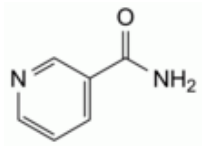
Edition: BP 2025 (Ph. Eur. 11.6 update)

Nicotinamide

General Notices

(Ph. Eur. monograph 0047)



$C_6H_6N_2O$ 122.1 *98-92-0*

Action and use

Component of vitamin B.

Preparations

Nicotinamide Tablets

Vitamins B and C Injection

Ph Eur

DEFINITION

Pyridine-3-carboxamide.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder or colourless crystals.

Solubility

Freely soluble in water and in anhydrous ethanol, slightly soluble in methylene chloride.

IDENTIFICATION

First identification: B.

Second identification: A, C.

A. Melting point (2.2.14): 128 °C to 131 °C.
B. Infrared absorption spectrophotometry (2.2.24).

Comparison nicotinamide CRS.

C. Thin-layer chromatography (2.2.27).

Test solution Dissolve 5 mg of the substance to be examined in a mixture of equal volumes of ethanol (96 per cent) R and water R and dilute to 5.0 mL with the same mixture of solvents.

Reference solution Dissolve 5 mg of nicotinamide CRS in a mixture of equal volumes of ethanol (96 per cent) R and water R and dilute to 5.0 mL with the same mixture of solvents.

Plate TLC silica gel F_{254} plate R.

Mobile phase water R, ethanol (96 per cent) R, methylene chloride R (4:45:48 *V/V/V*).

Application 5 µL.

Development Over 2/3 of the plate.

Drying In air.

Detection Examine in ultraviolet light at 254 nm.

Results The principal spot in the chromatogram obtained with the test solution is similar in position and size to the spot in the chromatogram obtained with the reference solution.

TESTS

Solution S

Dissolve 2.5 g in carbon dioxide-free water R and dilute to 50 mL with the same solvent.

Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution BY_7 (2.2.2, Method II).

pH (2.2.3)

6.0 to 7.5 for solution S.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 0.150 g of the substance to be examined in mobile phase A and dilute to 150.0 mL with mobile phase A.

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

Reference solution (b) Dissolve 5 mg of *isonicotinamide R* (impurity D) in the test solution and dilute to 100.0 mL with the test solution. Dilute 1.0 mL of this solution to 25.0 mL with the test solution.

Column:

— *size*: *l* = 0.15 m, Ø = 4.6 mm;

— *stationary phase*: *base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (3 µm).

Mobile phase:

— *mobile phase A*: mix 5.0 mL of *dilute acetic acid R* and 900 mL of *water for chromatography R*, then add 30 mL of *dilute ammonia R3* and 15 mL of *acetonitrile R*; dilute to 1 L with *water for chromatography R*;

— *mobile phase B*: *acetonitrile R*, mobile phase A (50:50 *V/V*);

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	98	2
2 - 16	98 → 0	2 → 100

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 264 nm.

Injection 20 µL.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peak due to impurity D.

Relative retention With reference to nicotinamide (retention time = about 7 min): impurity D = about 0.9.

System suitability Reference solution (b):

— *resolution*: minimum 2.0 between the peaks due to impurity D and nicotinamide.

Calculation of percentage contents:

— for each impurity, use the concentration of nicotinamide in reference solution (a).

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 0.05 per cent.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* for 18 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

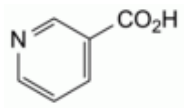
ASSAY

Dissolve 0.100 g in 50 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

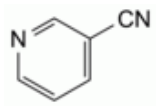
1 mL of *0.1 M perchloric acid* is equivalent to 12.21 mg of $C_6H_6N_2O$.

IMPURITIES

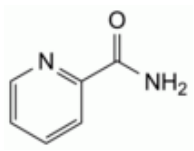
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) A, B, C, D, E.



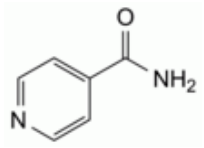
A. pyridine-3-carboxylic acid (nicotinic acid),



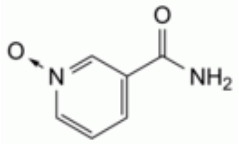
B. pyridine-3-carbonitrile,



C. pyridine-2-carboxamide (picolinamide),



D. pyridine-4-carboxamide (isonicotinamide),



E. pyridine-3-carboxamide 1-oxide (nicotinamide *N*-oxide).

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