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

Dapsone Tablets

General Notices

Action and use

Folic acid synthesis inhibitor; treatment of leprosy.

DEFINITION

Dapsone Tablets contain Dapsone.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of dapsone, $C_{12}H_{12}N_2O_2S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 0.1 g of Dapsone with 20 mL of *acetone*, filter and evaporate the filtrate to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of dapsone *(RS 084)*.

TESTS

Dissolution

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

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes, withdraw a sample of the medium and filter. Dilute with the dissolution medium, if necessary, to produce a solution expected to contain 0.0056% w/v of Dapsone.
(2) Dilute 1 volume of a solution containing 2.22% w/v of *dapsone BPCRS* in *acetonitrile* to 20 volumes with the dissolution medium, dilute 1 volume of this solution to 20 volumes with the dissolution medium.
(3) 0.0125% w/v each of *dapsone BPCRS* and *4-(4-aminobenzene-1-sulfonyl)phenol* (impurity A).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography with embedded polar groups* (3.5 µm) (Symmetry Shield RP18 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 35°.
(e) Use a detection wavelength of 230 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

25 volumes of *acetonitrile* and 75 volumes of 0.05M *potassium dihydrogen orthophosphate* previously adjusted to pH 3.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the retention time of dapsone is about 7 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to dapsone and impurity A is at least 1.5.

DETERMINATION OF CONTENT

Calculate the total content of dapsone, $C_{12}H_{12}N_2O_2S$, in the medium from the chromatograms obtained and using the declared content of $C_{12}H_{12}N_2O_2S$ in *dapsone BPCRS*.

LIMITS

The amount of dapsone 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 solutions prepared in solution A.

Solution A Equal volumes of *acetonitrile* and *water*.

(1) Shake a quantity of powdered tablets containing 40 mg of Dapsone in 30 mL. Dilute to 100 mL and filter (a 0.45-µm nylon syringe filter is suitable).
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) Dilute 1 volume of a solution containing 0.004% w/v each of *dapsone BPCRS*, *4-(4-aminobenzene-1-sulfonyl)phenol* (impurity A), *4-(benzenesulfonyl)aniline* (impurity B) and *4,4'-[oxybis[(4,1-phenylene)sulfonyl]]dianiline* (impurity C) to 10 volumes.
(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Discovery 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 an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A *water*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-10	75	25	isocratic
10-20	75→50	25→50	linear gradient
20-35	50	50	isocratic
35-36	50→75	50→25	linear gradient

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
36-50	75	25	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between the peaks due to dapsone and impurity A is at least 2.0;

in the chromatogram obtained with solution (4), the *signal-to-noise ratio* of the peak due to dapsone is at least 30.

CALCULATION OF IMPURITIES

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

For the reporting threshold, use the concentration of dapsone in solution (4).

For peak identification, use solution (3).

Dapsone retention time: about 7 minutes.

Relative retention: impurity A, about 1.1; impurity B, about 2.5 and impurity C, about 3.5.

Correction factors: impurity A, multiply by 1.9; impurity B, multiply by 2.7 and impurity C, multiply by 1.7.

LIMITS

— impurities A and B: not more than 0.4% of each;

— impurity C: not more than 0.3%;

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

— total impurities: not more than 2.0%;

— reporting threshold: 0.1%.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in *acetonitrile*.

(1) Mix, with the aid of ultrasound and frequent swirling, a quantity of powdered tablets containing 50 mg of Dapsone with 70 mL. Dilute to produce 100 mL and filter (a 0.45-µm nylon syringe filter is suitable).
(2) 0.05% w/v of *dapsone BPCRS*.
(3) 0.05% w/v each of *dapsone BPCRS* and *4-(4-aminobenzene-1-sulfonyl)phenol* (impurity A).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used with an injection volume of 5 µL.

SYSTEM SUITABILITY

The Assay is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to dapsone and impurity A is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{12}H_{12}N_2O_2S$ in the tablets from the chromatograms obtained and using the declared content of $C_{12}H_{12}N_2O_2S$ in *dapsone BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B and C listed under Dapsone.