IDENTIFICATION

A. Solution S (see Tests) is slightly alkaline (*2.2.4*).

B. Loss on drying (see Tests).

C. Solution S gives reaction (b) of phosphates (*2.3.1*).

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

TESTS

Solution S. Dissolve 5.0 g in *distilled water R* and dilute to 100 ml with the same solvent.

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

Reducing substances. To 5 ml of solution S add 5 ml of *dilute sulphuric acid R* and 0.25 ml of *0.02 M potassium permanganate* and heat on a water-bath for 5 min. The solution retains a slight red colour.

Monosodium phosphate: maximum 2.5 per cent.

From the volume of *1 M hydrochloric acid* (25 ml) and of *1 M sodium hydroxide* (n_1 ml and n_2 ml) used in the assay, calculate the following ratio:

$$\frac{n_2 - 25}{25 - n_1}$$

This ratio is not greater than 0.025.

Chlorides (*2.4.4*): maximum 400 ppm.

To 2.5 ml of solution S add 10 ml of *dilute nitric acid R* and dilute to 15 ml with *water R*.

Sulphates (*2.4.13*): maximum 0.1 per cent.

To 3 ml of solution S add 2 ml of *dilute hydrochloric acid R* and dilute to 15 ml with *distilled water R*.

Arsenic (*2.4.2, Method A*): maximum 4 ppm, determined on 5 ml of solution S.

Iron (*2.4.9*): maximum 40 ppm

Dilute 5 ml of solution S to 10 ml with *water R*.

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

12 ml of solution S complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): 19.5 per cent to 21.0 per cent, determined on 1.000 g by drying in an oven at 130 °C.

ASSAY

Dissolve 2.000 g (m) in 50 ml of *water R* and add 25.0 ml of *1 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*) using *1 M sodium hydroxide*. Read the volume added at the 1st inflexion point (n_1 ml). Continue the titration to the 2nd inflexion point (total volume of *1 M sodium hydroxide* required, n_2 ml).

Calculate the percentage content of Na_2HPO_4 from the following expression:

$$\frac{1420\,(25 - n_1)}{m\,(100 - d)}$$

d = percentage loss on drying.

01/2008:0118

DISODIUM PHOSPHATE DODECAHYDRATE

Dinatrii phosphas dodecahydricus

$Na_2HPO_4,12H_2O$ M_r 358.1
[7782-75-6]

DEFINITION

Content: 98.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance: colourless, transparent crystals, very efflorescent.

Solubility: very soluble in water, practically insoluble in ethanol (96 per cent).

IDENTIFICATION

A. Solution S (see Tests) is slightly alkaline (*2.2.4*).

B. Water (see Tests).

C. Solution S gives reaction (b) of phosphates (*2.3.1*).

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

TESTS

Solution S. Dissolve 5.0 g in *distilled water R* and dilute to 50 ml with the same solvent.

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

Reducing substances. To 5 ml of solution S add 5 ml of *dilute sulphuric acid R* and 0.25 ml of *0.02 M potassium permanganate* and heat on a water-bath for 5 min. The solution retains a slight red colour.

Monosodium phosphate: maximum 2.5 per cent.

From the volume of *1 M hydrochloric acid* (25 ml) and of *1 M sodium hydroxide* (n_1 ml and n_2 ml) used in the assay, calculate the following ratio:

$$\frac{n_2 - 25}{25 - n_1}$$

This ratio is not greater than 0.025.

Chlorides (*2.4.4*): maximum 200 ppm.

To 2.5 ml of solution S add 10 ml of *dilute nitric acid R* and dilute to 15 ml with *water R*.

Sulphates (*2.4.13*): maximum 500 ppm.

To 3 ml of solution S add 2 ml of *dilute hydrochloric acid R* and dilute to 15 ml with *distilled water R*.

Arsenic (*2.4.2, Method A*): maximum 2 ppm, determined on 5 ml of solution S.

Iron (*2.4.9*): maximum 20 ppm.

Dilute 5 ml of solution S to 10 ml with *water R*.

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

12 ml of solution S complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Water (*2.5.12*): 57.0 per cent to 61.0 per cent, determined on 50.0 mg. Use a mixture of 10 volumes of *anhydrous methanol R* and 40 volumes of *formamide R* as solvent.

ASSAY

Dissolve 4.00 g (*m*) in 25 ml of *water R* and add 25.0 ml of *1 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*) using *1 M sodium hydroxide*. Read the volume added at the 1st inflexion point (n_1 ml). Continue the titration to the 2nd inflexion point (total volume of *1 M sodium hydroxide* required, n_2 ml).

Calculate the percentage content of Na_2HPO_4 from the following expression:

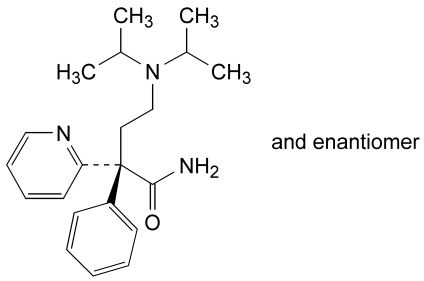
$$\frac{1420\,(25 - n_1)}{m\,(100 - d)}$$

d = percentage content of water.

01/2008:1006

DISOPYRAMIDE

Disopyramidum



and enantiomer

$C_{21}H_{29}N_3O$ M_r 339.5
[3737-09-5]

DEFINITION

Disopyramide contains not less than 98.5 per cent and not more than the equivalent of 101.5 per cent of (2*RS*)-4-[bis(1-methylethyl)amino]-2-phenyl-2-(pyridin-2-yl)butanamide, calculated with reference to the dried substance.

CHARACTERS

A white or almost white powder, slightly soluble in water, freely soluble in methylene chloride, soluble in alcohol.

IDENTIFICATION

First identification: B.

Second identification: A, C.

A. Dissolve 40.0 mg in a 5 g/l solution of *sulphuric acid R* in *methanol R* and dilute to 100.0 ml with the same solution. Dilute 5.0 ml of this solution to 50.0 ml with a 5 g/l solution of *sulphuric acid R* in *methanol R*. Examined between 240 nm and 350 nm (*2.2.25*), the solution shows an absorption maximum at 269 nm and a shoulder at 263 nm. The specific absorbance at the maximum is 190 to 210.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *disopyramide CRS*. Examine the substances as discs prepared by placing 50 µl of a 50 g/l solution in *methylene chloride R* on a disc of *potassium bromide R*. Dry the discs at 60 °C for 1 h before use.

C. Examine the chromatograms obtained in the test for related substances in ultraviolet light at 254 nm. The principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a). Spray with *dilute potassium iodobismuthate solution R*. Examine in daylight. The principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a).

TESTS

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution (a). Dissolve 0.20 g of the substance to be examined in *methanol R* and dilute to 10 ml with the same solvent.

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

Reference solution (a). Dissolve 20 mg of *disopyramide CRS* in *methanol R* and dilute to 10 ml with the same solvent.

Reference solution (b). Dilute 0.5 ml of test solution (b) to 20 ml with *methanol R*.

Apply to the plate 10 µl of each solution. Develop over a path of 15 cm using a mixture of 1 volume of *concentrated ammonia R*, 30 volumes of *acetone R* and 30 volumes of *cyclohexane R*. Dry the plate in a current of warm air and examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with test solution (a), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.25 per cent).

Heavy metals (*2.4.8*). 2.0 g complies with limit test C for heavy metals (10 ppm). Prepare the standard using 2 ml of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying at 80 °C over *diphosphorus pentoxide R* at a pressure not exceeding 0.7 kPa for 2 h.

Sulphated ash (*2.4.14*). Not more than 0.2 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.130 g in 30 ml of *anhydrous acetic acid R*. Add 0.2 ml of *naphtholbenzein solution R*. Titrate with *0.1 M perchloric acid* until the colour changes from yellow to green.

1 ml of *0.1 M perchloric acid* is equivalent to 16.97 mg of $C_{21}H_{29}N_3O$.

STORAGE

Store protected from light.