Column:

– *size*: *l* = 0.1 m, Ø = 4.0 mm;

– *stationary phase*: *base-deactivated octadecylsilyl silica gel for chromatography R* (3 µm).

Mobile phase:

– *mobile phase A*: 10 g/L solution of *ammonium acetate R*;

– *mobile phase B*: 0.2 per cent *V/V* solution of *glacial acetic acid R* in *acetonitrile R1*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 20	75 → 10	25 → 90
20 - 25	10	90

If necessary, adjust the concentration of glacial acetic acid in mobile phase B to obtain a horizontal baseline in the chromatogram.

Flow rate: 1.5 mL/min.

Detection: spectrophotometer at 230 nm.

Equilibration: with the mobile phase at the initial composition for at least 30 min.

Injection: 10 µL; inject *methanol R* as a blank.

Retention time: cinnarizine = about 11 min; flunarizine = about 11.5 min.

System suitability: reference solution (a):

– *resolution*: minimum 5.0 between the peaks due to cinnarizine and flunarizine; if necessary, adjust the time programme for the gradient elution.

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 (b) (0.25 per cent);

– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

– *disregard limit*: 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent); disregard any peak due to the blank.

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

Dissolve 1.0 g in a mixture of 15 volumes of *water R* and 85 volumes of *acetone R*. Add *dilute hydrochloric acid R* until dissolution is complete. Dilute to 20 mL with a mixture of 15 volumes of *water R* and 85 volumes of *acetone R*. 12 mL of the solution complies with test B. Prepare the reference solution using 10 mL of lead standard solution (1 ppm Pb) obtained by diluting *lead standard solution (100 ppm Pb) R* with a mixture of 15 volumes of *water R* and 85 volumes of *acetone R*.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven *in vacuo* at 60 °C for 4 h.

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

ASSAY

Dissolve 0.150 g in 50 mL of a mixture of 1 volume of *anhydrous acetic acid R* and 7 volumes of *ethyl methyl ketone R*. Titrate with *0.1 M perchloric acid*, using 0.2 mL of *naphtholbenzein solution R* as indicator.

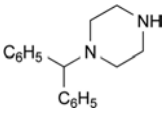
1 mL of *0.1 M perchloric acid* is equivalent to 18.43 mg of $C_{26}H_{28}N_2$.

STORAGE

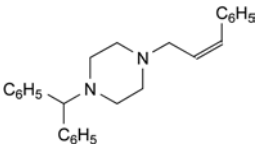
Protected from light.

IMPURITIES

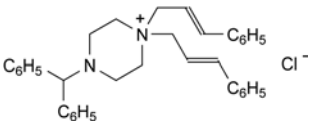
Specified impurities: *A, B, C, D, E.*



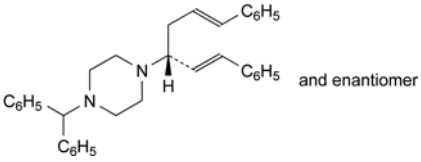
A. 1-(diphenylmethyl)piperazine,



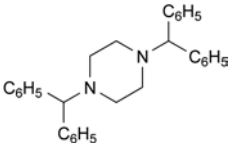
B. (*Z*)-1-(diphenylmethyl)-4-(3-phenylprop-2-enyl)piperazine,



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,

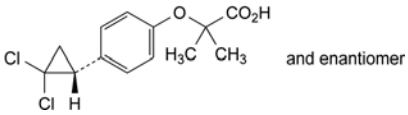


E. 1,4-bis(diphenylmethyl)piperazine.

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.

Sulfated 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*).

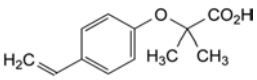
1 mL of *0.1 M sodium hydroxide* is equivalent to 28.92 mg of $C_{13}H_{14}Cl_2O_3$.

STORAGE

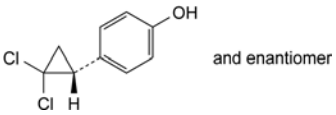
In an airtight container, protected from light.

IMPURITIES

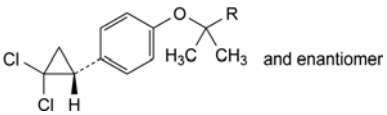
Specified impurities: A, B, C, D, E.



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



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



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

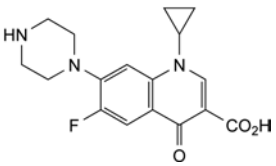
D. R = $CO\text{-}OCH_3$: methyl 2-[4-[(1*RS*)-2,2-dichlorocyclopropyl]phenoxy]-2-methylpropanoate,

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 anhydrous ethanol and in methylene chloride.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *ciprofloxacin CRS*.