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Validation of Solifenacin Succinate in Pharmaceutical Dosage Form

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Abstract – *Solifenacin in tablet dosage form was validated and found to be accurate, precise and robust with the help of a new HPLC method. Chromatographic separation with stationary phase maintained at ambient temperature with a mobile phase combination of acetonitrile containing buffer 0.1% perchloric acid in water (gradient mode) at a stream rate of 1.0 milliL/min, and the detection was carried out by using UV detector at 215 nm on a Inertsil ODS 3V column measuring C18 (250 millimeter × 4.6 millimeter, 5 µm) was utilized. The present ICH guidelines approved the accomplished method.*

Keywords – Chromatographic, Gradient, HPLC, Stationary, Validated.

I. INTRODUCTION

Solifenacin succinate is a focused muscarinic acetylcholine receptor, antagonically utilized in the treatment of overactive bladder with or without urge incontinence. Synthetically it is 1-azabicyclo [2.2.2]oct-8-yl(1S)- 1-phenyl-3,4-dihydro-1H-isoquinoline-2 carboxylate shown in Figure 1.

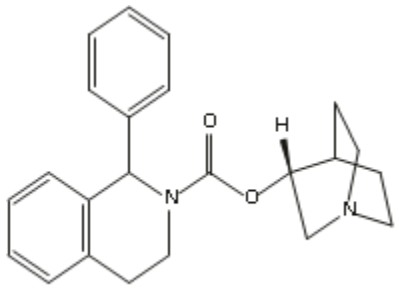

Fig: 1 Chemical structures of solifenacin.

The molecular formula of solifenacin succinate is C23H26N2O2 with its sub-atomic weight 362.46. Solifenacin is widely processed in the liver. The metabolites are observed as one pharmacologically dynamic metabolite (4Rhydroxy solifenacin), and three pharmacologically idle metabolites (N-glucuronide & the N-oxide and 4R-OH -N-oxide of solifenacin) occuring at low focuses in human plasma after oral dosing. After oral organization of vesicare to solid volunteers, top plasma levels (Cmax) of solifenacin are come to inside 3 to 8 hrs after organization and at enduring state ran from 32.3 to 62.9 ng/mLitre for the five and ten mg vesicare tablets, respectively. The terminal end half-existence of SF is roughly 45– 68 hours. Solifenacin is somewhere 98% (in vivo) bounded to proteins of human plasma, mainly to alpha-1-acid glycoprotein [1– 10].

Writing review uncovers that evaluation of solifenacin in human plasma [11, 12], rodent plasma [13], pharmaceutical mixes [14– 17], and mechanical waste streams [18] was accounted for. These strategies were accounted for by utilizing LC-MS/MS [11, 12, 18], HPLC [13– 16], and HPTLC [17]. Among all, evaluation of solifenacin by LC-MS/MS in organic frameworks [11– 13] was demonstrated best outcomes.

The detailed HPLC techniques [13– 16] have a few downsides as far as ruggedness, reproducibility, and affectability in long run. The principle objective of the present examination is to create and approve the novel basic, higher touchy, particular, tough, and reproducible diagnostic strategy for quantitative assurance of solifenacin in pharmaceutical mixes by HPLC. The created strategy would be connected in completed item and in quality control.

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II. EXPERIMENTAL

2.1 Instrumentation. Gradient quaternary pumps, having variable UV detector attached with data recorder and integrator software was used in HPLC methodology.

Table 1
Gradient program.

Time (mins)	% Mobile Phase A	% Mobile Phase B
0.01	70	30
25	53	47
35	30	70
50	30	70
52	70	30
60	70	30

2.2. Materials. Perchloric acid and acetonitrile were obtained from Merck. Commercially available solifenacin tablets were used for the dosage form analysis. HPLC grade solvents and ingredients & Milli-Q-water was used throughout the experiment. The tablet form studied contained 5 mg of solifenacin in it.

2.2.1. Mobile Phase Preparation

Solution A. Buffer 0.1% Perchloric acid in water

Solution B. Acetonitrile. Gradient program was shown in Table 1.

2.2.2. Diluent. Water:Acetonitrile (50:50 v/v)

2.2.3. Blank solution: Use diluent as blank.

2.3. Chromatographic Conditions. The mobile phase used was mixture of buffer 0.1% perchloric acid in water and acetonitrile in the ratio of gradient elution at a flow rate of 1.0 mL/min and the injection volume was 10 □L. Column used was Inertsil ODS 3V C18 (250 millimeter X 4.6 millimeter, 5 □m) at 250C temperature for analytical study. The detection was carried out at a wavelength of 215 nm for a run time of 60 mins. The retention time of solifenacin was found to be 21.544 min.

2.4. Standard Stock Solution. 50 mg of solifenacin succinate was weighed accurately and transferred it into 50 ml volumetric flask, 25 to 30 ml of diluent was added and further sonicated to dissolve & make with diluent till mark. Pipette out ten ml of this solution & dilute with diluent to fifty ml.

Calculations

$$\% \text{ Assay (OAB)} = \frac{AT}{AS} \times \frac{WS}{WT} \times \frac{P}{100 - KF} \times 100 \quad (1)$$

Where,

AT: Area of sample solution.

AS: Average area of standard solution.

WS: Weight of standard in mg.

WT: Weight of sample in mg.

P: as is basis purity of standard (%).

2.4.1. Assay of Pharmaceutical Dosage Form: Sample Preparation. 20 tablets were taken and its average weight was calculated. Fifty milligram of powdered tablet was transferred into 100 mL volumetric flask and sample solvent was added to

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extract solifenacin by ultrasonication for 10 minutes. 0.45 μ filter paper was utilized for filtration of resultant mixture. Take 10.0 mL of above solution and transfer it to 50 mL volumetric flask and make up the volume using mobile phase.

III. RESULTS AND DISCUSSION

3.1. Chromatographic Conditions. A few HPLC strategies were produced for the estimation of solifenacin utilizing methanol, water, acetonitrile and phosphate, acetic acid derivation, and OPA buffer. Hence KH2PO4 buffer and Inertsil ODS 3V C18 (250 mm × 4.6 mm, 5.5 m) segment to minimize the maintenance time and to get symmetric pinnacles having excellent resolution. Diverse trails were performed utilizing. distinctive extents of potassium phosphate buffer having distinctive pH with methanol and acetonitrile. The, mobile stage was observed to be acceptable and gave symmetric and well resolved peak for solifenacin.

The retention time of solifenacin was observed to be 21.544. The standard chromatogram was shown in Figure 2.

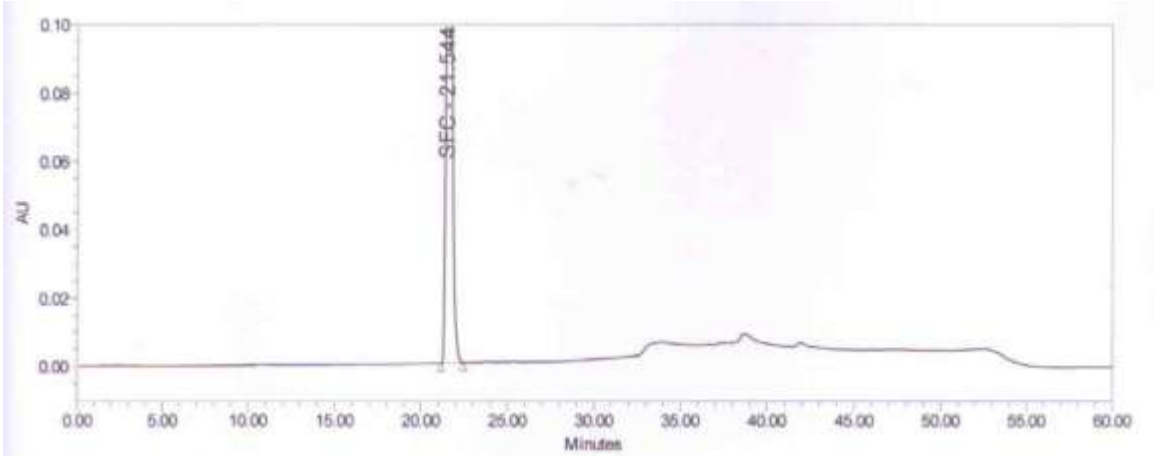

Fig: 2 Chromatogram of std. solifenacin

3.2. Evaluation of Proposed Method. The ICH guidelines were followed while developing the method. [19]

3.3. Linearity. Linearity test arrangements of solifenacin (10– 100 (μg/mL)) were set up from the stock arrangement at five distinctive focus levels. Graph of peak areas vs their concentration was developed which gave the idea of slope, *Y*-intercept, and correlation coefficient of the curve. The correlation coefficient was found to be 0.9827, intercept 4949.9627, slope value 40966.1903 & calibration curve for solifenacin is below in Figure 3.

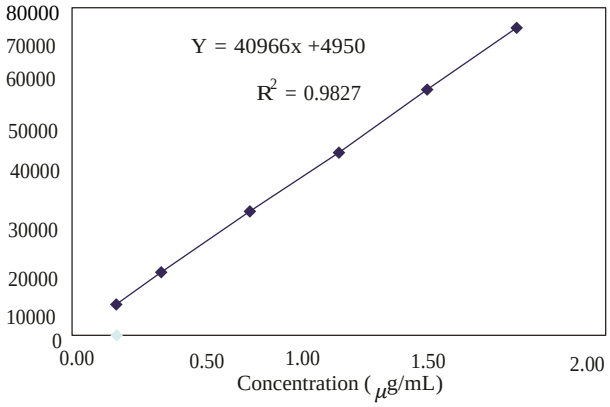

Fig: 3 Calibration curve of solifenacin

Linearity data: Three injections of six levels each level having similar concentrations yielded following results:

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LOQ level (0.25ppm) (3 injections) area obtained was 17408, 17720, 18063 having mean 17730 & %RSD 1.85
50% level (0.51ppm) (3 injections) area obtained was 24557, 24036, 25306 having mean 24633 & %RSD 2.59
80% level (0.81ppm) (3 injections) area obtained was 36587, 39151, 37776 having mean 37838 & %RSD 3.39
100% level (1.01ppm) (3 injections) area obtained was 42642, 42721, 41593 having mean 42319 & %RSD 1.49
120% level (1.21ppm) (3 injections) area obtained was 56232, 54085, 54604 having mean 54974 & %RSD 2.04
150% level (1.52ppm) (3 injections) area obtained was 69002, 69631, 69655 having mean 69429 & %RSD 0.53

3.4. Precision. A precision of any method developed analytically is the nearness of test results between series of measurements obtained from multiple samplings of same homogenous sample under the prescribed conditions. Resolution between the peak of solifenacin and impurity A from reference solution (a) was 6.02 which met the suitability criteria i.e. > 4.0. The RSD for peak area of SFC VI in reference solution of six replicate injection was 3.94% which was within limit i.e. not more than 15.0% which is concluded in Table 3.

Table 3
Precision data.

S. No.	Injection No.	Area of SFC
1	1	39172
2	2	39179
3	3	36915
4	4	41394
5	5 6	40774 39572
Average		39501.00
Standard deviation		1556.17
%RSD		**3.94**

Precision of solifenacin succinate observed in % in six solutions is as follows:

Test solution 1 Single max 0.03, Impurity A (4.8mins) 0.01, Impurity B (17.2 mins) ND, Impurity I (1.9 mins) ND and Total Impurity 0.04

Test solution 2 Single max 0.02, Impurity A (4.8mins) 0.01, Impurity B (17.2 mins) ND, Impurity I (1.9 mins) ND and Total Impurity 0.02

Test solution 3 Single max 0.04, Impurity A (4.8mins) 0.02, Impurity B (17.2 mins) ND, Impurity I (1.9 mins) ND and Total Impurity 0.06

Test solution 4 Single max 0.04, Impurity A (4.8mins) 0.01, Impurity B (17.2 mins) ND, Impurity I (1.9 mins) ND and Total Impurity 0.04

Test solution 5 Single max 0.01, Impurity A (4.8mins) 0.01, Impurity B (17.2 mins) ND, Impurity I (1.9 mins) ND and Total Impurity 0.02

Test solution 6 Single max 0.01, Impurity A (4.8mins) 0.02, Impurity B (17.2 mins) ND, Impurity I (1.9 mins) ND and Total Impurity 0.03

3.5. Intermediate Precision/Ruggedness. The halfway accuracy of the strategy was checked by deciding exactness on a similar instrument, utilizing the equivalent chromatographic conditions in various days. The %RSD of the drug was found lesser than 2 not withstanding when it is performed in diverse day. The strategy is said to be exact regarding the criteria of the middle accuracy. The results are given in Table 3.

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3.6. Accuracy. So as to pass judgment on the quality and relevance of technique the recuperation investigation was performed at three levels 50%, 100%, and 150% by standard expansion strategy. The % recuperations for solifenacin were determined by infusing the examples and it was observed to be inside the breaking points; the results are given in Table 4.

Table 4
Accuracy data.

Analyte	% Level	Nominal Value (mg)	Found (mg)	% Recovery	Mean Recovery %
Solifenacin	50	2.5	2.31	94.33	95.76
	100	5	4.93	99.51	
	150	7.5	6.99	93.44	

3.6.1. Robustness. The strength as a proportion of strategy ability to stay unaffected by little, yet conscious changes in chromatographic conditions was examined by testing impact of little changes in mobile phase composition (10 % absolute change in organic phase) and stream rate (±0.2 mL/min). The USP plate tally and USP following were inside the breaking points. Hence, the strategy was observed to be vigorous regarding fluctuations in every powerful condition.

3.6.2. LOD and LOQ. The LOD and LOQ of solifenacin were detected by injecting 6 level injections each level categorized into 3 injections of same concentrations and the result obtained is as follows:

30% level (0.30ppm) (3 injections) area obtained was 13109, 12351, 14581 having mean 13347 & %RSD 8.50

50% level (0.51ppm) (3 injections) area obtained was 22488, 20531, 22264 having mean 21761 & %RSD 4.92

80% level (0.81ppm) (3 injections) area obtained was 34514, 34951, 36382 having mean 35282 & %RSD 2.77

100% level (1.01ppm) (3 injections) area obtained was 41439, 40973, 41311 having mean 41241 & %RSD 0.58

120% level (1.21ppm) (3 injections) area obtained was 49779, 49964, 49205 having mean 49649 & %RSD 0.80

150% level (1.52ppm) (3 injections) area obtained was 63085, 62623, 62098 having mean 62602 & %RSD 0.79

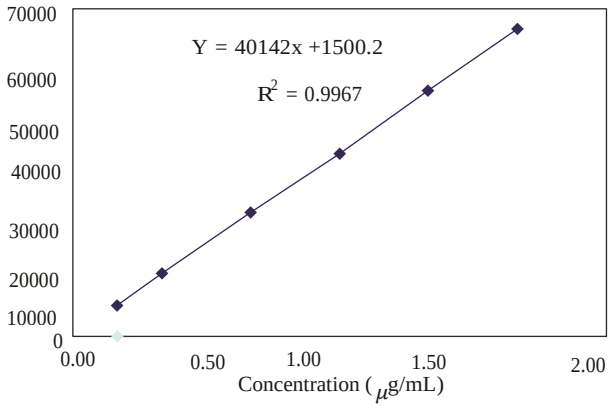

Fig no. 4 LOD & LOQ Of SFC

The graph yields intercept of 1500.2170, slope of 40142.2314, R^2 of 0.9967, LOD of 0.08ppm & LOQ of 0.25 ppm.

3.6.3. Assay of Pharmaceutical Formulation. The proposed approved strategy was effectively utilized to detect solifenacin in its tablet form. The outcome acquired for solifenacin was similar with the reference quantity and they are given as follows:

Amount taken – 10.0mg, Amount found – 9.75mg, % Assay – 97.50

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IV. CONCLUSION

The present work alludes to the way that the most exact, precise, and strong HPLC technique was produced and approved for estimation of solifenacin in pharmaceutical dosage form as per the ICH parameters. The technique was approved and observed to be straightforward, exact, and precise. Level of recuperation demonstrates that the strategy is free from obstruction of the excipients utilized in the formulation. Subsequently, the proposed strategy can be utilized for routine investigation of solifenacin in its dosage form.

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