Edition: BP 2025 (Ph. Eur. 11.6 update)

Solifenacin Oral Suspension

General Notices

Action and use

Muscarinic M_3 receptor antagonist; anticholinergic.

DEFINITION

Solifenacin Oral Suspension contains Solifenacin Succinate.

The oral suspension complies with the requirements stated under Oral Liquids and with the following requirements.

Content of solifenacin succinate, $C_{27}H_{32}N_2O_6$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Mix a volume of the oral suspension containing 20 mg of Solifenacin Succinate in 30 mL of a mixture of 2 volumes of *acetonitrile* and 3 volumes of 0.1M *hydrochloric acid*. Shake to disperse and centrifuge the mixture. To the supernatant add 5 mL of 5M *sodium hydroxide*. Extract with three 30-mL quantities of *dichloromethane*, shake the combined extracts with *anhydrous sodium sulfate*, filter and evaporate the filtrate to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the reference spectrum of solifenacin *(RS 508)*.

TESTS

Dissolution

Complies with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

Carry out the method for liquid chromatography, Appendix III D, using the following freshly prepared solutions.

(1) Shake the container containing the oral suspension being examined for 30 seconds and accurately place a volume equivalent to one dose into each dissolution vessel. After 15 minutes withdraw a sample of the medium and filter (0.45-µm PTFE is suitable). Dilute the filtrate, if necessary, to produce a solution containing the equivalent of 0.00056% w/v of Solifenacin Succinate.
(2) 0.00056% w/v of *solifenacin succinate BPCRS* in 0.1M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl amorphous organosilica polymer for chromatography* (3.5 µm) (Waters XTerra MS C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use an autosampler temperature of 5°.
(f) Use a detection wavelength of 210 nm.
(g) Inject 25 µL of each solution.

MOBILE PHASE

30 volumes of *acetonitrile R1* and 70 volumes of a 0.05M *ammonium dihydrogen orthophosphate* solution previously adjusted to pH 2.4 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions the retention time of the solifenacin is about 11 minutes.

DETERMINATION OF CONTENT

Calculate the total content of solifenacin succinate, $C_{27}H_{32}N_2O_6$, in the medium from the chromatograms obtained and using the declared content of $C_{27}H_{32}N_2O_6$ in *solifenacin succinate BPCRS*.

LIMITS

The amount of solifenacin succinate released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following freshly prepared solutions.

Solution A 20 volumes of *acetonitrile R1* and 30 volumes of 0.1M *hydrochloric acid*.

(1) To a quantity of the oral suspension containing 6 mg of Solifenacin Succinate, add 30 mL of solution A and shake. Dilute to 50 mL with solution A, centrifuge and use the supernatant liquid.
(2) Dilute 1 volume of solution (1) to 100 volumes with solution A. Further dilute 1 volume of this solution to 5 volumes with solution A.
(3) To 10 mg of *solifenacin succinate BPCRS* add 1 mL of *hydrogen peroxide (30%)*, 5 mL of 0.1M *sodium hydroxide*, 10 mL of *water* and 5 mL of *acetonitrile*. Stir uncovered for 10 minutes (generation of impurity I). Add 1 volume of this solution to 2.5 volumes of solution (1) and dilute to 25 volumes with solution A.
(4) 0.1% w/v of *solifenacin succinate impurity standard BPCRS* (containing impurities A and 1) in solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl amorphous organosilica polymer for chromatography* (3.5 µm) (Waters XTerra MS C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use an autosampler temperature of 5°.
(f) Use a detection wavelength of 210 nm.
(g) Inject 15 µL of each solution.

MOBILE PHASE

Mobile phase A 20 volumes of *acetonitrile R1* and 80 volumes of a 0.05M *ammonium dihydrogen orthophosphate* solution previously adjusted to pH 2.4 with *orthophosphoric acid*.

Mobile phase B *Acetonitrile R1*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-25	95-90	5-10	linear gradient

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
25-40	90-75	10-25	linear gradient
40-41	75-50	25-50	linear gradient
41-65	50	50	isocratic
65-66	50-95	50-5	linear gradient
66-75	95	5	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to solifenacin and impurity I is at least 2.0.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of solifenacin succinate in solution (2).

For the reporting threshold, use the concentration of solifenacin succinate in solution (2).

For peak identification, use solutions (3) and (4).

Solifenacin succinate retention time: about 26 minutes.

Relative retention: impurity A, about 0.2; impurity 1, about 0.5; impurity I, about 1.1.

Correction factor: impurity A, multiply by 0.7.

LIMITS

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 0.5%;

— reporting threshold: 0.1%.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions freshly prepared in solution A.

(1) To a weighed volume of the oral suspension containing 6 mg of Solifenacin Succinate, add 30 mL, shake to disperse and dilute to produce 50 mL. Centrifuge and dilute 1 volume of the supernatant liquid to 10 volumes.
(2) 0.0012% w/v of *solifenacin succinate BPCRS*.
(3) 0.0012% w/v of *solifenacin succinate BPCRS* and 0.00024% w/v of *propyl 4-hydroxybenzoate*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to solifenacin and propyl 4-hydroxybenzoate is at least 1.5.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_{27}H_{32}N_2O_6$, weight in volume, using the declared content of $C_{27}H_{32}N_2O_6$ in *solifenacin succinate BPCRS*.

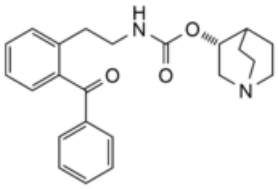
Supporting information for Dissolution and Assay

In developing the Dissolution and Assay methods, geometric scaling of column dimensions and chromatographic parameters to the validated method conditions have been explored in order to reduce the solvent needed and the

environmental impact. The "More resources" tab, available in the BP online monograph, provides additional information on the investigations carried out. Visit https://www.pharmacopoeia.com/guidance/environmentalhub for more information.

IMPURITIES

The impurities limited by the requirements of this monograph include impurity I listed under Solifenacin Succinate and:



1. (+)-(*R*)-quinuclidin-3-yl [2-(2-benzoylphenyl)ethyl]carbamate