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Research Article

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION BY RPHPLC FORDETERMINATION OF DISSOLUTIONOF SOLIFENACIN SUCCINATE IN SOLIFENACIN SUCCINATE TABLETS

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ABSTRACT

Solifenacin succinate 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 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. This article describes development and validation for the assay determination of Solifenacin succinate in Solifenacin succinate Tablets by using a high performance liquid chromatography. The high performance liquid chromatography was achieved on aInertsil ODS 3 150 x 4.6, 5µ, column with an isocratic elution at a flow rate of 1.0 mL/min. The detection was performed by a photo diode array Detector. The method was validated in the concentration range of 20% to 150% of working concentration. The intra and inter-day precision and accuracy were within Limit. The overall mean recoveries of Solifenacin succinate were in the range of 95.0% to 105.0% for 60%, 80%, 100% and 120%.

INTRODUCTION

Solifenacin succinate 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]. M2 and M3 receptors are mainly distributed in the bladder while M3 subtype is distributed predominantly in the salivary gland and that M3 subtype plays a major role in the physiological function of both organs. Solifenacin compared with oxybutynin binds to a greater extent to bladder M3 muscarinic receptors in the bladder while it may exert a relatively little activity to bind exocrine M3 muscarinic receptors [5-6]. Various methods are available for the analysis of Solifenacin in literature like LC–ESI-MS/MS, semi-micro high performance liquid chromatography. Analytical method for the estimation of Solifenacin in bulk drug was not reported by HPLC method or HPTLC method [7-8]. Analytical method is validated that allows the determination of Solifenacin succinate Dissolution in Solifenacin succinate Tablets. The validation parameters, Specificity, Linearity, Repeatability, Precision, Accuracy, Solution Stability and Robustness were validated [10-11].

MATERIALS AND METHOD

Working standard used in Experiments reported in table No.1. Apparatus and instruments used in experiment are listed in table No: 2. Reagents and solvents used: Water (HPLC grade, Milli Q), Potassium dihydrogen phosphate (AR grade), Sodium dihydrogen phosphate anhydrous (AR grade), Acetonitrile (HPLC grade), Methanol (HPLC grade), Triethyl amine (AR Grade), Orthophosphoric Acid (AR Grade).

Table 1 Standard details

S No.	Name of Standards	Potency (%)
1	Solifenacin succinate	99.7

Table 2 List of Instruments used

Sr No	Instrument	Make	Software	Detector/Model No
1	HPLC	Waters	Empower Software	2489 dual wavelength
2	HPLC	Waters	Empower Software	2998 PDA Detector
3	Sonicator	Lab India	NA	NA
4	Weight balance	Mettler Toledo	NA	ML204

Development Trial

Literature reference was considered from the published assay paper "RPHPLC method development and validation for Assay

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determination of Solifenacin Succinate inSolifenacin Succinate Tablets", International Journal of Current Advanced Research [9], DOI: http://dx.doi.org/10.24327/ijcar.2017.2346.0005
Same Chromatographic conditions were used and dissolution media was selected form the office of Generic Drugs.

Peak shape and % dissolution was found satisfactory and methodology was finalised

Final Methodology

Preparation of Buffer: Added 4.0ml of triethylamine in 2.0 liters of water and adjust pH 3.0 with orthophosphoric acid.
Preparation of Mobile phase:Prepare a mixture of Buffer: Acetonitrile in the ratio (60: 40)

Preparation of Standard Stock Solution: Weigh accurately and transfer about 25 mg of Solifenacin succinate working standard into a 100 mL volumetric flask, add 50ml methanol and sonicate it to dissolve. Cool and make up to the mark with methanol and mix.

Preparation of Standard solution: (for 10mg)Accurately transfer 2 ml of Standard stock solution into 50 mL volumetric flask and dilute up to mark with media and mix.

Preparation of Standard solution: (for 5mg)Accurately transfer 2 ml of Standard stock solution into 100 mL volumetric flask and dilute up to mark with media and mix.

Dissolution Parameters:

Apparatus	:	USP II, Paddle
Dissolution Medium	:	Water, 900 mL
Speed	:	50 rpm
Interval	:	45 minutes
Temperature	:	37° C ± 0.5°C

Preparation of Sample Solution: Set the dissolution apparatus as per parameters. Place one tablet in each dissolution vessel and carry out dissolution. Withdraw 10 mL of solution after specified interval and inject.

Chromatographic Conditions:

Column	:	Inertsil ODS 3 150 x 4.6, 5µ
Flow Rate	:	1 mL / min.
Detection	:	215 nm.
Column Temp	:	30°C.
Injection Volume	:	20 µL.
Run Time	:	5 min.
Retention time	:	About 3 minutes

Procedure: Separately inject given volumes of Blank (Media), five replicates of Standard and Sample solution into the chromatograph and record the chromatograms. Measure the area counts for Solifenacin succinate peak.

Evaluation of System Suitability: Inject the five replicates injections of standard solution into the chromatograph and record the chromatograms. Measure the area counts for Solifenacin succinate peak. The RSD of five replicate injections should not be more than 2.0%.

Calculation

Calculate the percentage of Solifenacin succinate in solifenacin succinate Tablets as follows:

For 10mg

$$\% LC = \frac{AT}{AS} \times \frac{\text{Std. wt (mg)}}{100\ mL} \times \frac{2\ mL}{50\ mL} \times \frac{900\ mL}{1Tab} \times \frac{P}{100} \times \frac{100}{LC}$$

For 5mg

$$\% LC = \frac{AT}{AS} \times \frac{\text{Std. wt (mg)}}{100\ mL} \times \frac{2\ mL}{100\ mL} \times \frac{900\ mL}{1Tab} \times \frac{P}{100} \times \frac{100}{LC}$$

Where,

AT = Area count of Solifenacin succinate in the sample solution.
AS = Average area count of Solifenacin succinate in the standard solution.
P = Percent potency of Solifenacin succinate working standard on as is basis.
LC = Label claim of Solifenacin succinate in mg.

RESULT AND DISCUSSION

Specificity: Specificity is the ability of the method to measure the analyte in the presence of dissolution media and placebo.No interference was observed from Dissolution media and Placebo at the retention time of Solifenacin Succinate peak. Therefore, the HPLC method for the dissolution of Solifenacin SuccinateTablets is specific.Data is reported in Table no 2& Figure No 1, 2&3.

Table No.2 Table for Specificity

Sr. No.	Sample Name	Purity Angle	Purity Threshold
1	Standard Preparation	0.193	1.291
2	Sample Preparation	0.153	1.208

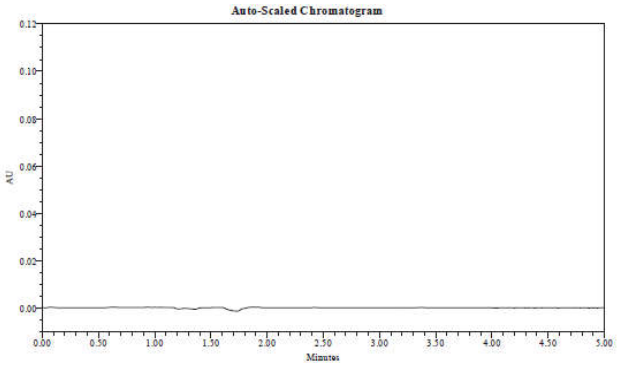

Figure No 1 Blank

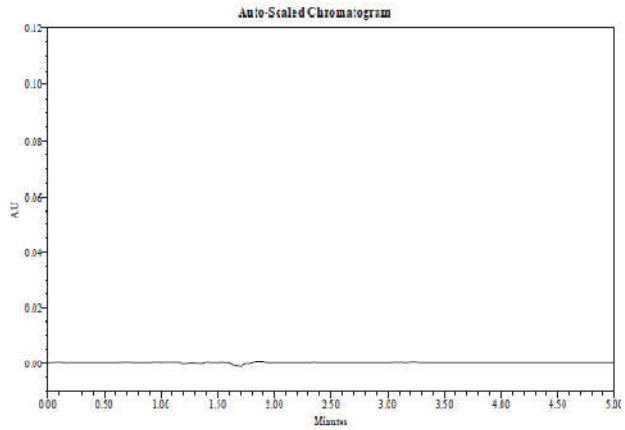

Figure No 2 Placebo

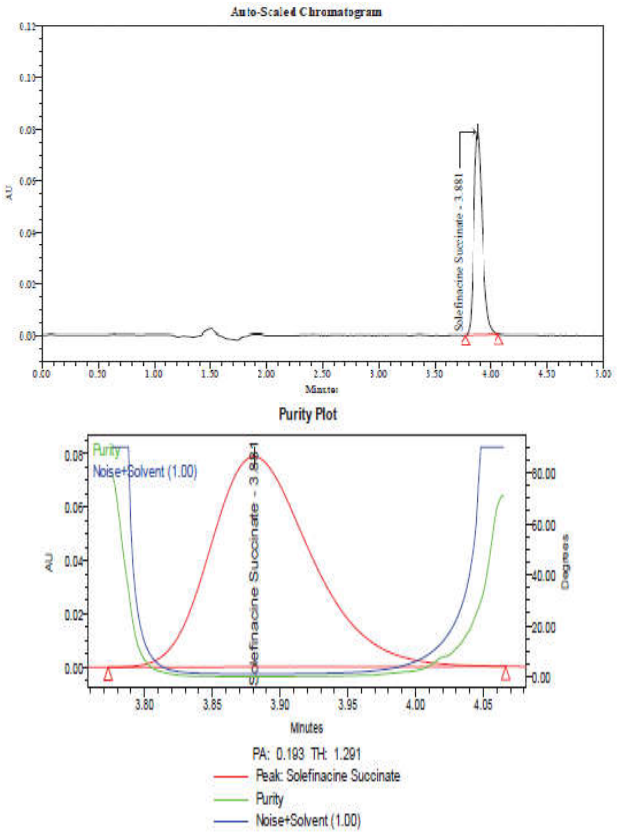

Figure No 3 Standard Solution

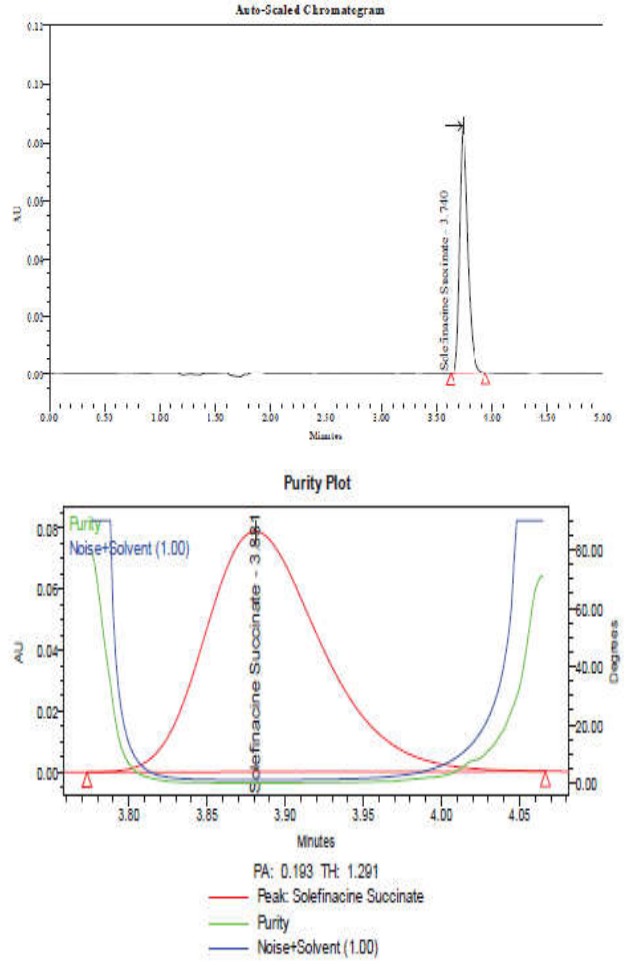

Figure No 4 Sample Solution

Linearity: The response for the drug was found to be strictly linear in the investigated concentration range. The values of the area under the curve and concentration are given in Table 2 and Figure No.5. The Correlation coefficient is 0.99961. Therefore, the HPLC method for the dissolution of Solifenacin Succinate Tablets is linear.

Table No 4 Linearity Table

% Linearity Range	Concentration (µg per ml)	Response (Area)	Statistical analysis	
1	1.001	37544		
2	2.002	83831	**Slope**	**42704**
3	5.006	202228		
4	8.009	338299	**Intercept**	**-6287**
5	10.012	418740		
6	12.014	497379		
7	15.018	643911	**Correlation Coefficient**	**0.99961**

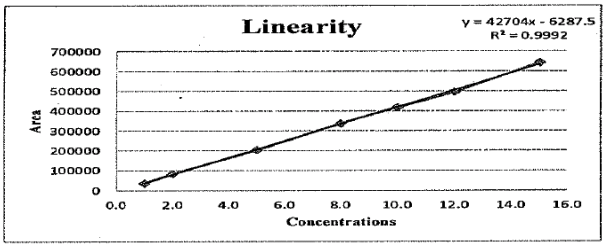

Figure No 5 Linearity Graph

Accuracy: As shown from the data in Table 4, the mean recovery is 99.7 % were made at various added concentrations from a range of 60% to 120%, despite the fact that the drug was fortified to a mixture that contained the drug as well as the test formulation. Therefore, the HPLC method for the dissolution of Solifenacin Succinate Tablets is accurate.

Table No 5 Accuracy of Solifenacin Succinate

Sample No.	Amount added (mg)	Amount recovered (mg)	% Recovery
Recovery-60 %	5.988	6.003	100.3
Recovery-60 %	5.988	6.152	102.7
Recovery-60 %	5.988	6.052	101.1
Recovery -80 %	7.984	8.050	100.8
Recovery -80 %	7.984	7.870	98.6
Recovery -80 %	7.984	8.066	101.0
Recovery-100 %	9.980	10.072	100.9
Recovery-100 %	9.980	10.013	100.3
Recovery-100 %	9.980	10.100	101.2
Recovery-120 %	11.977	11.562	96.5
Recovery-120 %	11.977	11.527	96.2
Recovery-120 %	11.977	11.544	96.4
	Mean		99.7
	SD		2.192
	% RSD		2.20

Precision: Precision is the closeness of agreement between a series of measurements obtained from multiple sampling of same sample under the prescribed conditions.The percent relative standard deviation (RSD) was determined for the Dissolution of Solifenacin Succinate Tablets.To evaluate the intermediate precision, the same experiment was repeated with a different analyst, lot of column and a different instrument in the same laboratory.Precision and Ruggedness data reported in table no.5.

Table No. 6 Over all %RSD Comparison for Dissolution in Precision and Ruggedness study

Sample	Analyst -1 % Drug release	Analyst -2 % Drug release
1	98	97
2	95	97
3	90	98
4	94	96
5	97	97
6	93	98
Mean	95	97
SD	2.881	0.753
% RSD	3.049	0.775
Overall Mean	96	
Overall SD	2.443	
Overall % RSD	2.545	
Difference between two Analyst	2.0	

Stability of Analytical solution: The solution stability of sample and standard solution provide an indication of the method's reliability in normal usage during the storage of the solutions used in the method. The sample and standard preparations for Solifenacin Succinate Tabletswere to be stored at room temperature and injected in to RPHPLC at regular intervals of times for at least 48 hours. No significant changes were experienced during solution stability.
Standard and sample solutions were stable up to 42 hours at room temperature.

Filter equivalency: Filtration is an essential component of the dissolution test. The dissolutionprocess stops at the moment that a sample is withdrawn and immediately filtered. The sample, once clarified of solid particles and excipient material, is now ready for the second phase of the test analysis of the filtered sample. Sample from one dissolution vessel were filtered in triplicate through one or more different types of filters such as Nylon 0.45µ, Teflon 0.45µ filter discarding first two mL of the filtrate. Additionally the solution from the same dissolution vessel was centrifuged in triplicate. The filtrate and the centrifugate were analysed as described under Methodology. Results are reported in table no.6.

Table No 7 Filter equivalency

Sample No.	% Drug release		
	Centrifuged	Nylon 0.45µ	Teflon 0.45µ
1	91	106	70
2	95	121	83
3	96	120	91
Mean	94	116	81
% Correlation with centrifuged	--	123	86

Conclusion: The Percent correlation is not within limits for Nylon 0.45µ and Teflon 0.45µ. Therefore, centrifuge sample has to be used for injection in HPLC system.

System Suitability: Record the RSD of five replicate injections of standard solution. System Suitability of Different parameters are reported in table no 7.

Table No.8 System suitability data

Experiment	%RSD of Standard Theoretical plates
Accuracy, Linearity	0.210
Specificity &Precision	0.180
Ruggedness and solution stability	0.387

CONCLUSION

The Validated HPLC method for Dissolutionof Solifenacin Succinateis linear, precise, accurate and specific. The results of the method are well within the acceptance limits and as per the International Conference on Harmonization requirements.

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List of abbreviations

No.	Number
Hrs	Hours
mL	MilliLiter
RPHPLC	Reverse Phase High performance Liquid Chromatography
SD	Standard Deviation
RSD	Relative Standard Deviation

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