

Column:

- size: $l = 0.25$ m, $\varnothing = 4.6$ mm;
- stationary phase: end-capped octylsilyl silica gel for chromatography R (5 μ m).

Mobile phase: mix 34 volumes of a solution containing 0.5 g/L of phosphoric acid R and 0.8 g/L of sodium dihydrogen phosphate R, adjusted to pH 2.5 with phosphoric acid R, and 66 volumes of methanol R.

Flow rate: 1 mL/min.

Detection: spectrophotometer at 254 nm.

Injection: 20 μ L.

Run time: 1.5 times the retention time of diclofenac.

Retention time: impurity A = about 12 min; diclofenac = about 25 min.

System suitability: reference solution (b):

- resolution: minimum 6.5 between the peaks due to impurity A and diclofenac.

Limits:

- impurities A, B, C, D, E: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
- total: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);
- disregard limit: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Heavy metals (2.4.8): maximum 10 ppm.

2.0 g complies with test C. Use a quartz crucible. Prepare the reference solution using 2 mL of lead standard solution (10 ppm Pb) 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 3 h.

ASSAY

Dissolve 0.250 g in 30 mL of anhydrous acetic acid R. Titrate with 0.1 M perchloric acid, determining the end-point potentiometrically (2.2.20).

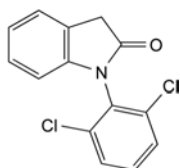
1 mL of 0.1 M perchloric acid is equivalent to 33.42 mg of $C_{14}H_{10}Cl_2KNO_2$.

STORAGE

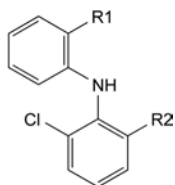
In an airtight container, protected from light.

IMPURITIES

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



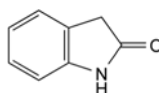
A. 1-(2,6-dichlorophenyl)-1,3-dihydro-2H-indol-2-one,



B. R1 = CHO, R2 = Cl: 2-[(2,6-dichlorophenyl)amino]benzaldehyde,

C. R1 = CH₂OH, R2 = Cl: 2-[(2,6-dichlorophenyl)amino]phenylmethanol,

D. R1 = CH₂-CO₂H, R2 = Br: 2-[(2-bromo-6-chlorophenyl)amino]phenylacetic acid,

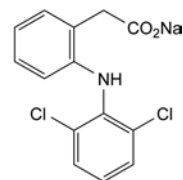


E. 1,3-dihydro-2H-indol-2-one.

01/2008:1002

DICLOFENAC SODIUM

Diclofenacum natricum



$C_{14}H_{10}Cl_2NNaO_2$
[15307-79-6]

M_r 318.1

DEFINITION

Sodium 2-[(2,6-dichlorophenyl)amino]phenyl]acetate.

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

CHARACTERS

Appearance: white or slightly yellowish, slightly hygroscopic, crystalline powder.

Solubility: sparingly soluble in water, freely soluble in methanol, soluble in ethanol (96 per cent), slightly soluble in acetone.

mp: about 280 °C, with decomposition.

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (2.2.24).

Preparation: discs.

Comparison: diclofenac sodium CRS.

B. Thin-layer chromatography (2.2.27).

Test solution. Dissolve 25 mg of the substance to be examined in methanol R and dilute to 5 mL with the same solvent.

Reference solution (a). Dissolve 25 mg of diclofenac sodium CRS in methanol R and dilute to 5 mL with the same solvent.

Reference solution (b). Dissolve 10 mg of indometacin R in reference solution (a) and dilute to 2 mL with the same solution.

Plate: TLC silica gel GF₂₅₄ plate R.

Mobile phase: concentrated ammonia R, methanol R, ethyl acetate R (10:10:80 V/V/V).

Application: 5 μ L.

Development: over a path of 10 cm.

Drying: in air.

Detection: examine in ultraviolet light at 254 nm.

System suitability: reference solution (b):

- the chromatogram shows 2 clearly separated spots.

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

C. Dissolve about 10 mg in 10 mL of ethanol (96 per cent) R. To 1 mL of this solution add 0.2 mL of a mixture, prepared immediately before use, of equal volumes of a 6 g/L solution of potassium ferricyanide R and a 9 g/L solution of ferric chloride R. Allow to stand protected from light for 5 min.

Add 3 mL of a 10 g/L solution of *hydrochloric acid R*. Allow to stand, protected from light, for 15 min. A blue colour develops and a precipitate is formed.

D. Dissolve 60 mg in 0.5 mL of *methanol R* and add 0.5 mL of *water R*. The solution gives reaction (b) of sodium (2.3.1).

TESTS

Appearance of solution. The solution is clear (2.2.1) and its absorbance (2.2.25) at 440 nm is not greater than 0.05.

Dissolve 1.25 g in *methanol R* and dilute to 25.0 mL with the same solvent.

Related substances. Liquid chromatography (2.2.29).

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

Reference solution (a). Dilute 2.0 mL of the test solution to 100.0 mL with *methanol R*. Dilute 1.0 mL of this solution to 10.0 mL with *methanol R*.

Reference solution (b). Dilute 1.0 mL of the test solution to 200.0 mL with *methanol R*. In 1.0 mL of this solution dissolve the contents of a vial of *diclofenac impurity A CRS*.

Column:

- size: $l = 0.25$ m, $\varnothing = 4.6$ mm;
- stationary phase: end-capped octylsilyl silica gel for chromatography R (5 μ m).

Mobile phase: mix 34 volumes of a solution containing 0.5 g/L of *phosphoric acid R* and 0.8 g/L of *sodium dihydrogen phosphate R*, adjusted to pH 2.5 with *phosphoric acid R*, and 66 volumes of *methanol R*.

Flow rate: 1 mL/min.

Detection: spectrophotometer at 254 nm.

Injection: 20 μ L.

Run time: 1.5 times the retention time of diclofenac.

Retention times: impurity A = about 12 min; diclofenac = about 25 min.

System suitability: reference solution (b):

- resolution: minimum 6.5 between the peaks due to impurity A and diclofenac.

Limits:

- impurities A, B, C, D, E: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
- total: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);
- disregard limit: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Heavy metals (2.4.8): maximum 10 ppm.

2.0 g complies with test C. Use a quartz crucible. Prepare the reference solution using 2 mL of *lead standard solution (10 ppm Pb) 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 3 h.

ASSAY

Dissolve 0.250 g in 30 mL of *anhydrous acetic acid R*. Titrate with 0.1 M *perchloric acid*, determining the end-point potentiometrically (2.2.20).

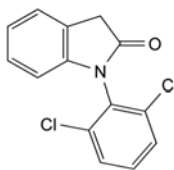
1 mL of 0.1 M *perchloric acid* is equivalent to 31.81 mg of $C_{14}H_{10}Cl_2NNaO_2$.

STORAGE

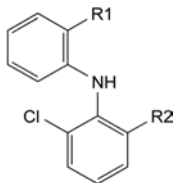
In an airtight container, protected from light.

IMPURITIES

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



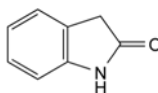
A. 1-(2,6-dichlorophenyl)-1,3-dihydro-2H-indol-2-one,



B. R1 = CHO, R2 = Cl: 2-[(2,6-dichlorophenyl)amino]benzaldehyde,

C. R1 = CH₂OH, R2 = Cl: [2-[(2,6-dichlorophenyl)amino]phenyl]methanol,

D. R1 = CH₂-CO₂H, R2 = Br: 2-[2-[(2-bromo-6-chlorophenyl)amino]phenyl]acetic acid,

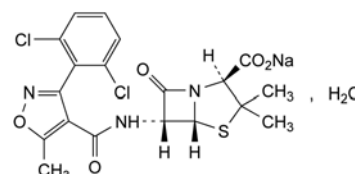


E. 1,3-dihydro-2H-indol-2-one.

01/2008:0663
corrected 6.0

DICLOXACILLIN SODIUM

Dicloxacillinum natrium



$C_{19}H_{16}Cl_2N_3NaO_5S \cdot H_2O$
[13412-64-1]

M_r 510.3

DEFINITION

Sodium (2S,5R,6R)-6-[[[3-(2,6-dichlorophenyl)-5-methylisoxazol-4-yl]carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate monohydrate.

Semi-synthetic product derived from a fermentation product.

Content: 95.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, hygroscopic, crystalline powder.

Solubility: freely soluble in water, soluble in ethanol (96 per cent) and in methanol.

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (2.2.24).

Preparation: discs.

Comparison: dicloxacillin sodium CRS.

B. Thin-layer chromatography (2.2.27).

Test solution. Dissolve 25 mg of the substance to be examined in 5 mL of *water R*.