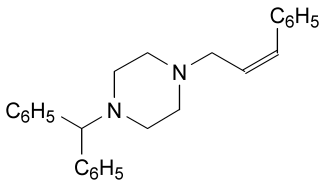
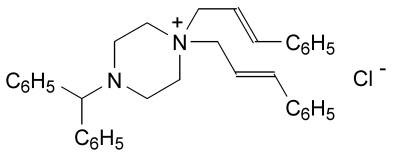
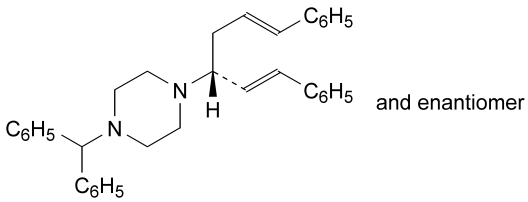


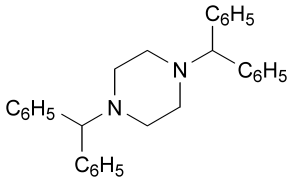
B. (*Z*)-1-(diphenylmethyl)-4-(3-phenylprop-2-enyl)piperazine,



C. (4-(diphenylmethyl)-1,1-bis[(*E*)-3-phenylprop-2-enyl]piperazinium chloride,



D. 1-(diphenylmethyl)-4-[(1*RS*,3*E*)-4-phenyl-1-[(*E*)-2-phenylethenyl]but-3-enyl]piperazine,

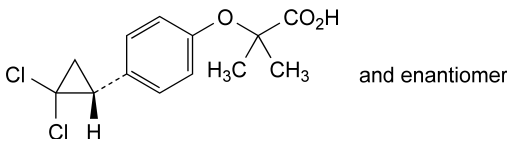


E. 1,4-bis(diphenylmethyl)piperazine.

01/2008:2013

CIPROFIBRATE

Ciprofibratum



$C_{13}H_{14}Cl_2O_3$ M_r 289.2
[52214-84-3]

DEFINITION

2-[4-[(1*RS*)-2,2-Dichlorocyclopropyl]phenoxy]-2-methylpropanoic acid.

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

CHARACTERS

Appearance: white or slightly yellow, crystalline powder.

Solubility: practically insoluble in water, freely soluble in anhydrous ethanol, soluble in toluene.

mp: about 115 °C.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *ciprofibrate CRS*.

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution BY_4 (*2.2.2, Method II*).

Dissolve 1.0 g in *anhydrous ethanol R* and dilute to 10.0 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.125 g of the substance to be examined in a mixture of equal volumes of *acetonitrile R* and *water R* and dilute to 50 ml with the same mixture of solvents.

Reference solution (a). Dilute 1.0 ml of the test solution to 100.0 ml with a mixture of equal volumes of *acetonitrile R* and *water R*. Dilute 1.0 ml of this solution to 10.0 ml with a mixture of equal volumes of *acetonitrile R* and *water R*.

Reference solution (b). Dissolve the contents of a vial of *ciprofibrate for system suitability CRS* in 2.0 ml of a mixture of equal volumes of *acetonitrile R* and *water R*.

Column:

– *size*: *l* = 0.15 m, Ø = 4.6 mm,
– *stationary phase*: *octylsilyl silica gel for chromatography R* (5 µm).

Mobile phase:

– *mobile phase A*: 1.36 g/l solution of *potassium dihydrogen phosphate R* adjusted to pH 2.2 with *phosphoric acid R*,
– *mobile phase B*: *acetonitrile R*,

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 30	75 → 30	25 → 70
30 - 40	30	70
40 - 42	30 → 75	70 → 25

Flow rate: 1.5 ml/min.

Detection: spectrophotometer at 230 nm.

Injection: 10 µl.

Identification of impurities: use the chromatogram supplied with *ciprofibrate for system suitability CRS* to identify the peaks due to impurities A, B, C, D and E.

Relative retention with reference to ciprofibrate (retention time = about 18 min): impurity A = about 0.7; impurity B = about 0.8; impurity C = about 0.95; impurity D = about 1.3; impurity E = about 1.5.

System suitability: reference solution (b):

– *resolution*: baseline separation between the peaks due to impurity C and ciprofibrate.

Limits:

– *correction factor*: for the calculation of content, multiply the peak area of impurity A by 2.3,
– *impurities A, C, D*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent),
– *impurity B*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent),
– *impurity E*: not more than 8 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.8 per cent),

– *any other impurity*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent),
– *total of other impurities*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent),
– *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Chlorides (*2.4.4*): maximum 350 ppm.

To 0.190 g add 20 ml of *water R* and treat in an ultrasonic bath for 8 min. Filter. 15 ml of the filtrate complies with the test.

Water (*2.5.12*): maximum 0.5 per cent, determined on 1.000 g.

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in a mixture of 20 ml of *water R* and 40 ml of *anhydrous ethanol R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

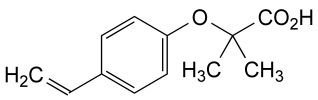
1 ml of *0.1 M sodium hydroxide* is equivalent to 28.92 mg of $C_{13}H_{14}Cl_2O_3$.

STORAGE

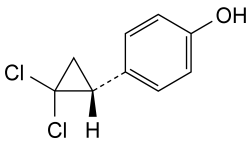
In an airtight container, protected from light.

IMPURITIES

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

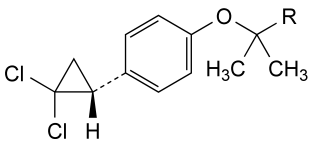


A. 2-(4-ethenylphenoxy)-2-methylpropanoic acid,



and enantiomer

B. 4-[(1*RS*)-2,2-dichlorocyclopropyl]phenol,



and enantiomer

C. R = CH_2OH: 2-[4-[(1*RS*)-2,2-dichlorocyclopropyl]phenoxy]-2-methylpropan-1-ol,

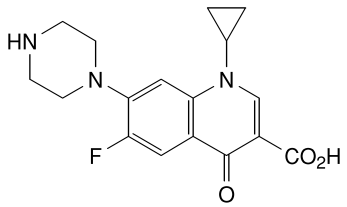
D. R = $CO\text{-}OCH_3$: methyl 2-[4-[(1*RS*)-2,2-dichlorocyclopropyl]phenoxy]-2-methylpropanoate,

E. R = $CO\text{-}OC_2H_5$: ethyl 2-[4-[(1*RS*)-2,2-dichlorocyclopropyl]phenoxy]-2-methylpropanoate.

01/2008:1089

CIPROFLOXACIN

Ciprofloxacinum



$C_{17}H_{18}FN_3O_3$ M_r 331.4
[85721-33-1]

DEFINITION

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

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

CHARACTERS

Appearance: almost white or pale yellow, crystalline powder, slightly hygroscopic.

Solubility: practically insoluble in water, very slightly soluble in ethanol and in methylene chloride.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *ciprofloxacin CRS*.

TESTS

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*).

Dissolve 0.25 g in *0.1 M hydrochloric acid* and dilute to 20 ml with the same solvent.

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

Test solution. Dissolve 50 mg of the substance to be examined in *dilute ammonia R1* 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 second 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).