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Penicillamine Capsules

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DEFINITION

Penicillamine Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of penicillamine ($C_5H_{11}NO_2S$).

IDENTIFICATION

• A. THIN-LAYER CHROMATOGRAPHY

Standard solution: 100 mg of [USP Penicillamine RS](#) in 10 mL of [methanol](#). Add 2 drops of [3 N hydrochloric acid](#) and mix.

Sample solution: Transfer a portion of Capsule contents, containing nominally about 100 mg of penicillamine, to a 10-mL volumetric flask, and dilute with [methanol](#) to volume. Add 2 drops of [3 N hydrochloric acid](#), mix, and filter. Use the filtrate.

Chromatographic system

(See [Chromatography \(621\), General Procedures, Thin-Layer Chromatography](#).)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture, heated at 105° for 30 min, and allowed to cool before use

Application volume: 10 µL

Developing solvent system: [Butyl alcohol](#), [glacial acetic acid](#), and [water](#) (8:2:2)

Spray reagent: 3-mg/mL solution of [ninhydrin](#) in [dehydrated alcohol](#)

Analysis

Samples: *Standard solution* and *Sample solution*

Separately apply the *Sample solution* and the *Standard solution* to the plate. Develop the chromatogram in the *Developing solvent system* until the solvent front has moved three-fourths the length of the plate. Remove the plate, mark the solvent front, allow the solvent to evaporate, and place the plate in an atmosphere of iodine vapors. After a few minutes, spray the plate with *Spray reagent*, heat it at 105° for 10 min, allow it to cool, and examine it.

Acceptance criteria: The R_F values, colors, and intensities of the principal spots from the *Sample solution* correspond to those from the *Standard solution*.

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

• PROCEDURE

Mobile phase: 6.9 g/L of [monobasic sodium phosphate](#) and 0.2 g/L of [sodium 1-hexanesulfonate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 3.0 ± 0.1 .

Diluent: 1.0 g/L of [edetate disodium](#) in [water](#)

System suitability solution: 1 mg/mL of [USP Penicillamine RS](#) and 0.1 mg/mL of [USP Penicillamine Disulfide RS](#) in *Diluent*

Standard solution: 1.25 mg/mL of [USP Penicillamine RS](#) in *Diluent*

Sample solution: Nominally equivalent to 1.25 mg/mL of penicillamine in *Diluent* prepared as follows. Transfer the contents of Capsules (NLT 10) to a suitable volumetric flask. Add the empty Capsule shells to the flask, and add sufficient *Diluent* to the flask to fill it to three-fourths of its capacity. Shake for 1 min, and allow the mixture to stand for 90 min. Dilute with *Diluent* to volume. Pass a portion of this solution through a suitable filter of 1-µm or finer pore size, and use the clear filtrate.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 3.9-mm × 30-cm; 10-µm packing [L1](#)

Flow rate: 1.6 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for penicillamine and penicillamine disulfide are 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between penicillamine and penicillamine disulfide, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of penicillamine ($C_5H_{11}NO_2S$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of penicillamine from the *Sample solution*

r_S = peak response of penicillamine from the *Standard solution*

C_S = concentration of [USP Penicillamine RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of penicillamine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

▲ Test 1 ▲ (RB 1-Aug-2023)

Medium: 0.1 N [hydrochloric acid](#); 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Procedure for a pooled sample

Dilute hydrochloric acid: Dilute 37 mL of [hydrochloric acid](#) with [water](#) to 1 L.

Dilute sulfuric acid: Dilute 1 mL of [sulfuric acid](#) with [water](#) to 50 mL.

Ammonium sulfamate reagent: 2.5 mg/mL of [ammonium sulfamate](#) in *Dilute hydrochloric acid*

N-(1-Naphthyl)ethylenediamine dihydrochloride reagent: 1 mg/mL of [N-\(1-naphthyl\)ethylenediamine dihydrochloride](#) in *Dilute hydrochloric acid*

Sulfanilamide–mercuric chloride reagent: 1 mg/mL of [sulfanilamide](#) and 1 mg/mL of [mercuric chloride](#) in *Dilute hydrochloric acid*

Sodium nitrite reagent: 2 mg/mL of [sodium nitrite](#) in *Dilute sulfuric acid*. Prepare fresh.

Standard solution: 250 µg/mL of [USP Penicillamine RS](#) in 0.1 N [hydrochloric acid](#)

Sample solution: Withdraw a portion of the solution under test, containing nominally about 278 µg of penicillamine, and pass through a suitable filter.

Blank: Volume of 0.1 N hydrochloric acid equivalent to a volume of the *Sample solution*

Instrumental conditions

Mode: UV-Vis

Analytical wavelength: 540 nm

Cell: 1 cm

Analysis: Pipet the *Sample solution* into a 100-mL volumetric flask. Into a similar flask, transfer the reagent *Blank*, and into a third 100-mL volumetric flask, pipet 1 mL of *Standard solution*. Treat each flask as follows. Add by pipet 3 mL of *Sodium nitrite reagent*, and mix by swirling occasionally. After 5 min, add 10 mL of *Ammonium sulfamate reagent*, swirl, and allow to stand for an additional 5 min. Add 5 mL of *Sulfanilamide–mercuric chloride reagent*, swirl, and immediately add 10 mL of *N-(1-Naphthyl)ethylenediamine dihydrochloride reagent*. Dilute with water to volume and mix. Determine the absorbances of both solutions against the *Blank*.

Calculate the percentage of the labeled amount of penicillamine ($C_5H_{11}NO_2S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*