– *impurity B*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (c) (0.01 per cent);
– *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (d) (0.05 per cent);
– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (d) (0.1 per cent);
– *disregard limit of impurities other than B*: 0.6 times the area of the principal peak in the chromatogram obtained with reference solution (d) (0.03 per cent).

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

Dissolve 2.0 g in a mixture of 25 volumes of *water R* and 75 volumes of *ethanol (96 per cent) R* and dilute to 20 mL with the same mixture of solvents. 12 mL of the solution complies with test B. Prepare the reference solution using lead standard solution (1 ppm Pb) obtained by diluting *lead standard solution (100 ppm Pb) R* with a mixture of 25 volumes of *water R* and 75 volumes of *ethanol (96 per cent) R*.

Water (*2.5.12*): maximum 0.5 per cent, determined on 2.00 g.

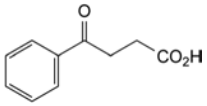
ASSAY

Disperse 0.150 g in 50 mL of *anhydrous acetic acid R*. The opalescence of the solution disappears during the titration. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

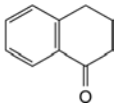
1 mL of *0.1 M perchloric acid* is equivalent to 18.62 mg of $C_{10}H_{11}NaO_2$.

IMPURITIES

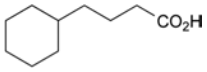
Specified impurities: A, B, C.



A. 4-oxo-4-phenylbutanoic acid (3-benzoylpropionic acid),



B. 3,4-dihydronaphthalen-1(2*H*)-one (α-tetralone),

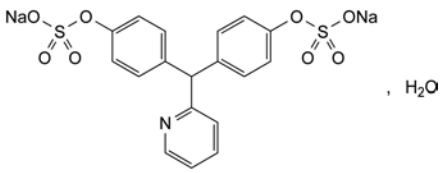


C. 4-cyclohexylbutanoic acid.

07/2009:1031

SODIUM PICOSULFATE

Natrii picosulfas



$C_{18}H_{13}NNa_2O_8S_2,H_2O$ M_r 499.4

DEFINITION

4,4′-[(Pyridin-2-yl)methylene]diphenyl bis(sodium sulfate) monohydrate.

Content: 98.5 per cent to 100.5 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

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

IDENTIFICATION

First identification: A, E.

Second identification: B, C, D, E.

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *sodium picosulfate CRS*.

B. Thin-layer chromatography (*2.2.27*).
Test solution. Dissolve 20 mg of the substance to be examined in *methanol R* and dilute to 5 mL with the same solvent.
Reference solution. Dissolve 20 mg of *sodium picosulfate CRS* in *methanol R* and dilute to 5 mL with the same solvent.
Plate: *TLC silica gel GF_{254} plate R*.
Mobile phase: *anhydrous formic acid R, water R, methanol R, ethyl acetate R* (2.5:12.5:25:60 *V/V/V/V*).
Application: 5 µL.
Development: over half of the plate.
Drying: in a current of hot air for 15 min.
Detection: examine in ultraviolet light at 254 nm.
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 the reference solution.

C. To 5 mL of solution S (see Tests) add 1 mL of *dilute hydrochloric acid R* and heat to boiling. Add 1 mL of *barium chloride solution R1*. A white precipitate is formed.

D. To about 10 mg add 3 mL of *sulfuric acid R* and 0.1 mL of *potassium dichromate solution R1*. A violet colour develops.

E. Solution S gives reaction (a) of sodium (*2.3.1*).

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* prepared from *distilled water R* and dilute to 50 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution GY_7 (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.05 mL of *phenolphthalein solution R*. The solution is colourless. Not more than 0.25 mL of *0.01 M sodium hydroxide* is required to change the colour of the indicator to pink.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 50 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

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

Reference solution (b). Dissolve the contents of a vial of *picosulfate for system suitability CRS* (containing impurities A and B) in 1.0 mL of the mobile phase.

Column:
– *size*: *l* = 0.25 m, Ø = 4.0 mm;
– *stationary phase*: spherical *end-capped octadecylsilyl silica gel for chromatography R1* (5 µm);
– *temperature*: 40 °C.

Mobile phase: dissolve 2.3 g of *disodium hydrogen phosphate dihydrate R* in 800 mL of *water for chromatography R*, add 0.2 g of *cetyltrimethylammonium bromide R*, adjust to pH 7.5 with *phosphoric acid R* and dilute to 1000 mL with *water for chromatography R*; mix 550 mL of this solution and 450 mL of *acetonitrile R* (if necessary vary the buffer/acetonitrile proportion in 10 mL increments in order to fulfil the resolution requirement).

Flow rate: 1.0 mL/min.

Detection: spectrophotometer at 263 nm.

Injection: 40 µL.

Run time: twice the retention time of picosulfate.

Identification of impurities: use the chromatogram supplied with *picosulfate for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A and B.

Relative retention with reference to picosulfate (retention time = about 7.4 min): impurity B = about 0.5; impurity A = about 0.7.

System suitability: reference solution (b):

– *resolution*: minimum 4.0 between the peaks due to impurities B and A.

Limits:

– *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 0.7; impurity B = 0.5;
– *impurities A, B*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
– *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);
– *total*: 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 200 ppm.

Dilute 5 mL of solution S to 15 mL with *water R*.

Sulfates (*2.4.13*): maximum 400 ppm.

Dilute 7.5 mL of solution S to 15 mL with *distilled water R*.

Water (*2.5.12*): 3.0 per cent to 5.0 per cent, determined on 0.500 g.

ASSAY

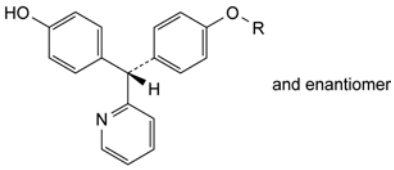
Dissolve 0.400 g in 80 mL of *methanol R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 48.14 mg of $C_{18}H_{13}NNa_2O_8S_2$.

IMPURITIES

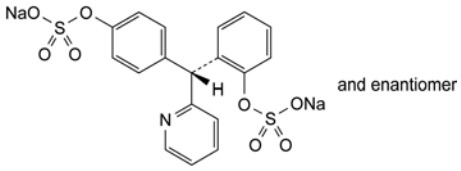
Specified impurities: A, B.

Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical use (2034)*. It is therefore not necessary to identify these impurities for demonstration of compliance. See also *5.10. Control of impurities in substances for pharmaceutical use*): *C*.



A. R = SO_3Na: 4-[(*RS*)-(4-hydroxyphenyl)(pyridin-2-yl)methyl]phenyl sodium sulfate,

B. R = H: 4,4′-[(pyridin-2-yl)methylene]diphenol,



C. 2-[(*RS*)-(pyridin-2-yl)[4-(sulfonatooxy)phenyl]methyl]phenyl disodium sulfate.

01/2009:1909

SODIUM POLYSTYRENE SULFONATE

Natrii polystyrenesulfonas

DEFINITION

Polystyrene sulfonate resin prepared in the sodium form.

Exchange capacity: 2.8 mmol to 3.4 mmol of potassium per gram (dried substance).

Content: 9.4 per cent to 11.0 per cent of Na (dried substance).

CHARACTERS

Appearance: almost white or light brown powder.

Solubility: practically insoluble in water, in ethanol (96 per cent) and in methylene chloride.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Preparation: discs using finely ground substance.
Comparison: *Ph. Eur. reference spectrum of sodium polystyrene sulfonate*.

B. Suspend 0.1 g in *water R*, add 2 mL of a 150 g/L solution of *potassium carbonate R*, and heat to boiling. Allow to cool and filter. To the filtrate add 4 mL of *potassium pyroantimonate solution R* and heat to boiling. Allow to cool in iced water and if necessary rub the inside of the test-tube with a glass rod. A dense white precipitate is formed.

TESTS

Styrene. Liquid chromatography (*2.2.29*).

Test solution. Shake 10.0 g of the substance to be examined with 10 mL of *acetone R* for 30 min, centrifuge and use the supernatant liquid.

Reference solution. Dissolve 10 mg of *styrene R* in *acetone R* and dilute to 100 mL with the same solvent. Dilute 1 mL of this solution to 100 mL with *acetone R*.

Column:

– *size*: *l* = 0.25 m, Ø = 4 mm;
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: *acetonitrile R, water R* (1:1 *V/V*).

Flow rate: 2 mL/min.

Detection: spectrophotometer at 254 nm.

Injection: 20 µL.

Limit:

– *styrene*: not more than the area of the principal peak in the chromatogram obtained with the reference solution (1 ppm).

Calcium: maximum 0.10 per cent.

Atomic emission spectrometry (*2.2.22, Method I*).

Test solution. To 1.10 g add 5 mL of *hydrochloric acid R*, heat to boiling, cool and add 10 mL of *water R*. Filter, wash the filter and residue with *water R* and dilute the filtrate and washing to 25.0 mL with *water R*.

Reference solutions. Prepare the reference solutions using *calcium standard solution (400 ppm Ca) R*, diluted as necessary with *water R*.

Wavelength: 422.7 nm.