Solifenacin Oral Suspension, Sustainability Case Study – BP 2025

Dissolution and Assay Scaled Method Information

The Dissolution and Assay methods for the Solifenacin Oral Suspension monograph published in the BP 2025 were assessed using geometric scaling of column dimensions and chromatographic parameters, with the intention of reducing solvent use and environmental impact. This work is complementary to section 3.3 of the Environmental sustainability information pack - British Pharmacopoeia.

Appendix III Chromatographic Separation Techniques (Ph. Eur. method 2.2.46) details the extent to which the various parameters of a chromatographic test may be adjusted without fundamentally modifying the pharmacopoeial analytical procedure. Users are advised to refer to this text when investigating scaled method approaches to determine whether full revalidation is needed.

We would be grateful for any feedback you have on the content of this additional information and interested to hear your own case studies. Please contact us by email at BPsustainability@mhra.gov.uk.

The purpose of the case study was to give an illustration of the solvent, energy and efficiency savings that can be obtained through scaling down column dimensions and chromatographic conditions without fundamentally modifying the pharmacopoeial analytical procedure. A full validation of the scaled method has not been carried out.

Case Study Selection Criteria

The Solifenacin Oral Suspension Dissolution and Assay method was identified as a candidate for scaling based on the following criteria:

- The LC method is isocratic
- The method is used for Assay, Dissolution and/or Uniformity of Content
- The original column dimensions are big enough to allow for scaling reductions
- The Assay and Related Substances methods in the monograph published in the BP 2025 are not harmonised
- The injection volume is less than 100 µL

Experimental Procedure

The viability of scaled conditions for the Solifenacin Oral Suspension Dissolution and Assay method was investigated by reducing the column dimensions and, by extension, the flow rate and total mobile phase consumption. A column was used with a smaller internal diameter (2.1 mm) than the one specified in the published monograph (4.6 mm).

A freely available online HPLC Method Transfer Calculator was used to provide a modified flow rate, injection volume and run time as per the allowed changes in Appendix III of the British Pharmacopoeia. The Sigma Aldrich tool was used for the purpose of this investigation, however many equivalent tools are available. After applying these changes, the flow rate was then increased by the maximum allowable amount (50%) as outlined in Appendix III, to further reduce the run time, giving the final method parameters listed below:

Table 1 Method Transfer Calculator Output, Shaded

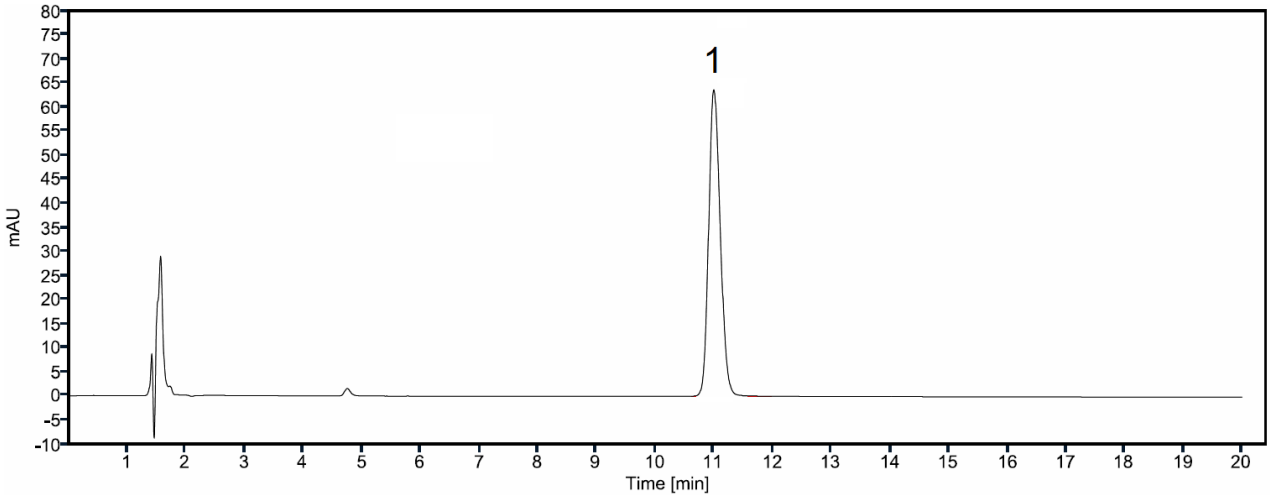
	Published method	**Scaled method**	**Scaled method with adjusted flow rate**
Column length (cm)	15	As per published method	
Column I.D. (mm)	4.6	2.1	2.1
Particle size (µm)	3.5	As per published method	
Flow rate (mL/min)	1.0	0.2	0.3
Injection volume (µL)	25	5	5
Pressure	149	149	221[1]

[1] The experimental value obtained was 152 bar, with the same instrument used throughout.

(bar)			
Run time (min)	20	20	13
Time saved per injection (min)		0	7
Solvent saved per injection (mL)		16 ~80% reduction	16 ~80% reduction

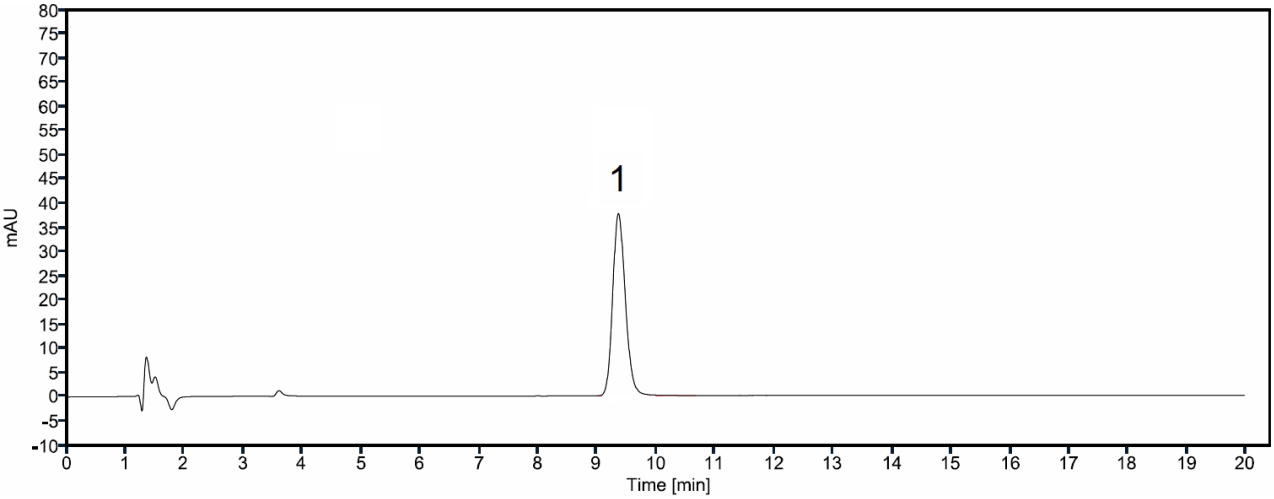
Results

A typical chromatogram for solution (2) from the Assay test for Solifenacin Oral Suspension as published in BP 2025.



Peak ID: 1: Solifenacin.

A typical chromatogram for solution (2) from the Assay test for Solifenacin Oral Suspension using scaled chromatographic conditions with an adjusted flow rate.



Peak ID: 1: Solifenacin.

Table 2 Published versus Scaled Chromatographic Conditions

	Published	**Scaled with adjusted flow rate**
Column	Waters XTerra MS C18 (15 cm x 4.6 mm, 3.5 µm)	Waters XTerra MS C18 (15 cm x 2.1 mm, 3.5 µm)
Method reference	BP 2025 monograph, Assay for Solifenacin Oral Suspension	
Buffer	0.05M ammonium dihydrogen orthophosphate adjusted to pH 2.4 with orthophosphoric acid	
Mobile phase	acetonitrile: buffer (3:7, v/v)	
Diluent (solution A)	acetonitrile: 0.1M hydrochloric acid (20:30, v/v)	
Flow rate	1.0 mL/min	0.3 mL/min
Column temp	40°C	
Autosampler temp	5°C	
Injection volume	25 µL	5 µL
Detection	210 nm	

Chromatograms are provided for information only as an aid to analysts and are intended as guidance.

A summary of the differences in the method parameters and results between the published monograph method and scaled conditions is given below:

Table 3 Summary of Results

Parameter	**Published**	**Scaled with adjusted flow rate**
Resolution between solifenacin and propyl 4-hydroxybenzoate (>1.5)	7.5	4.5
Retention time (min)	11	9
Peak asymmetry (0.8 - 1.8)	1.2	1.2
Theoretical plates	14849	9243
Linearity ($r^2 \geq 0.99$, 0 - 120% test solution concentration)	1.0	1.0
Injector repeatability (% RSD ≤ 1.0%, 6 injections of solution 2)	0.10	0.24

Scaling the method resulted in a reduction of mobile phase consumption of ~80%, and a reduction in run time of ~30% whilst maintaining acceptable chromatography.