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

Penicillamine Tablets

General Notices

Action and use

Disease-modifying antirheumatic drug; chelating agent; treatment of Wilson's disease; heavy metal poisoning; cystinuria.

DEFINITION

Penicillamine Tablets contain Penicillamine. They are coated.

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

Content of penicillamine, $C_5H_{11}NO_2S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Shake a quantity of the powdered tablets containing 20 mg of Penicillamine with 4 mL of *water* and filter. Add to the filtrate 2 mL of *phosphotungstic acid solution* and allow to stand for a few minutes. A deep blue colour is produced.
B. Dissolve a quantity of the powdered tablets containing 10 mg of Penicillamine in 5 mL of *water* and add 0.3 mL of 5M *sodium hydroxide* and 20 mg of *ninhydrin*. An intense blue or violet-blue colour is produced immediately.

TESTS

Mercuric salts

Not more than 10 ppm, calculated with reference to the content of penicillamine, when determined by the following method. Disperse a quantity of the powdered tablets containing 1 g of Penicillamine in 10 mL of *water* in a stoppered flask, add 0.2 mL of 9M *perchloric acid* and swirl to dissolve. Add 1 mL of *ammonium pyrrolidinedithiocarbamate solution*, mix, add 2 mL of *4-methylpentan-2-one*, shake well for 1 minute and add sufficient *water* to produce 25 mL. Determine by *atomic absorption spectrophotometry*, Appendix II D, introducing the methylpentanone layer into the flame, measuring at 254 nm and using *4-methylpentan-2-one* in place of *water*. Use *mercury standard solution (10 ppm Hg)* for the standard solutions, adjusted to contain the same concentrations of 9M perchloric acid, ammonium pyrrolidinedithiocarbamate solution and 4-methylpentan-2-one as the solution being examined.

Penicillamine disulfide

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

(1) Shake a quantity of the powdered tablets containing 40 mg of Penicillamine with 10 mL of the mobile phase, filter and use the filtrate.
(2) 0.004% w/v of *penicillamine disulfide EPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Lichrospher 5 C8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

0.01% w/v of *disodium edetate* and 0.2% w/v of *methane sulfonic acid*.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to penicillamine disulfide is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

ASSAY

Weigh and powder 20 tablets. Dissolve a quantity of the powder containing 0.1 g of Penicillamine as completely as possible in 50 mL of *water* and filter. Add to the filtrate 5 mL of 1M *sodium hydroxide* and 0.2 mL of a 0.1% w/v solution of *dithizone* in *ethanol* (*96%*) and titrate with *0.02M mercury(II) nitrate VS*. Each mL of *0.02M mercury(II) nitrate VS* is equivalent to 5.968 mg of $C_5H_{11}NO_2S$.