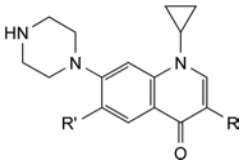
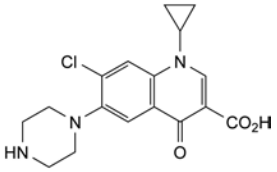


B. R = CO_2H, R′ = H: 1-cyclopropyl-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid (desfluoro compound),

E. R = H, R′ = F: 1-cyclopropyl-6-fluoro-7-(piperazin-1-yl)quinolin-4(1*H*)-one (decarboxylated compound),

F. R = CO_2H, R′ = OH: 1-cyclopropyl-6-hydroxy-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid,

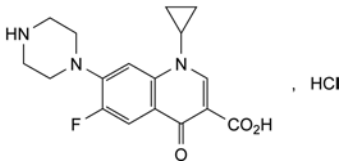


D. 7-chloro-1-cyclopropyl-4-oxo-6-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid.

01/2008:0888

CIPROFLOXACIN HYDROCHLORIDE

Ciprofloxacini hydrochloridum



$C_{17}H_{19}ClFN_3O_3$ M_r 367.8
[86393-32-0]

DEFINITION

1-Cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid hydrochloride.

Content: 98.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: pale yellow, crystalline powder, slightly hygroscopic.

Solubility: soluble in water, slightly soluble in methanol, very slightly soluble in anhydrous ethanol, practically insoluble in acetone, in ethyl acetate and in methylene chloride.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Preparation: discs.
Comparison: *ciprofloxacin hydrochloride CRS*.

B. 0.1 g gives reaction (b) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 0.5 g in *carbon dioxide-free water R* and dilute to 20 mL with the same solvent.

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution GY_5 (*2.2.2, Method II*).

Dilute 10 mL of solution S to 20 mL with *carbon dioxide-free water R*.

pH (*2.2.3*): 3.5 to 4.5 for solution S.

Impurity A. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 50 mg of the substance to be examined in *water R* and dilute to 5 mL with the same solvent.

Reference solution. Dissolve 10 mg of *ciprofloxacin impurity A CRS* in a mixture of 0.1 mL of *dilute ammonia R1* and 90 mL of *water R* and dilute to 100 mL with *water R*. Dilute 2 mL of the solution to 10 mL with *water R*.

Plate: *TLC silica gel F_{254} plate R*.

Application: 5 µL.

At the bottom of a chromatographic tank, place an evaporating dish containing 50 mL of *concentrated ammonia R*. Expose the plate to the ammonia vapour for 15 min in the closed tank. Withdraw the plate, transfer to a 2nd chromatographic tank and proceed with development.

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

Development: over 3/4 of the plate.

Drying: in air.

Detection: examine in ultraviolet light at 254 nm.

Limit:

– *impurity A*: any spot corresponding to impurity A is not more intense than the principal spot in the chromatogram obtained with the reference solution (0.2 per cent).

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 25.0 mg of the substance to be examined in the mobile phase and dilute to 50.0 mL with the mobile phase.

Reference solution (a). Dissolve 25.0 mg of *ciprofloxacin hydrochloride CRS* in the mobile phase and dilute to 50.0 mL with the mobile phase.

Reference solution (b). Dissolve 5 mg of *ciprofloxacin hydrochloride for peak identification CRS* in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution (c). Dilute 1.0 mL of the test solution to 50.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *base-deactivated octadecylsilyl silica gel for chromatography R* (5 µm);
– *temperature*: 40 °C.

Mobile phase: mix 13 volumes of *acetonitrile R* and 87 volumes of a 2.45 g/L solution of *phosphoric acid R*, previously adjusted to pH 3.0 with *triethylamine R*.

Flow rate: 1.5 mL/min.

Detection: spectrophotometer at 278 nm.

Injection: 50 µL.

Run time: twice the retention time of ciprofloxacin.

Identification of impurities: use the chromatogram supplied with *ciprofloxacin hydrochloride for peak identification CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities B, C, D and E.

Relative retention with reference to ciprofloxacin (retention time = about 9 min): impurity E = about 0.4; impurity F = about 0.5; impurity B = about 0.6; impurity C = about 0.7; impurity D = about 1.2.

System suitability: reference solution (b):

– *resolution*: minimum 1.3 between the peaks due to impurity B and impurity C.

Limits:

– *correction factors*: for the calculation of contents, multiply the peak areas of the following impurities by the corresponding correction factor: impurity B = 0.7; impurity C = 0.6; impurity D = 1.4; impurity E = 6.7;
– *impurities B, C, D, E*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.2 per cent);
– *unspecified impurities*: not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent);

– *total*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 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).

Heavy metals (*2.4.8*): maximum 20 ppm.

Dissolve 0.25 g in *water R* and dilute to 30 mL with the same solvent. Carry out the prefiltration. The filtrate complies with test E. Prepare the reference solution using 5 mL of *lead standard solution (1 ppm Pb) R*.

Water (*2.5.12*): maximum 6.7 per cent, determined on 0.200 g.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g in a platinum crucible.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modifications.

Injection: 10 µL of the test solution and reference solution (a).

Calculate the percentage content of $C_{17}H_{19}ClFN_3O_3$.

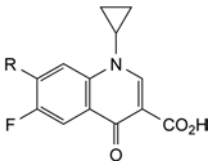
STORAGE

In an airtight container, protected from light.

IMPURITIES

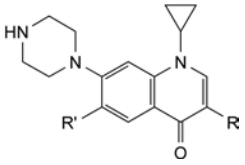
Specified impurities: A, B, C, D, E.

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*): *F.*



A. R = Cl: 7-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (fluoroquinolonic acid),

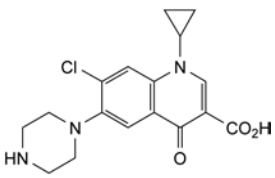
C. R = NH-$[CH_2]_2$-NH_2: 7-[(2-aminoethyl)amino]-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (ethylenediamine compound),



B. R = CO_2H, R′ = H: 1-cyclopropyl-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid (desfluoro compound),

E. R = H, R′ = F: 1-cyclopropyl-6-fluoro-7-(piperazin-1-yl)quinolin-4(1*H*)-one (decarboxylated compound),

F. R = CO_2H, R′ = OH: 1-cyclopropyl-6-hydroxy-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid,



D. 7-chloro-1-cyclopropyl-4-oxo-6-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid.

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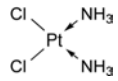
corrected 7.0

CISPLATIN

Cisplatinum



$PtCl_2(NH_3)_2$ M_r 300.0
[15663-27-1]

DEFINITION

cis-Diamminedichloroplatinum(II).

Content: 97.0 per cent to 102.0 per cent.

CHARACTERS

Appearance: yellow powder, or yellow or orange-yellow crystals.

Solubility: slightly soluble in water, sparingly soluble in dimethylformamide, practically insoluble in ethanol (96 per cent).

Carry out identification test B, the tests (except that for silver) and the assay protected from light.

IDENTIFICATION

First identification: A, B.

Second identification: B, C.

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *cisplatin CRS*.

B. Thin-layer chromatography (*2.2.27*).
Test solution. Dilute 1 mL of solution S2 (see Tests) to 10 mL with *dimethylformamide R*.
Reference solution. Dissolve 10 mg of *cisplatin CRS* in 5 mL of *dimethylformamide R*.
Plate: *cellulose for chromatography R1* as the coating substance.
Pretreatment: activate the plate by heating at 150 °C for 1 h.
Mobile phase: *acetone R, dimethylformamide R* (10:90 *V/V*).
Application: 2 µL.
Development: over 2/3 of the plate.
Drying: in air.
Detection: spray with a 50 g/L solution of *stannous chloride R* in a mixture of equal volumes of *dilute hydrochloric acid R* and *water R*. Examine after 1 h.
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 the reference solution.

C. Add 50 mg to 2 mL of *dilute sodium hydroxide solution R* in a glass dish. Evaporate to dryness. Dissolve the residue in a mixture of 0.5 mL of *nitric acid R* and 1.5 mL of *hydrochloric acid R*. Evaporate to dryness. The residue is orange. Dissolve the residue in 0.5 mL of *water R* and add 0.5 mL of *ammonium chloride solution R*. A yellow, crystalline precipitate is formed.

TESTS

Solution S1. Dissolve 25 mg in a 9 g/L solution of *sodium chloride R* in *carbon dioxide-free water R* and dilute to 25 mL with the same solvent.

Solution S2. Dissolve 0.20 g in *dimethylformamide R* and dilute to 10 mL with the same solvent.

Appearance of solution S1. Solution S1 is clear (*2.2.1*) and not more intensely coloured than reference solution GY_5 (*2.2.2, Method II*).

Appearance of solution S2. Solution S2 is clear (*2.2.1*).