Research Article

# Validated RP-HPLC Method for Routine Analysis of Solifenacin in Bulk and Finished Products

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**Received:** 10-04-2026; **Revised:** 22-06-2026; **Accepted:** 29-06-2026; **Published online:** 20-07-2026.

**ABSTRACT**

A simple, rapid, precise, and accurate reverse-phase high-performance liquid chromatographic (RP-HPLC) method was developed and validated for the routine quantitative estimation of solifenacin succinate in bulk drug and pharmaceutical dosage forms. Chromatographic separation was achieved using a Sunfire C8 column (150 mm × 4.8 mm, 5 µm) with a mobile phase consisting of buffer, methanol, and acetonitrile in the ratio of 45:45:10 (v/v), delivered at an optimized flow rate. Detection was carried out using a UV detector, and solifenacin showed a well-resolved peak with a retention time of approximately 3.2 minutes. The method was validated in accordance with ICH guidelines for parameters including linearity, precision, accuracy, robustness, limit of detection (LOD), and limit of quantification (LOQ). The calibration curve was found to be linear over the concentration range of 20–100 µg/mL with a correlation coefficient of 0.9996. The %RSD for precision was less than 2%, indicating good repeatability and reproducibility. Accuracy studies showed recovery values within acceptable limits (98–102%), confirming the reliability of the method. The LOD and LOQ were found to be 0.93 µg/mL and 3.07 µg/mL, respectively, demonstrating adequate sensitivity. The developed method was successfully applied for the assay of solifenacin in marketed tablet formulations, showing satisfactory results consistent with labeled claims. Stability studies under various stress conditions indicated that the method is stability-indicating. Overall, the proposed RP-HPLC method is simple, sensitive, robust, and suitable for routine quality control analysis of solifenacin in bulk and pharmaceutical formulations.

**Keywords:** Solifenacin, RP-HPLC, Method Validation, Chromatography.

## INTRODUCTION

Solifenacin succinate is a competitive muscarinic acetylcholine receptor antagonist used in the treatment of overactive bladder with or without urge incontinence. Chemically it is 1-azabicyclo[2.2.2]oct-8-yl(1S)-1-phenyl-3,4-dihydro-1Hisoquinoline-2 carboxylate. The molecular formula of solifenacin succinate is C23H26N2O2 with its molecular weight 362.46. Solifenacin is extensively metabolized in the liver. The metabolites observed as one pharmacologically active metabolite (4Rhydroxy solifenacin), and three pharmacologically inactive metabolites (N-glucuronide and the N-oxide and 4R-hydroxy-N-oxide of solifenacin) occurring at low concentrations in human plasma after oral dosing. After oral administration of vesicare to healthy volunteers, peak plasma levels (Cmax) of solifenacin are reached within 3 to 8 hours after administration and at steady state ranged from 32.3 to 62.9 ng/mL for the 5 and 10 mg vesicare tablets, respectively. The terminal elimination half-life of SF is approximately 45–68 hours. Solifenacin is approximately 98% (in vivo) bound to human plasma proteins, principally to alpha-1-acid glycoprotein [1–10].

Literature survey reveals that quantification of solifenacin in human plasma [11, 12,] rat plasma [13], pharmaceutical compounds [14–17], and industrial waste streams [18] was reported. These methods were reported by using LC-MS/MS [11, 12, 18], HPLC [13–16] and HPTLC [17]. Among all, quantification of solifenacin by LC-MS/MS in biological matrices [11–13] was proved best results.

The reported HPLC methods [13–16] have some drawbacks in terms of ruggedness, reproducibility, and sensitivity in long run. The main goal of the present study is to develop and validate the novel simple, higher sensitive, selective, rugged, and reproducible analytical method for quantitative determination of solifenacin in pharmaceutical compounds by HPLC. The developed method would be applied in finished product and in quality control.

## MATERIALS AND METHODS

### Instrumentation:

The Waters HPLC system equipped with autosampler and UV or DAD was used for method development and method validation. The output signal was monitored and processed by using Empower software.

### Materials

Solifenacin succinate bulk drug was made available from Pharma Train, Hyderabad; orthophosphoric acid, potassium phosphate monobasic, methanol, and acetonitrile were obtained from Merk. Commercially available solifenacin tablets were used for the dosage form analysis. All chemicals and reagents used were of HPLC grade; Milli-Q-water was used throughout the experiment. The pharmaceutical dosage form assayed in the study is test formulation containing 5 mg of solifenacin.

**PREPARATION OF BUFFER AND MOBILE PHASE:**

A 0.1% trifluoroacetic acid solution was prepared on addition of 1mL trifluoroacetic acid to a 1000mL flask containing Milli-Q water; then, pH was corrected to 3.0 using orthophosphoric acid.

**Preparation of Mobile phase:**

450mL (45%) of prepared buffer, 450mL (45%) of methanol, and 100mL (10%) of acetonitrile were combined to make the mobile phase for 1000mL.

**Preparation of Standard solution:**

Solifenacin Succinate, 25mg, was added to a 25mL flask and then diluted to the desired concentration (primary stock solution). 0.6mL was also taken in a 10mL flask from the stock solution. The resulting solution is 60 µg/mL of Solifenacin Succinate.

**Sample Preparation:**

In a 25mL flask, five Solifenacin Succinate tablets are weighed, broken up, and transferred to a 25mg Solifenacin Succinate equivalent (marketed formulation = 308.8mg pill Powder) 308.8 mg in weight (Stock solution). From the above information, 60µg/mL of Solifenacin Succinate was diluted in a 10mL flask and, therefore, 0.6mL was obtained.

**Assay of Pharmaceutical Dosage Form:** Sample Preparation. Take 20 tablets and calculate the average weight. Crush the tablets and accurately weigh 50 mg of tablet powder and transfer it into 100 mL volumetric flask and add sample solvent to extract solifenacin by ultrasonication for 10 min. The resultant mixture was filtered through 0.45 $\mu$ filter. From this, take 10.0 mL and transfer it to 50 mL volumetric flask and make up the volume using mobile phase.

## RESULTS AND DISCUSSION

**Optimization of Chromatographic Conditions:**

Several HPLC methods were developed for the estimation of solifenacin using methanol, water, acetonitrile and phosphate, acetate, and OPA buffer. Hence, we have selected Reverse phase sunfire C8 (150 mm × 4.8 mm, 5 $\mu$m) column to decrease the retention time and to obtain symmetric peaks having good resolution.

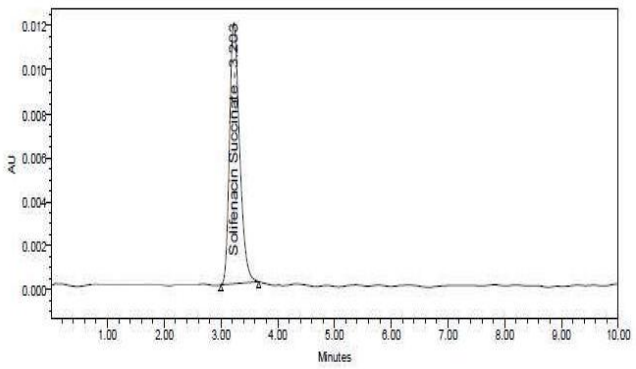


**Figure 1:** Optimized chromatogram of Solifenacin Succinate

Different trails were performed using different proportions of potassium phosphate buffer having different pH with methanol and acetonitrile. The mobile phase containing buffer: Methanol: Acetonitrile (45: 45: 10 v/v) at ph 6.0 was found to be satisfactory and gave symmetric and well resolved peak for solifenacin. The retention time of solifenacin was found to be 3.203. The standard chromatogram was shown in Figure 1.

**Validation of Proposed Method:**

The proposed method was validated according to the International Conference on Harmonization (ICH) guidelines[19].

**Linearity:** Linearity test solutions of solifenacin (20 – 100 ($\mu$g/mL)) were prepared from the stock solution at five different concentration levels. The calibration curves were constructed by plotting peak areas versus their corresponding concentrations. The slope, $Y$-intercept, and correlation coefficient of the calibration curve were calculated. The correlation coefficient was found to be 0.9996 and the calibration curve for solifenacin is given in Figure 2 and Table 1.

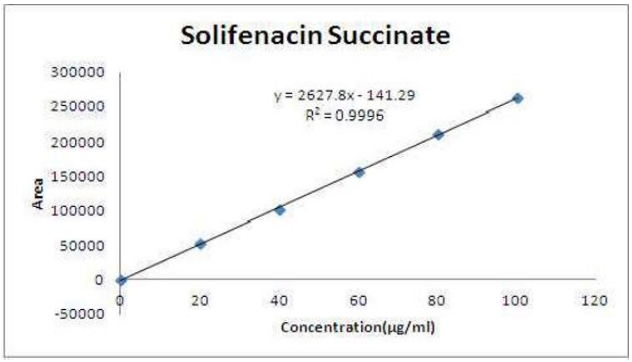


**Figure 2:** Calibration curve of Solifenacin

**Table 1:** Calibration curve data of Solifenacin

| S. No | Conc. ($\mu$g/mL) | Average peak area | Rt (minutes) |
|---|---|---|---|
| 1 | 20 | 54694 | 3.219 |
| 2 | 40 | 101930 | 3.227 |
| 3 | 60 | 156336 | 3.228 |
| 4 | 80 | 211765 | 3.222 |
| 5 | 100 | 262769 | 3.220 |

**Precision:**

Precision was evaluated by injecting five replicate injections of solifenacin of standard concentration under the same chromatographic conditions and calculated by the % RSD. The % RSD indicates that the developed method is repeatable. The % RSD for assay of solifenacin was found to be 0.7. The results are shown in Table 2.

**Table 2:** Results of precision data

| Sample No. | Conc. (µg/mL) | System Precision (Repeatability) | Method Precision (Reproducibility) | Intermediate precision |
|---|---|---|---|---|
| Injection-1 | 60 | 152826 | 152826 | 156293 |
| Injection-2 | 60 | 152093 | 152635 | 153299 |
| Injection-3 | 60 | 152078 | 152763 | 153034 |
| Injection-4 | 60 | 153435 | 153722 | 154244 |
| Injection-5 | 60 | 152934 | 154264 | 155261 |
| Injection-6 | 60 | 154964 | 152877 | 153566 |
| Mean± SD | | 153055.0 ±1071.0 | 153322.3±656.2 | 154282.8±1268.1 |
| % RSD | | 0.7 | 0.4 | 0.8 |

**Table 3:** Results of Accuracy data

| Conc. Taken (µg/mL) | Recovery level | Amount added (µg/mL) | Amount found (µg/mL) | Peak area (n=3) | % Recovery | % RSD |
|---|---|---|---|---|---|---|
| **60** | 50% | 12.5 | 12.62 | 77170.3 | 100.95 | 0.45 |
| | 100% | 25 | 25.16 | 153884.7 | 100.65 | |
| | 150% | 37.5 | 37.52 | 229433 | 100.05 | |

**Intermediate Precision:**

The intermediate precision of the method was checked by determining precision on the same instrument, using the same chromatographic conditions in different day. The %RSD of solifenacin was found to be below 2 even when it is performed in different day. The method is said to be precise with respect to the criteria of the intermediate precision. The results are given in Table 2.

**Accuracy:**

In order to judge the quality and applicability of method the recovery analysis was performed at three levels 50%, 100%, and 150% by standard addition method. The % recoveries for solifenacin were calculated by injecting the samples and it was found to be within the limits; the results are given in Table 3 and chromatogram in Figure 3, 4 & 5.

**Robustness:**

The robustness as a measure of method capability to remain unaffected by small, but deliberate changes in chromatographic conditions was studied by testing influence of small changes in mobile phase composition (10% absolute change in organic phase) and flow rate (±0.2 mL/min). The USP plate count and USP tailing were within the limits. So, the method was found to be robust with respect to variability in all robust conditions. Results are shown in Table 4.

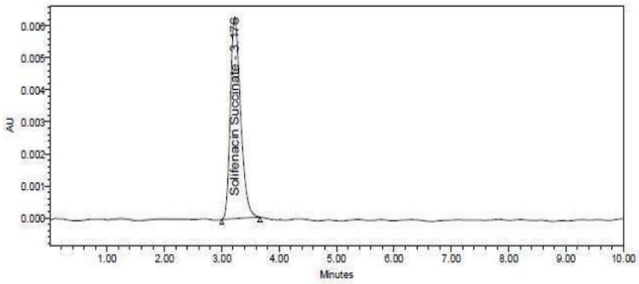


**Figure 3:** Chromatogram showing 50% Accuracy

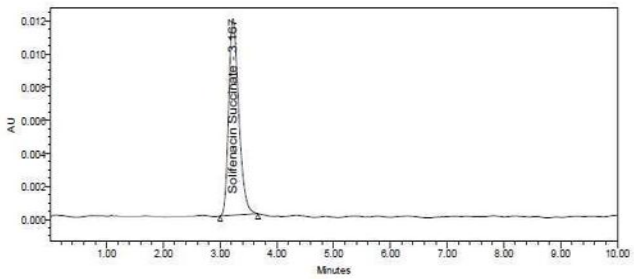


**Figure 4:** Chromatogram showing 100% Accuracy

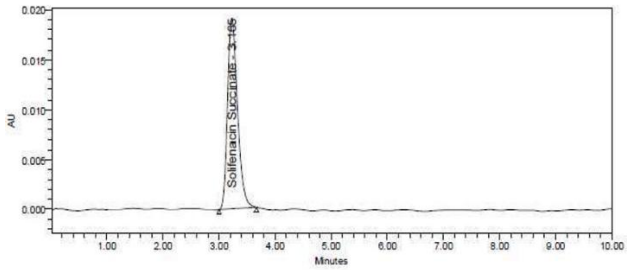


**Figure 5:** Chromatogram showing 150% Accuracy

**Table 4:** Results of Robustness data

| Parameter | Condition | Rt (min) | Plate Count | Tailing | Peak Area |
|---|---|---|---|---|---|
| Optimized | 1 mL/min<br>Buffer: methanol: Acetonitrile (45:45:10, v/v) | 3.198 | 3551.15 | 1.38 | 153515 |
| Flow rate | 0.9 mL/min | 3.545 | 3494.29 | 1.41 | 177559 |
| | 1.1 mL/min | 2.885 | 3466.64 | 1.44 | 130464 |
| Mobile phase | Buffer: methanol: Acetonitrile (55: 35:10, v/v) | 5.159 | 3890.88 | 1.20 | 161067 |
| | Buffer: methanol: Acetonitrile (35:55:10, v/v) | 2.254 | 3173.07 | 1.49 | 164207 |

**LOD and LOQ:**

The LOD and LOQ of solifenacin were determined by using the signal to noise approach as defined in ICH guidelines. The concentration with signal to noise ratio of LOD and LOQ at S/N was 3 and 10, respectively. The results are given in Table 5 & Figure 6 & 7.

**Assay of Pharmaceutical Formulation:**

The proposed validated method was successfully applied to determine solifenacin in its tablet dosage form. The result obtained for solifenacin was comparable with the corresponding labeled amounts and they are given in Table 6.

**Stability Studies:**

Solifenacin resistance to various degradation routes is evaluated for the current project to understand its stability requirements better. Results are shown Table 11.

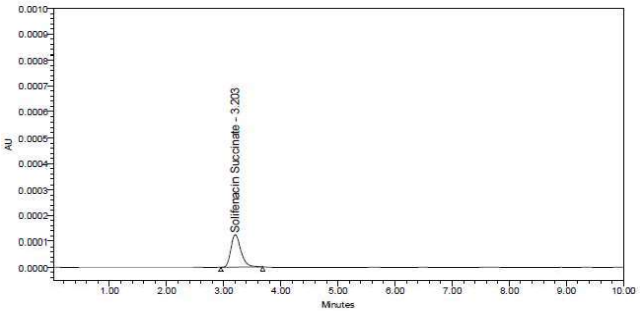


**Figure 6:** Chromatogram of LOD

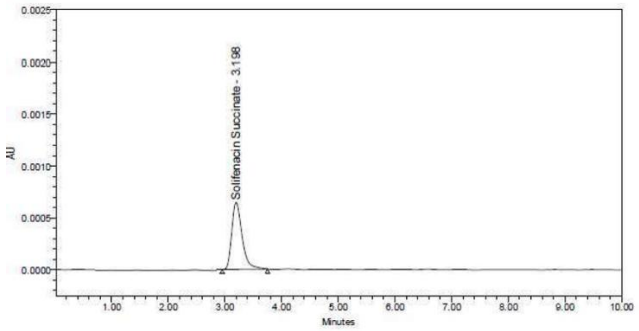


**Figure 7:** Chromatogram of LOQ

**Table 5:** Results of LOD & LOQ

| Parameter | (µg/mL) | S/N Ratio | Area |
|---|---|---|---|
| LOD (µg/mL) | 0.93 | 2.98 | 152603 |
| LOQ (µg/mL) | 3.07 | 10 | 163515 |

**Table 6:** Results of Assay

| Drug | Labelled claim | Test Conc. | Amount recovered (mg) | % Recovery |
|---|---|---|---|---|
| Solifenacin | 10mg | 60 | 10.04 | 100.4 |

**Table 11:** Results of stability studies

| Stress Conditions | Peak Area | % Degradation | % Recovery |
|---|---|---|---|
| Acidic / 0.1N HCl for 24hrs at room temperature | 139575 | 8.52 | 91.48 |
| Basic / 1N NaOH for 24hrs at room temperature | 136484 | 10.55 | 89.45 |
| Oxidative 3% v/v Hydrogen peroxide for 24 hrs at room temperature | 141187 | 7.47 | 92.53 |
| Thermal at 110 ° C for 24 hrs | 135599 | 11.13 | 88.87 |
| Photo: Sunlight for 24 hrs | 142982 | 6.29 | 93.71 |

## CONCLUSION

The present work refers to the fact that the most accurate, precise, and robust HPLC method was developed and validated for estimation of solifenacin in pharmaceutical dosage form in accordance with the ICH parameters. The method was validated and found to be simple, accurate, and precise. Percentage of recovery shows that the method is free from interference of the excipients used in the formulation. Therefore, the proposed method can be used for routine analysis of solifenacin in its dosage form.

**Source of Support:** The author(s) received no financial support for the research, authorship, and/or publication of this article

**Conflict of Interest:** The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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