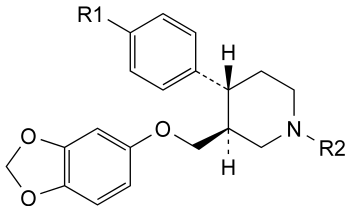
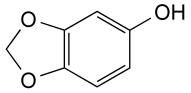


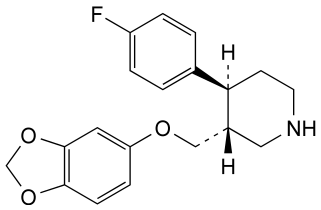
A. R1 = R2 = H: (3*S*,4*R*)-3-[(1,3-benzodioxol-5-yloxy)methyl]-4-phenylpiperidine (desfluoroparoxetine),

C. R1 = F, R2 = CH_2-C_6H_5: (3*S*,4*R*)-3-[(1,3-benzodioxol-5-yloxy)methyl]-1-benzyl-4-(4-fluorophenyl)piperidine (*N*-benzylparoxetine),

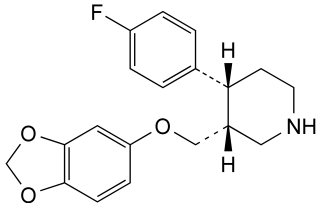
F. R1 = H, R2 = CH_2-C_6H_5: (3*S*,4*R*)-3-[(1,3-benzodioxol-5-yloxy)methyl]-1-benzyl-4-phenylpiperidine (*N*-benzyldesfluoroparoxetine),



B. 1,3-benzodioxol-5-ol (sesamol),

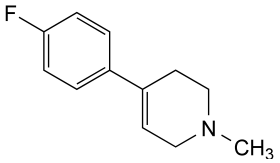


D. (3*R*,4*S*)-3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)piperidine ((+)-*trans*-paroxetine),

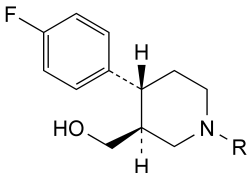


and enantiomer

E. (3*RS*,4*RS*)-3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)piperidine (*cis*-paroxetine),

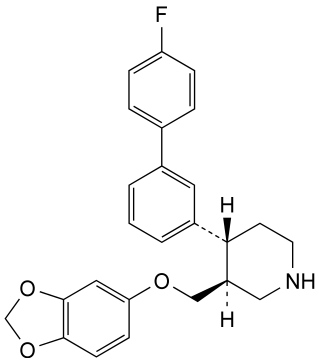


G. 4-(4-fluorophenyl)-1-methyl-1,2,3,6-tetrahydropyridine,



H. R = CH_2-C_6H_5: [(3*S*,4*R*)-1-benzyl-4-(4-fluorophenyl)-piperidin-3-yl]methanol,

I. R = H: [(3*S*,4*R*)-4-(4-fluorophenyl)piperidin-3-yl]methanol,

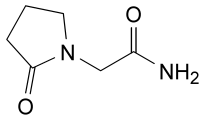


J. (3*S*,4*R*)-3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4′-fluorobiphenyl-3-yl)piperidine.

04/2006:1733

PIRACETAM

Piracetamum



$C_6H_{10}N_2O_2$ M_r 142.2

DEFINITION

2-(2-Oxopyrrolidin-1-yl)acetamide.

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

CHARACTERS

Appearance: white or almost white, powder.

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

It shows polymorphism.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *piracetam CRS*.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *ethanol (96 per cent) R*, evaporate to dryness on a water-bath and record new spectra using the residues.

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Dissolve 2.0 g in *water R* and dilute to 10 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution (a). Dissolve 50.0 mg of the substance to be examined in a mixture of 10 volumes of *acetonitrile R1* and 90 volumes of *water R* and dilute to 100.0 ml with the same mixture of solvents.

Test solution (b). Dilute 10.0 ml of test solution (a) to 50.0 ml with a mixture of 10 volumes of *acetonitrile R1* and 90 volumes of *water R*.

Reference solution (a). Dissolve 5 mg of the substance to be examined and 10 µl of *2-pyrrolidone R* in a mixture of 10 volumes of *acetonitrile R1* and 90 volumes of *water R* and dilute to 100.0 ml with the same mixture of solvents.

Reference solution (b). Dilute 1.0 ml of test solution (a) to 100.0 ml with a mixture of 10 volumes of *acetonitrile R1* and 90 volumes of *water R*. Dilute 5.0 ml of this solution to 50.0 ml with a mixture of 10 volumes of *acetonitrile R1* and 90 volumes of *water R*.

Reference solution (c). Dissolve 50.0 mg of *piracetam CRS* in a mixture of 10 volumes of *acetonitrile R1* and 90 volumes of *water R* and dilute to 100.0 ml with the same mixture of solvents. Dilute 10.0 ml of this solution to 50.0 ml with a mixture of 10 volumes of *acetonitrile R1* and 90 volumes of *water R*.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm,

– *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: mix 10 volumes of *acetonitrile R1* and 90 volumes of a 1.0 g/l solution of *dipotassium hydrogen phosphate R*; adjust to pH 6.0 with *dilute phosphoric acid R*.

Flow rate: 1.0 ml/min.

Detection: spectrophotometer at 205 nm.

Injection: 20 µl of test solution (a) and reference solutions (a) and (b).

Run time: 8 times the retention time of piracetam.

Relative retention with reference to piracetam (retention time = about 4 min): impurity D = about 0.8; impurity A = about 1.15; impurity B = about 2.8; impurity C = about 6.3.

System suitability: reference solution (a):

– *resolution*: minimum 3.0 between the peaks due to piracetam and impurity A,

– *symmetry factor*: maximum 2.0 for the peak due to piracetam.

Limits:

– *impurities A, B, C, D*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent),

– *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent),

– *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent),

– *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Heavy metals (*2.4.8*): maximum 10 ppm.

Dissolve 2.0 g in 20 ml of *water R*. 12 ml of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 100-105 °C.

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

ASSAY

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

Injection: test solution (b) and reference solution (c).

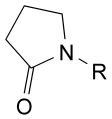
Calculate the percentage content of $C_6H_{10}N_2O_2$ from the areas of the peaks and the declared content of *piracetam CRS*.

STORAGE

Protected from light.

IMPURITIES

Specified impurities: A, B, C, D.



A. R = H: pyrrolidin-2-one (2-pyrrolidone),

B. R = CH_2-CO-O-CH_3: methyl (2-oxopyrrolidin-1-yl)acetate,

C. R = CH_2-CO-O-C_2H_5: ethyl (2-oxopyrrolidin-1-yl)acetate,

D. R = CH_2-CO_2H: (2-oxopyrrolidin-1-yl)acetic acid.

04/2006:0428

POLYSORBATE 80

Polysorbatum 80

DEFINITION

Mixture of partial esters of fatty acids, mainly *Oleic acid (0799)*, with sorbitol and its anhydrides ethoxylated with approximately 20 moles of ethylene oxide for each mole of sorbitol and sorbitol anhydrides.

CHARACTERS

Appearance: oily, yellowish or brownish-yellow, clear or slightly opalescent liquid.

Solubility: dispersible in water, in anhydrous ethanol, in ethyl acetate and in methanol, practically insoluble in fatty oils and in liquid paraffin.

Relative density: about 1.10.

Viscosity: about 400 mPa·s at 25 °C.

IDENTIFICATION

First identication: A, D.

Second identification: B, C, D, E.

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *Ph. Eur. reference spectrum of polysorbate 80*.

B. Hydroxyl value (see Tests).

C. Saponification value (see Tests).

D. Composition of fatty acids (see Tests).

E. Dissolve 0.1 g in 5 ml of *methylene chloride R*. Add 0.1 g of *potassium thiocyanate R* and 0.1 g of *cobalt nitrate R*. Stir with a glass rod. The solution becomes blue.

TESTS

Acid value (*2.5.1*): maximum 2.0.

Dissolve 5.0 g in 50 ml of the prescribed mixture of solvents.

Hydroxyl value (*2.5.3, Method A*): 65 to 80.

Peroxide value: maximum 10.0.

Introduce 10.0 g into a 100 ml beaker, dissolve with *glacial acetic acid R* and dilute to 20 ml with the same solvent. Add 1 ml of *saturated potassium iodide solution R* and allow to stand for 1 min. Add 50 ml of *carbon dioxide-free water R* and a magnetic stirring bar. Titrate with *0.01 M sodium*