ASSAY

Dissolve 80.0 mg in 10 ml of *anhydrous acetic acid R* with gentle heating and dilute to 70 ml with the same acid. Titrate with *0.1 M perchloric acid* using 0.25 ml of *naphtholbenzein solution R* as indicator until the colour changes from brownish-yellow to green.

1 ml of *0.1 M perchloric acid* is equivalent to 9.705 mg of $C_4H_{10}N_2,6H_20$.

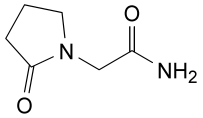
STORAGE

Store in an airtight container, protected from light.

01/2008:1733
corrected 6.0

PIRACETAM

Piracetamum



$C_6H_{10}N_2O_2$ M_r 142.2
[7491-74-9]

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 (*5.9*).

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 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).

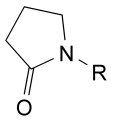
Calculate the percentage content of $C_6H_{10}N_2O_2$ from the areas of the peaks and the declared content of *piracetam CRS*.

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,

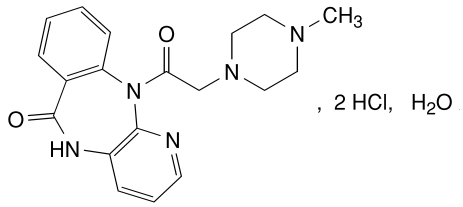
C. R = CH_2-CO-O-C_2H_5: ethyl (2-oxopyrrolidin-1-yl)acetate,

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

01/2008:2001

PIRENZEPINE DIHYDROCHLORIDE MONOHYDRATE

Pirenzepini dihydrochloridum monohydricum



$C_{19}H_{23}Cl_2N_5O_2,H_2O$ M_r 442.3

DEFINITION

11-[(4-Methylpiperazin-1-yl)acetyl]-5,11-dihydro-6*H*-pyrido[2,3-*b*][1,4]benzodiazepin-6-one dihydrochloride monohydrate.

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

CHARACTERS

Appearance: white or yellowish, crystalline powder.

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

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Dissolve 30.0 mg in *methanol R* and dilute to 100.0 ml with the same solvent. Dilute 10.0 ml of the solution to 100.0 ml with *methanol R*. Examined between 240 nm and 360 nm (*2.2.25*), the solution shows an absorption maximum at 283 nm. The specific absorbance at the maximum is 190 to 205 (anhydrous substance).

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *pirenzepine dihydrochloride monohydrate CRS*.

C. Examine the chromatograms obtained in the test for impurity D.

Results: the principal band obtained in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal band in the chromatogram obtained with reference solution (d).

D. To 0.2 ml of solution S (see Tests) add 1.8 ml of *water R*. The solution gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 25 ml with the same solvent.

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

pH (*2.2.3*): 1.0 to 2.0 for solution S.

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

Test solution (a). To 0.10 g add 0.1 ml of *concentrated ammonia R* and dilute to 10 ml with *methanol R*.

Test solution (b). Dilute 1 ml of test solution (a) to 10 ml with *methanol R*.

Reference solution (a). To 0.1 g of *pirenzepine dihydrochloride monohydrate CRS* add 0.1 ml of *concentrated ammonia R* and dilute to 10 ml with *methanol R*.

Reference solution (b). Dissolve 25 mg of *methylpiperazine R* in *methanol R* and dilute to 25 ml with the same solvent. Dilute 2.0 ml of the solution to 100 ml with *methanol R*.

Reference solution (c). Dilute 5 ml of test solution (a) to 100 ml with *methanol R*. Dilute 4 ml of this solution to 100 ml with *methanol R*. Mix 1 ml with 1 ml of reference solution (b).

Reference solution (d). Dilute 1 ml of reference solution (a) to 10 ml with *methanol R*.

Plate: *TLC silica gel plate R*.

Mobile phase: *concentrated ammonia R, methanol R, ethyl acetate R, toluene R* (7:25:28:40 *V/V/V/V*).

Application: 20 µl as bands of 20 mm by 2 mm.

Development: over 2/3 of the plate.

Drying: in air.

Detection: expose the plate to iodine vapour until the band in the chromatogram obtained with reference solution (b) is clearly visible (at most 60 min).

System suitability: the test is not valid unless the chromatogram obtained with reference solution (c) shows 2 clearly separated bands.

Limit:

– *impurity D*: any band corresponding to impurity D in the chromatogram obtained with test solution (a) is not more intense than the band in the chromatogram obtained with reference solution (b) (0.2 per cent).

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.30 g of the substance to be examined in *water R* and dilute to 10.0 ml with the same solvent. To 1.0 ml of the solution add 5 ml of *methanol R* and dilute to 10.0 ml with mobile phase A.

Reference solution (a). Dilute 2.0 ml of the test solution to 100.0 ml with mobile phase A. Dilute 1.0 ml of this solution to 10.0 ml with mobile phase A.

Reference solution (b). Dissolve 0.1 g of *1-phenylpiperazine R* in *methanol R* and dilute to 10 ml with the same solvent. Mix 1 ml of the solution with 1 ml of the test solution, add 5 ml of *methanol R* and dilute to 10 ml with mobile phase A.

Column:

– *size*: *l* = 0.125 m, Ø = 4.6 mm,

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