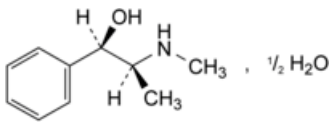
Edition: BP 2025 (Ph. Eur. 11.6 update)

Ephedrine Hemihydrate

General Notices

(Ph. Eur. monograph 0489)

NOTE: *The name Ephedrine was formerly used in the United Kingdom.*



$C_{10}H_{15}NO,½H_2O$ 174.2 *50906-05-3*

Action and use

Adrenoceptor agonist.

Ph Eur

DEFINITION

Ephedrine hemihydrate contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of (1*R*,2*S*)-2-(methylamino)-1-phenylpropan-1-ol, calculated with reference to the anhydrous substance.

CHARACTERS

A white or almost white, crystalline powder or colourless crystals, soluble in water, very soluble in ethanol (96 per cent).

It melts at about 42 °C, determined without previous drying.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D, E.

A. Specific optical rotation (see Tests).
B. Examine by infrared absorption spectrophotometry (2.2.24), comparing with the spectrum obtained with the base isolated from *ephedrine hydrochloride CRS*. Examine the substances in discs prepared as follows: dissolve 40 mg of the substance to be examined in 1 mL of *water R*, add 1 mL of *dilute sodium hydroxide solution R* and 4 mL of *chloroform R* and shake; dry the organic layer over 0.2 g of *anhydrous sodium sulfate R*; prepare a blank disc using about 0.3 g of *potassium bromide R*; apply dropwise to the disc 0.1 mL of the organic layer, allowing the solvent to evaporate between applications; dry the disc at 50 °C for 2 min. Repeat the operations using 50 mg of *ephedrine hydrochloride CRS*.
C. Examine the chromatograms obtained in the test for related substances. The principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained wit reference solution (a).

D. Dissolve about 10 mg in 1 mL of *water R*. Add 0.2 mL of *strong sodium hydroxide solution R* and 0.2 mL of *copper sulfate solution R*. A violet colour is produced. Add 2 mL of *ether R* and shake. The ether layer is purple and the aqueous layer blue.
E. Water (see Tests).

TESTS

Appearance of solution

Dissolve 0.25 g in *water R* and dilute to 10 mL with the same solvent. The solution is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Specific optical rotation (*2.2.7*)

Dissolve 2.25 g in 15 mL of *dilute hydrochloric acid R* and dilute to 50.0 mL with *water R*. The specific optical rotation is -4 to -43, calculated with reference to the anhydrous substance.

Related substances

Examine by thin-layer chromatography (*2.2.27*), using *silica gel G R* as the coating substance.

Test solution (a) Dissolve 0.2 g of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent.

Test solution (b) Dilute 1 mL of test solution (a) to 10 mL with *methanol R*.

Reference solution (a) Dissolve 25 mg of *ephedrine hydrochloride CRS* in *methanol R* and dilute to 10 mL with the same solvent.

Reference solution (b) Dilute 1.0 mL of test solution (a) to 200 mL with *methanol R*.

Apply separately to the plate 10 µL of each solution. Develop over a path of 15 cm using a mixture of 5 volumes of *chloroform R*, 15 volumes of *concentrated ammonia R* and 80 volumes of *2-propanol R*. Allow the plate to dry in air and spray with *ninhydrin solution R*. Heat at 110 °C for 5 min. Any spot in the chromatogram obtained with test solution (a), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.5 per cent). Disregard any spot of lighter colour than the background.

Chlorides

Dissolve 0.18 g in 10 mL of *water R*. Add 5 mL of *dilute nitric acid R* and 0.5 mL of *silver nitrate solution R1*. Allow to stand for 2 min, protected from bright light. Any opalescence in the solution is not more intense than that in a standard prepared at the same time and in the same manner using 10 mL of *chloride standard solution (5 ppm Cl) R*, 5 mL of *dilute nitric acid R* and 0.5 mL of *silver nitrate solution R1* (280 ppm).

Water (*2.5.12*)

4.5 per cent to 5.5 per cent, determined on 0.300 g by the semi-micro determination of water.

Sulfated ash (*2.4.14*)

Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 5 mL of *alcohol R* and add 20.0 mL of *0.1 M hydrochloric acid*. Using 0.05 mL of *methyl red solution R* as indicator, titrate with *0.1 M sodium hydroxide* until a yellow colour is obtained.

1 mL of *0.1 M hydrochloric acid* is equivalent to 16.52 mg of $C_{10}H_{15}NO$.

STORAGE

Store protected from light.