Tamsulosin hydrochloride
Analytical wavelength	250 nm	265 nm
Beer's law limit	10-100 µg/ml	2-10 µg/ml
Regression line equation Y = mx + c	y=0.00003x -0.000001	y=0.0017x+0.0009
Correlation coefficient	R ² = 0.996	R ² = 0.9988
LOD(µg/ml)	1.054	0.101
LOQ(µg/ml)	3.196	0.308

TABLE 2: INTRADAY AND INTERDAY PRECISION DATA

DRUG	Concentration (µg/ml)	Inter-day		Intra-day	
		Concentration estimated*(µg/ml±SD)	% RSD	Concentration estimated* (µg/ml)±SD	% RSD
Solifenacin Succinate	40	40.06±0.11	0.27	40.12±0.08	0.19
	60	59.98±0.38	0.63	39.93±0.35	0.87
	80	79.97±0.29	0.36	79.92±0.56	0.70
Tamsulosin Hydrochloride	2	2.05±0.03	1.7	1.98±0.02	1.01
	4	4.06±0.06	1.47	3.94±0.05	1.29
	6	5.91±0.05	0.84	6.09±0.09	1.47

*Average of three determinations

TABLE 3: RECOVERY DATA OF SOLIFENACIN SUCCINATE AND TAMSULOSIN

DRUG	Level	Amount of sample taken (µg/ml)	Amount of standard spiked (µg/ml)	Amount recovered* (µg/ml)	% Mean recovery* ± SD
Solifenacin Succinate	50 %	60	30	29.83	98.33 ± 1.791
	100 %	60	60	59.84	99.20 ± 0.613
	150 %	60	90	89.92	99.75 ± 0.519
Tamsulosin Hydrochloride	50 %	4	2	1.98	98.93 ± 0.210
	100 %	4	4	3.965	98.58 ± 0.297
	150 %	4	6	5.971	99.03 ± 0.154

* Mean of three determinations

TABLE 4: RESULTS OF COMMERCIAL FORMULATION ANALYSIS

Parameters	Drug	
	Solifenacin Succinate	Tamsulosin HCl
Label Claim(mg/tablet)	6	0.4
Drug Content* % ± SD	99.89 ± 1.473	99.69 ± 1.912
%RSD	1.475	1.918

* Average of six determinations

method. Known amounts of standard solutions of solifenacin succinate (30, 60 and 90 µg/ml) and tamsulosin hydrochloride (2, 4, 6 µg/ml) were added to prequantified sample solutions of solifenacin succinate (60 µg/ml) and tamsulosin hydrochloride (4 µg/ml). The amount of solifenacin succinate and tamsulosin hydrochloride was determined by applying obtained values to the regression equation of the calibration curve. The accuracy was repeated for three times at each level. The recovery study was carried out for three times and percentage mean recovery was calculated and results are shown in Table 3. The value of standard deviation and percentage recovery studies were indicates that the proposed method is accurate.

Limit of Detection (LOD) and the Limit of Quantification (LOQ) of the solifenacin succinate and tamsulosin hydrochloride were calculated using the following equations as per International Council for Harmonisation (ICH) guidelines. $LOD=3.3 \times \sigma/S$; $LOQ=10 \times \sigma/S$

Where, σ = The Standard deviation of y-intercepts of calibration curves. S = Average slope of calibration curve.

LOD values for solifenacin succinate and tamsulosin hydrochloride were found to be 1.054 and 0.101 µg/ml, respectively and LOQ values for solifenacin succinate and tamsulosin hydrochloride were found to be 3.196 and 0.308 µg/ml respectively. These data reveals that proposed method is sensitive for the determination of solifenacin succinate and tamsulosin hydrochloride.

The proposed validated method was successfully applied to determine concentration of solifenacin succinate and tamsulosin hydrochloride in their combined dosage form. The assay results obtained for solifenacin succinate and tamsulosin hydrochloride were comparable with the corresponding labeled

amounts indicates that the method is suitable for simultaneous estimation of solifenacin succinate and tamsulosin hydrochloride without interference of excipients normally present in tablets. The results are shown in Table 4.

The developed first order derivative spectrophotometric method was found to be simple in nature and produced more accurate results. Hence the method is effective for routine analysis of solifenacin succinate and tamsulosin hydrochloride in combined dosage form.

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