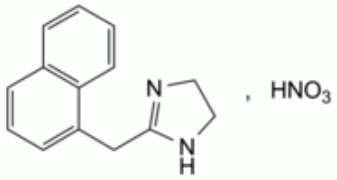
Edition: BP 2025 (Ph. Eur. 11.6 update)

Naphazoline Nitrate

General Notices

(Ph. Eur. monograph 0147)



$C_{14}H_{15}N_3O_3$ 273.3 *5144-52-5*

Action and use

Alpha-adrenoceptor agonist.

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DEFINITION

2-(Naphthalen-1-ylmethyl)-4,5-dihydro-1*H*-imidazole nitrate.

Content

99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Sparingly soluble in water, soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: C.

Second identification: A, B, D.

A. Melting point (2.2.14): 167 °C to 170 °C.
B. Ultraviolet and visible absorption spectrophotometry (2.2.25).

Test solution Dissolve 50.0 mg in *0.01 M hydrochloric acid* and dilute to 250.0 mL with the same acid. Dilute 25.0 mL of the solution to 100.0 mL with *0.01 M hydrochloric acid*.

Spectral range 230-350 nm.

Absorption maximum At 270 nm, 280 nm, 287 nm and 291 nm.

Absorbance ratio:

— A_{270}/A_{280} = 0.82 to 0.86,

— A_{291}/A_{280} = 0.65 to 0.69.

C. Infrared absorption spectrophotometry (2.2.24).

Comparison *naphazoline nitrate CRS*.

D. Dissolve 45 mg of the substance to be examined in 2 mL of *water R*. Add 1 mL of *sulfuric acid R*. Shake carefully and allow to cool. Add 1 mL of *ferrous sulfate solution R2* dropwise along the walls of the container. At the junction of the 2 liquids, a brown colour develops.

TESTS

Solution S

Dissolve 0.5 g in *carbon dioxide-free water R*, warming gently, and dilute to 50 mL with the same solvent.

Appearance of solution

Solution S is clear (2.2.1) and colourless (*2.2.2, Method II*).

pH (2.2.3)

5.0 to 6.5 for solution S.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 50.0 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a) Dissolve 5 mg of *1-naphthylacetic acid R* in the mobile phase, add 5 mL of the test solution and dilute to 100 mL with the mobile phase.

Reference solution (b) Dissolve 5.0 mg of *naphazoline impurity A CRS* in the mobile phase and dilute to 100.0 mL with the same solvent. Dilute 5.0 mL of this solution to 100.0 mL with the mobile phase.

Reference solution (c) Dilute 2.0 mL of the test solution to 10.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 100.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.0 mm,

— *stationary phase*: *base-deactivated end-capped octylsilyl silica gel for chromatography R* (4 µm) with a pore size of 6 nm.

Mobile phase Dissolve 1.1 g of *sodium octanesulfonate R* in a mixture of 5 mL of *glacial acetic acid R*, 300 mL of *acetonitrile R* and 700 mL of *water R*.

Flow rate 1 mL/min.

Detection Spectrophotometer at 280 nm.

Injection 20 µL.

Run time 3 times the retention time of naphazoline.

Relative retention With reference to naphazoline (retention time = about 14 min): impurity A = about 0.76; impurity D = about 1.24; impurity B = about 1.27; impurity C = about 2.8.

System suitability Reference solution (a):

— *resolution*: minimum 5.0 between the peaks due to naphazoline and impurity B.

Limits:

— *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent),

— *unspecified impurities*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.10 per cent),

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (1.0 per cent),

— *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.05 per cent); disregard the peak due to the nitrate ion.

Chlorides (*2.4.4*)

Maximum 330 ppm, determined on solution S.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 30 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 27.33 mg of $C_{14}H_{15}N_3O_3$.

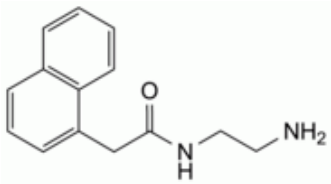
STORAGE

Protected from light.

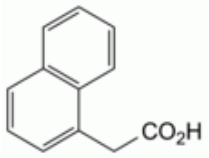
IMPURITIES

Specified impurities A.

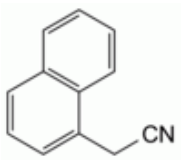
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) B, C, D.



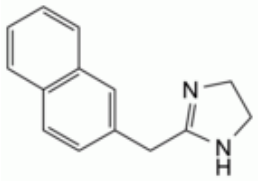
A. *N*-(2-aminoethyl)-2-(naphthalen-1-yl)acetamide (naphthylacetylethylenediamine),



B. (naphthalen-1-yl)acetic acid (1-naphthylacetic acid),



C. (naphthalen-1-yl)acetonitrile (1-naphthylacetonitrile),



D. 2-(naphthalen-2-ylmethyl)-4,5-dihydro-1*H*-imidazole (β-naphazoline).

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