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ASSAY METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF SOLIFENACIN SUCCINATE IN TABLETS BY UV SPECTROPHOTOMETRY

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Abstract:

The main objective this article is to develop a simple and cheap UV spectrophotometric method for the quantitative estimation of Solifenacin succinate in tablets and validate as per ICH guidelines. The optimized method uses a solvent 0.1 N HCl for the estimation of assay of Solifenacin succinate in tablets at a detection wavelength of 210 nm. System, intraday and inter day precision are exemplified by relative standard deviation of 1.069, 0.58 and 0.77% respectively. The developed method exhibited linearity in the range of 5-15µg/ml. Percentage Mean recovery was found to be in the range of 98-102, during accuracy studies. Accordingly, it is concluded that a simple and a cheap UV spectrophotometric method was developed and validated for the quantitative estimation of Solifenacin succinate in tablets as per ICH guidelines and hence it can be used for the routine analysis in various pharmaceutical industries.

Keywords: *UV, Solifenacin succinate, 0.1N HCl, method development, validation.*

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INTRODUCTION

Solifenacin succinate (Figure 1) is a competitive muscarinic acetylcholine receptor antagonist. Muscarinic receptor antagonists are widely used for treatment of the syndrome of overactive bladder and urge urinary incontinence [1-4]. The binding of acetylcholine to these receptors, particularly the M3 receptor subtype, plays a critical role in the contraction of smooth muscle. By preventing the binding of acetylcholine to these receptors, Solifenacin reduces smooth muscle tone in the bladder, allowing the bladder to retain larger volumes of urine and reducing the number of incontinence episodes. IUPAC name of Solifenacin succinate is Butanedioic acid, compound with (1S)-(3R)-1-azabicyclo [2.2.2] oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-iso-quinolinecarboxylate (1:1), having an empirical formula of $C_{23}H_{26}N_2O_2.C_4H_6O_4$and a molecular weight of 480.55. It is freely soluble at room temperature in water, Glacial acetic acid, dimethyl sulfoxide and methanol [1-4].

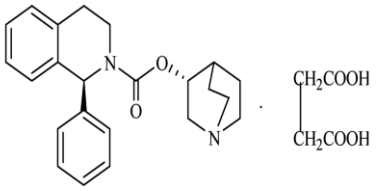

Fig 1: Structure of Solifenacin Succinate

Literature survey reveals chromatographic methods for the analysis of Solifenacin succinate in various pharmaceutical dosage forms [1-7]. Few literatures is cited on spectrophotometric methods [8-10]. Reported methods employ water and triethylammonium phosphate buffer (pH 2.5) as solvents respectively [8-10]. The main objective of this article is to study assay method and validation using 0.1N HCl which is not reported anywhere in the literature. Accordingly, we here report a new, cheap, simple, accurate and precise UV method for the determination of assay of solifenacin succinate in tablets and validate the developed method as per ICH guidelines.

MATERIALS AND METHODS

Materials

Instrument

A double beam UV-visible spectrophotometer (Shimadzu, model 1800) having two matched quartz cells with 1 cm light path and loaded with UV probe software (version 2.41) was used for recording of spectra and measuring absorbance. An electronic analytical weighing balance (0.1mg sensitivity, Shimadzu AY 220), digital pH meter (DELUX model 101) and a sonicator (sonica, model 2200 MH) were used in this study.

Chemicals and Reagents

Analytically pure sample of Solifenacin succinate with purities greater than 99% was obtained as gift sample from RACHEM pharma, Hyderabad, India and tablet formulation [SOLITEN] was procured from MEDPLUS, Hyderabad, India with labelled amount 5mg of Solifenacin succinate. Concentrated HCl (LR Grade) were obtained from SD Fine chemicals (Hyderabad, India).0.45µm Nylon membrane filters were obtained from Spincotech Private Limited, Hyderabad, India.

Method

Solvent

1.825 ml of HCl is taken in 1000ml volumetric flask. To this 800 ml of distilled water is added, and mixed properly later it was made up to 1000ml by using distilled water.

Selection of Suitable Detection Wavelength

Suitable wavelength for the total experiment was determined by recording UV spectrum in the range of 200-400 nm for Solifenacin succinate standard and sample and suitable wavelength selected was 210 nm (**Figure 2-3**).

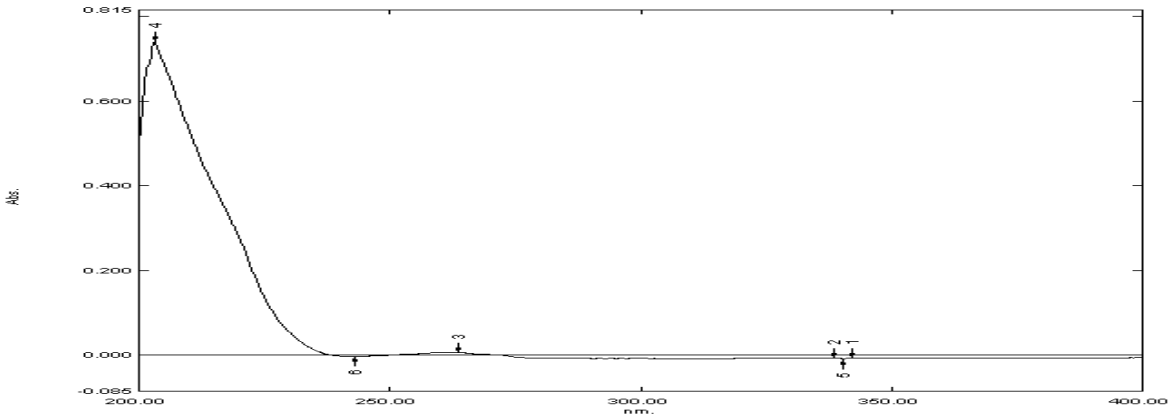

Fig. 2: UV Spectrum of Solifenacin Succinate Standard

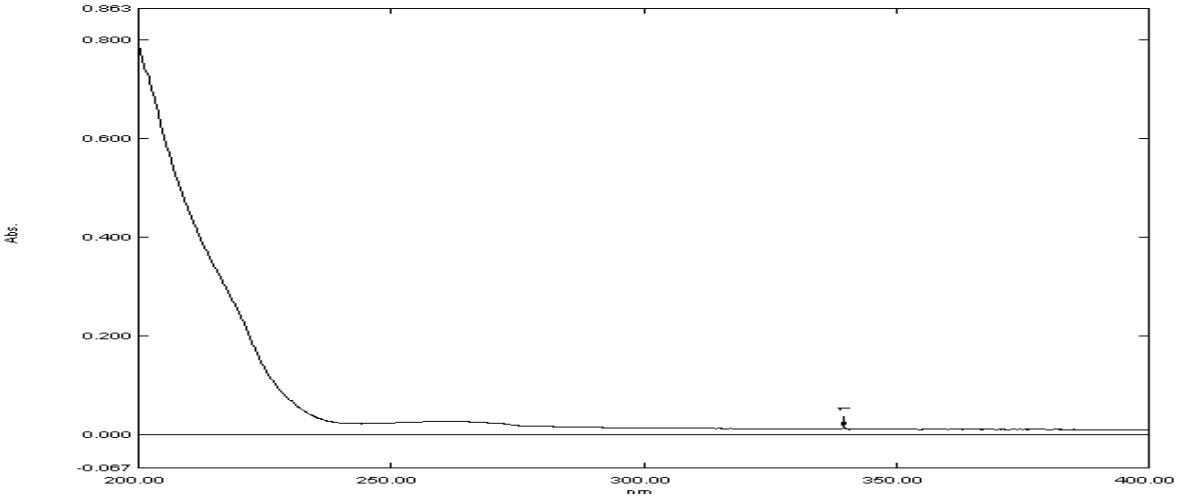

Fig. 3:UV spectrum of Solifenacin Succinate sample

Preparation of Working Standard Solution

10mg of Solifenacin succinate was accurately weighed and taken in 100ml clean and dry volumetric flask containing 80ml of solvent and then the solution was made up to the mark using the solvent. This is considered as standard stock solution (100µg/ml). From this 1ml was pipetted out and made to 10ml using solvent to get 10µg/ml concentration, treated as working standard, 100% target concentration.

Preparation of Stock and Working Sample Solution

Ten tablets were weighed and equivalent weight was determined. Weight equivalent to 5mg of Eplerenone was weighed from the ten tablets grinded in a pestle and mortar was transferred to a 50ml volumetric flask containing 40ml diluent and then sonicated for 5 minutes, later made upto the mark and then filtered through 0.45µ nylon membrane filter to get sample stock solution of 100µg/ml. 1 ml of the above stock solution was pipetted out and made up to 10 ml to get working sample solution equivalent to a concentration of working standard of 10µg/ml.

RESULTS AND DISCUSSION

Method Development

Various solvents were explored including water, 0.05N HCl, 0.1N HCl, 0.1N NaOH and 0.05N NaOH. Solifenacin succinate was found to be soluble and stable for minimum of 1 hour at room temperature using 0.05N HCl and 0.1N HCl and hence this solvent was initiated for the determination of suitable detection wavelength and working concentration of standard. In order to test the applicability of the developed method to a commercial formulation, SOLITEN tablets (5mg) was studied at working concentration. Assay of Solifenacin succinate in tablets was found to be in the range of 95-105% using 0.1NHCl solvent when the tablets were extracted for 5 minutes, while the assay was approximately 80% when 0.05N HCl was used. Hence 0.1N HCl was selected as a solvent. The protocol affords reproducible quantification of the drug in the sample ranging between 95 and 105%, which is the standard level in any pharmaceutical quality control. Hence the method is optimized.

Method Validation

Validation of the analytical method is the process that establishes by laboratory studies in which the performance characteristics of the method meet the requirements for the intended analytical application. UV spectrophotometric method developed was validated according to International Conference on Harmonization (ICH) guidelines [11] for validation of analytical procedures. The method was validated for parameters like linearity, accuracy, system precision, intra-day and inter-day precision / ruggedness as per ICH guidelines.

Precision

System Precision

Six replicate recording of absorbances at 210nm of standard solution at working concentration showed % RSD(Relative Standard Deviation) less than 2 for the drug, which indicates the acceptable reproducibility and thereby the precision of the system. System precision results are tabulated in **Table 1**.

Method Precision

Method precision was determined by performing assay of sample under the tests of repeatability (Intra day precision) and Inter day precision (Intermediate precision / Ruggedness) at working concentration.

Table 1: System Precision Results of Solifenacin Succinate.

	Absorbance
1	0.553
2	0.564
3	0.552
4	0.549
5	0.557
6	0.548
Average	**0.553**
SD	**0.005913**
% RSD	**1.069**

Repeatability (Intra Day Precision)

Six consecutive recording of absorbances at 210nm of the sample from the same homogeneous mixture at working concentration showed % RSD less than 2 concerning % assay for the drug which indicate that the method developed is method precise by the test of repeatability and hence can be understood that the method gives consistently reproducible results (**Table 2**).

Table 2: Intraday Precision Results of Solifenacin Succinate.

n	% Assay
1	101.5
2	100.4
3	101.3
4	100.3
5	100.3
Average	**100.7**
S.D.	**0.589915**
% RSD	**0.5854**

Intermediate Precision (Inter day precision / Ruggedness)

Assay precision between two consecutive days performed by different analysts of the sample showed % RSD less than 2, which indicate the method developed is inter day precise / rugged (**Table 3)**.

Table 3: Inter Day Precision/ Ruggedness Results

n	Analyst 1	Analyst 2
1	101.5	97.9
2	100.4	96.6
3	101.3	98.3
4	100.3	97.1
5	100.3	98.3
Average	**100.7**	**97.64**
SD	**0.589915**	**0.76**
% RSD	**0.5854**	**0.77**

Linearity

Standard solutions of Solifenacin succinate at different concentrations level (50%, 75%, 100%, 125% and 150%) were prepared. Calibration curve was plot by concentration level of drug versus corresponding absorbance at 210nm. The results show an excellent correlation between absorbance and concentration level of drug within the concentration range (5-15µg/ml) and the results are given in **Table 4** and **Figure 4.** The correlation coefficients were greater than 0.995, which meet the method validation acceptance criteria and hence the method is said to be linear in the range of 5-15µg/ml.

Table 4: Calibration Data for Solifenacin succinate

% Level	Concentration (µg/ml)	Absorbance
50	5	0.271
75	7.5	0.409
100	10	0.541
125	12.5	0.652
150	15	0.757
Regression equation		**Y=0.0486X+0.04**
Regression coefficient		**0.996265**

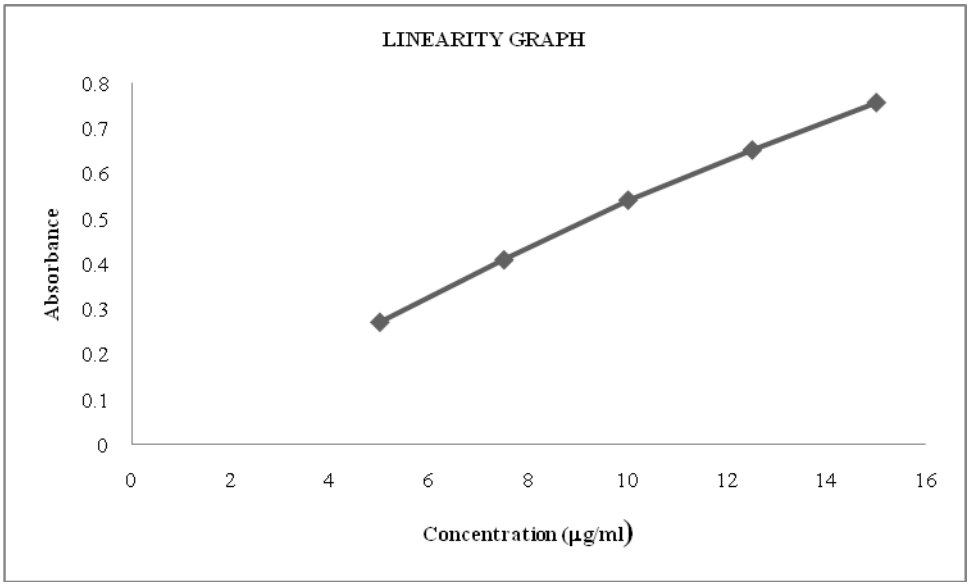

Figure 4: Linearity graph of Solifenacin Succinate

Accuracy

Accuracy was determined by means of recovery experiments using percentage method at three different levels (50-150%). At each level, three determinations were performed. Percent mean recovery was calculated as shown in **Table 5.** The accepted limits of recovery are 98% -102% and all observed data are within the required range which indicates good recovery values and hence the accuracy of the method developed. **Table 6** summarizes all the results regarding validation parameters as per ICH guidelines.

Table 5: Accuracy Studies

LEVEL (%)	Absorbance	% Recovery	*%MEAN RECOVERY
50	0.271	96.05	99.35
	0.290	102.78	
	0.280	99.24	
100	0.544	96.40	99.06
	0.560	99.24	
	0.573	101.54	
150	0.723	101.90	100.53
	0.735	100.67	
	0.723	99.02	

Table 6: Optical Characteristics and Validation Parameters of Solifenacin Succinate.

Parameters	Results
Detection wavelength (nm)	210
Beer's Law limits (µg/ml)	5-15
Regression equation (y = mx+c)	y=0.0486x+0.04
Correlation coefficient (r^2)	0.996
Slope (m)	0.0486
Intercept (c)	0.04
% Relative Standard Deviation (% RSD) System precision	1.06
(% RSD) Intra-day precision	0.5854
(% RSD) Inter-day precision	0.77
Accuracy (% Mean Recovery)	
50 % Level	99.35
100 % Level	99.06
150 % Level	100.53

CONCLUSION

A cheap and a rapid UV spectrophotometric method was developed and validated for the quantitative estimation of Solifenacin succinate in tablets as per ICH guidelines using 0.01N HCl as solvent. System, intraday and inter day precision are exemplified by relative standard deviation of 1.069, 0.58 and 0.77% respectively. The developed method exhibited linearity in the range of 5-15µg/ml. Percentage Mean recovery was found to

be in the range of 98-102, during accuracy studies. Accordingly it is concluded that the developed UV Spectrophotometric method is accurate, precise, linear and therefore the method can be used for the routine analysis of Solifenacin succinate in tablets in various pharmaceutical industries.

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