Ampicillin (Ampicillinum)

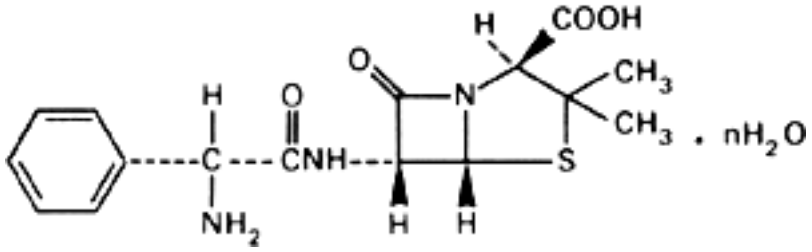
Ampicillin anhydrous

Ampicillin trihydrate

Molecular formula. $C_{16}H_{19}N_3O_4S$ (anhydrous); $C_{16}H_{19}N_3O_4S,3H_2O$ (trihydrate).

Relative molecular mass. 349.4 (anhydrous); 403.5 (trihydrate).

Graphic formula.



n = 0 (anhydrous)

n = 3 (trihydrate)

Chemical name.

(2*S*,5*R*,6*R*)-6-[(*R*)-2-Amino-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid; [2*S*-[2*α*,5*α*,6*β* (*S**)]]-6-[(aminophenylacetyl)amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0]-heptane-2-carboxylic acid; CAS Reg. No. 69-53-4 (anhydrous).

(2*S*,5*R*,6*R*)-6-[(*R*)-2-Amino-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate; [2*S*-[2*α*,5*α*,6*β* (*S**)]]-6-[(aminophenylacetyl)amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate; CAS Reg. No. 7177-48-2 (trihydrate).

Description. A white or almost white, crystalline powder; odourless or almost odourless.

Solubility. Slightly soluble in water; practically insoluble in ethanol (~750 g/l) TS and ether R.

Category. Antibiotic.

Storage. Ampicillin should be kept in a tightly closed container, protected from light.

Labelling. The designation on the container of Ampicillin should state whether the substance is in the anhydrous form or is the trihydrate.

Additional information. Even in the absence of light, Ampicillin is gradually degraded on exposure to a humid atmosphere, the decomposition being faster at higher temperatures.

Requirements

Definition. Ampicillin contains not less than 95.0% and not more than 102.0% of $C_{16}H_{19}N_3O_4S$, calculated with reference to the anhydrous substance.

Identity tests

• Either test A or test B may be applied.

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. For the anhydrous form the infrared absorption spectrum is concordant with the spectrum obtained from ampicillin RS or with the *reference spectrum* of ampicillin.

For the trihydrate the infrared absorption spectrum is concordant with the spectrum obtained from ampicillin trihydrate RS or with the *reference spectrum* of ampicillin trihydrate.

B. To 2 mg in a test-tube add 1 drop of water followed by 2 mL of sulfuric acid (~1760 g/l) TS and mix; the solution is colourless. Immerse the test-tube for 1 minute in a water-bath; the solution remains colourless. Place 2 mg in a second test-tube, add 1 drop of water and 2 mL of formaldehyde/sulfuric acid TS and mix; the solution is colourless to slightly pink. Immerse the test-tube for 1 minute in a water-bath; an orange-yellow colour is produced.

Specific optical rotation. Use a 2.5 mg/mL solution and calculate with reference to the anhydrous substance: $[\alpha]_D^{20\,°C}$ = +280° to +305°.

Water. Determine as described under 2.8 Determination of water by the Karl Fischer method, Method A.

For the anhydrous form use about 0.8 g of the substance; the water content is not more than 15 mg/g.

For the trihydrate use about 0.1 g of the substance; the water content is not less than 120 mg/g and not more than 150 mg/g.

pH value. pH of a 2.5 mg/mL solution, 3.5-6.0.

Assay. Dissolve about 0.12 g, accurately weighed, in sufficient water to produce 500 mL. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, add 10 mL of buffer borate, pH 9.0, TS, 1 mL of acetic anhydride/dioxan TS, allow to stand for 5 minutes at room temperature and dilute to volume with water.

Transfer two 2.0-mL aliquots of this solution into separate stoppered tubes. To one tube add 10.0 mL of imidazole/mercuric chloride TS, mix, stopper the tube, and place in a water-bath at 60°C for exactly 25 minutes. Cool the tube rapidly to 20°C (solution A).

To the second tube add 10.0 mL of water and mix (solution B).

Without delay, measure the absorbance of a 1-cm layer at the maximum at about 325 nm, against a solvent cell containing a mixture of 2.0 mL of water and 10.0 mL of imidazole/mercuric chloride TS for solution A and water for solution B.

From the difference between the absorbance of solution A and that of solution B, calculate the amount of $C_{16}H_{19}N_3O_4S$ in the substance being tested by comparison with ampicillin RS similarly and concurrently examined. In an adequate calibrated spectrophotometer the absorbance of the reference solution should be 0.29 ± 0.02.