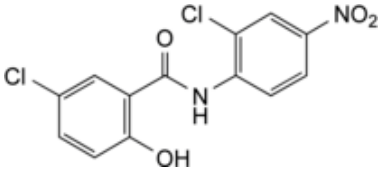
Edition: BP 2025 (Ph. Eur. 11.6 update)

Niclosamide

General Notices

Anhydrous Niclosamide

(Ph. Eur. monograph 0679)



$C_{13}H_8Cl_2N_2O_4$ 327.1 *50-65-7*

Action and use

Anthelminthic.

Preparation

Niclosamide Tablets

Ph Eur

DEFINITION

5-Chloro-*N*-(2-chloro-4-nitrophenyl)-2-hydroxybenzamide.

Content

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

CHARACTERS

Appearance

Yellowish-white or yellowish, fine crystals.

Solubility

Practically insoluble in water, sparingly soluble in acetone, slightly soluble in anhydrous ethanol.

IDENTIFICATION

First identification: B, E.

Second identification: A, C, D, E.

A. Melting point (2.2.14): 227 °C to 232 °C.
B. Infrared absorption spectrophotometry (2.2.24).

Preparation Discs prepared using about 0.5 mg of substance and 0.3 g of *potassium bromide R*.

Comparison *anhydrous niclosamide CRS*.

C. To 50 mg add 5 mL of *1 M hydrochloric acid* and 0.1 g of *zinc powder R*, heat in a water-bath for 10 min, cool and filter. To the filtrate add 1 mL of a 5 g/L solution of *sodium nitrite R* and allow to stand for 3 min; add 2 mL of a 20 g/L solution of *ammonium sulfamate R*, shake, allow to stand for 3 min and add 2 mL of a 5 g/L solution of *naphthylethylenediamine dihydrochloride R*. A violet colour is produced.
D. Heat the substance on a copper wire in a non-luminous flame. The flame becomes green.
E. Loss on drying (see Tests).

TESTS

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 50 mg of the substance to be examined in *methanol R*, heating gently, cool and dilute to 50.0 mL with the same solvent.

Reference solution Dilute 1.0 mL of the test solution to 100.0 mL with *acetonitrile R*. Dilute 1.0 mL of this solution to 20.0 mL with *acetonitrile R*.

Column:

— *size*: *l* = 0.125 m, Ø = 4 mm;

— *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase Mixture of equal volumes of *acetonitrile R* and a solution containing 2 g/L of *potassium dihydrogen phosphate R*, 1 g/L of *disodium hydrogen phosphate dodecahydrate R* and 2 g/L of *tetrabutylammonium hydrogen sulfate R*.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 20 µL.

Run time Twice the retention time of niclosamide.

Limits:

— *total*: not more than 4 times the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent);

— *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with the reference solution (0.005 per cent).

5-Chlorosalicylic acid

Maximum 60 ppm.

Test solution To 1.0 g add 15 mL of *water R*, boil for 2 min, cool, filter through a membrane filter (nominal pore size 0.45 µm), wash the filter and dilute the combined filtrate and washings to 20.0 mL with *water R*.

Reference solution Dissolve 30 mg of *5-chlorosalicylic acid R* in 20 mL of *methanol R* and dilute to 100.0 mL with *water R*. Dilute 1.0 mL of this solution to 100.0 mL with *water R*.

To 10.0 mL of the test solution and to 10.0 mL of the reference solution add separately 0.1 mL of *ferric chloride solution R2*. Any violet colour in the test solution is not more intense than that in the reference solution.

2-Chloro-4-nitroaniline

Maximum 100 ppm.

Test solution To 0.250 g add 5 mL of *methanol R*, heat to boiling, cool, add 45 mL of *1 M hydrochloric acid*, heat again to boiling, cool, filter and dilute the filtrate to 50.0 mL with *1 M hydrochloric acid*.

Reference solution Dissolve 50 mg of *2-chloro-4-nitroaniline R* in *methanol R* and dilute to 100.0 mL with the same solvent. Dilute 1.0 mL of the solution to 100.0 mL with *methanol R*. Dilute 2.0 mL of this solution to 20.0 mL with *1 M hydrochloric acid*.

To 10.0 mL of the test solution and to 10.0 mL of the reference solution add separately 0.5 mL of a 5 g/L solution of *sodium nitrite R* and allow to stand for 3 min. Add 1 mL of a 20 g/L solution of *ammonium sulfamate R*, shake, allow to stand for 3 min and add 1 mL of a 5 g/L solution of *naphthylethylenediamine dihydrochloride R*. Any pinkish-violet colour in the test solution is not more intense than that in the reference solution.

Chlorides (*2.4.4*)

Maximum 500 ppm.

To 2 g add a mixture of 1.2 mL of *acetic acid R* and 40 mL of *water R*, boil for 2 min, cool and filter. Dilute 2 mL of the filtrate to 15 mL with *water R*.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 4 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.3000 g in 80 mL of a mixture of equal volumes of *acetone R* and *methanol R*. Titrate with 0.1 M tetrabutylammonium hydroxide, determining the end-point potentiometrically (*2.2.20*).

1 mL of 0.1 M tetrabutylammonium hydroxide is equivalent to 32.71 mg of $C_{13}H_8Cl_2N_2O_4$.

STORAGE

In an airtight container, protected from light.

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