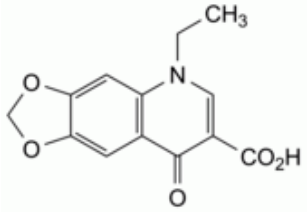
Edition: BP 2025 (Ph. Eur. 11.6 update)

Oxolinic Acid

General Notices

(Ph. Eur. monograph 1353)



$C_{13}H_{11}NO_5$ 261.2 *14698-29-4*

Action and use

Antibacterial.

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DEFINITION

5-Ethyl-8-oxo-5,8-dihydro-1,3-dioxolo[4,5-*g*]quinoline-7-carboxylic acid.

Content

98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance

Almost white or pale yellow, crystalline powder.

Solubility

Practically insoluble in water, very slightly soluble in methylene chloride, practically insoluble in ethanol (96 per cent). It dissolves in dilute solutions of alkali hydroxides.

IDENTIFICATION

First identification: B.

Second identification: A, C.

A. Ultraviolet and visible absorption spectrophotometry (2.2.25).

Test solution Dissolve 25.0 mg in 5 mL of *0.1 M sodium hydroxide*, heating on a water-bath. Allow to cool and dilute to 100.0 mL with *methanol R*. Dilute 2.0 mL of this solution to 100.0 mL with *0.1 M hydrochloric acid*.

Spectral range 220-350 nm.

Absorption maxima At 260 nm, 322 nm and 336 nm.

Absorbance ratio A_{260}/A_{336} = 4.9 to 5.2.

B. Infrared absorption spectrophotometry (2.2.24).

Comparison *oxolinic acid CRS*.

C. Thin-layer chromatography (2.2.27).

Test solution Dissolve 10 mg of the substance to be examined in 3 mL of *dilute sodium hydroxide solution R* and dilute to 20 mL with *ethanol (96 per cent) R*.

Reference solution (a) Dissolve 10 mg of *oxolinic acid CRS* in 3 mL of *dilute sodium hydroxide solution R* and dilute to 20 mL with *ethanol (96 per cent) R*.

Reference solution (b) Dissolve 5 mg of *ciprofloxacin hydrochloride CRS* in *methanol R* and dilute to 10 mL with the same solvent. Dilute 1 mL of this solution to 2 mL with reference solution (a).

Plate *TLC silica gel plate R*.

Mobile phase *acetonitrile R*, *concentrated ammonia R*, *methanol R*, *methylene chloride R* (10:20:40:40 *V/V/V/V*).

Application 10 µL.

Development At the bottom of a chromatographic tank, place an evaporating dish containing 50 mL of *concentrated ammonia R* and expose the plate to the ammonia vapour for 15 min in the closed tank; withdraw the plate, transfer to a second chromatographic tank and proceed with development over a path of 15 cm.

Drying In air.

Detection Examine in ultraviolet light at 254 nm.

System suitability Reference solution (b):

— the chromatogram shows 2 clearly separated principal spots.

Results The principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a).

TESTS

Solution S

Dissolve 0.6 g in 20 mL of a 40 g/L solution of *sodium hydroxide R*.

Appearance of solution

Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution B_7 (*2.2.2, Method II*).

Related substances

Thin-layer chromatography (*2.2.27*).

Test solution Dissolve 0.10 g of the substance to be examined in 3 mL of *dilute sodium hydroxide solution R* and dilute to 10 mL with *ethanol (96 per cent) R*.

Reference solution (a) Dilute 1 mL of the test solution to 50.0 mL with *ethanol (96 per cent) R*. Dilute 1.0 mL of this solution to 5.0 mL with *ethanol (96 per cent) R*.

Reference solution (b) Dissolve 2 mg of *oxolinic acid impurity B CRS* in *ethanol (96 per cent) R* and dilute to 10 mL with the same solvent. Dilute 1.0 mL of this solution to 10 mL with *ethanol (96 per cent) R*.

Reference solution (c) Dissolve 5 mg of the substance to be examined and 5 mg of *oxolinic acid impurity A CRS* in 2 mL of *dilute sodium hydroxide solution R* and dilute to 40 mL with *ethanol (96 per cent) R*.

Plate *cellulose for chromatography R* as the coating substance.

Mobile phase *ammonia R*, *water R*, *propanol R* (15:30:55 *V/V/V*).

Application 5 µL, in sufficiently small portions to obtain small spots.

Development Over 2/3 of the plate.

Drying In air.

Detection Examine in ultraviolet light at 254 nm.

System suitability Reference solution (c):

— the chromatogram shows 2 clearly separated principal spots.

Limits:

— *impurity B*: any spot due to impurity B is not more intense than the corresponding spot in the chromatogram obtained with reference solution (b) (0.2 per cent);

— *impurities A, C*: any spot due to impurities A or C is not more intense than the principal spot in the chromatogram obtained with reference solution (a) (0.4 per cent).

Loss on drying (*2.2.32*)

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

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

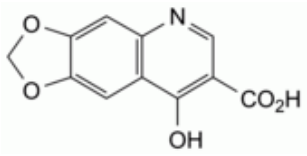
Dissolve 0.200 g in 150 mL of *dimethylformamide R*. Titrate with *0.1 M tetrabutylammonium hydroxide*, determining the end-point potentiometrically (*2.2.20*). Use a glass indicator electrode and a suitable reference electrode.

1 mL of *0.1 M tetrabutylammonium hydroxide* is equivalent to 26.12 mg of $C_{13}H_{11}NO_5$.

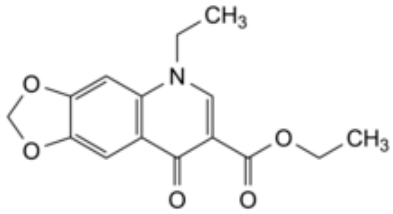
STORAGE

Protected from light.

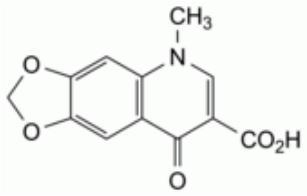
IMPURITIES



A. 8-hydroxy-1,3-dioxolo[4,5-*g*]quinoline-7-carboxylic acid,



B. ethyl 5-ethyl-8-oxo-5,8-dihydro-1,3-dioxolo[4,5-*g*]quinoline-7-carboxylate,



C. 5-methyl-8-oxo-5,8-dihydro-1,3-dioxolo[4,5-*g*]quinoline-7-carboxylic acid.

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