TESTS

Solution S. Dissolve 10.0 g in *carbon dioxide-free water R* prepared from *distilled water R* and dilute to 100.0 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_6 (*2.2.2, Method II*).

pH (*2.2.3*): 6.8 to 7.8 for solution S.

Oxidisable substances. To 1 mL of solution S, add 10 mL of *water R*, 1 mL of *dilute sulfuric acid R* and 0.25 mL of a 3.0 g/L solution of *potassium permanganate R*. Mix. After 5 min, the violet colour of the mixture is still visible.

Sucrose and reducing sugars. To 5 mL of solution S add 2 mL of *hydrochloric acid R1* and dilute to 10 mL with *water R*. Heat to boiling for 5 min and allow to cool. Add 10 mL of *sodium carbonate solution R*. Allow to stand for 5 min, dilute to 25 mL with *water R* and filter. To 5 mL of the filtrate add 2 mL of *cupri-tartaric solution R* and heat to boiling for 1 min. No red precipitate is formed.

Chlorides (*2.4.4*): maximum 50 ppm.

Dilute 10 mL of solution S to 15 mL with *water R*.

Sulfates (*2.4.13*): maximum 200 ppm.

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

Magnesium and alkali metals: maximum 1.0 per cent.

To 10 mL of solution S, add 80 mL of *water R*, 10 mL of *ammonium chloride solution R* and 1 mL of *ammonia R*. Heat to boiling. To the boiling solution, add dropwise 50 mL of warm *ammonium oxalate solution R*. Allow to stand for 4 h, then dilute to 200 mL with *water R* and filter. To 100 mL of the filtrate, add 0.5 mL of *sulfuric acid R*. Evaporate to dryness on a water-bath and ignite to constant mass at 600 ± 50 °C. The residue weighs a maximum of 5.0 mg.

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*.

Loss on drying (*2.2.32*): 11.0 per cent to 12.5 per cent, determined on 0.200 g by drying at 105 °C.

Pyrogens (*2.6.8*). If intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of pyrogens, it complies with the test for pyrogens. Inject per kilogram of the rabbit's mass 4 mL of a solution containing per millilitre 50 mg of the substance to be examined.

ASSAY

Dissolve 0.240 g in 50 mL of *water R*. Carry out the complexometric titration of calcium (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 27.03 mg of $C_{10}H_{14}CaO_6$.

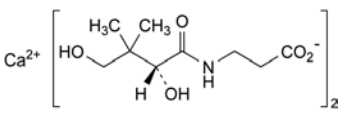
STORAGE

Protected from light.

01/2008:0470
corrected 6.0

CALCIUM PANTOTHENATE

Calcii pantothenas



$C_{18}H_{32}CaN_2O_{10}$ M_r 476.5
[137-08-6]

DEFINITION

Calcium pantothenate contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of calcium bis[3-[[(2*R*)-2,4-dihydroxy-3,3-dimethylbutanoyl]amino]propanoate], calculated with reference to the dried substance.

CHARACTERS

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

IDENTIFICATION

A. Specific optical rotation (see Tests).

B. Examine the chromatograms obtained in the test for 3-aminopropionic acid. 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).

C. To 1 mL of solution S (see Tests) add 1 mL of *dilute sodium hydroxide solution R* and 0.1 mL of *copper sulfate solution R*. A blue colour develops.

D. It gives reaction (a) of calcium (*2.3.1*).

TESTS

Solution S. Dissolve 2.50 g in *carbon dioxide-free water R* and dilute to 50.0 mL with the same solvent.

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

pH (*2.2.3*). The pH of solution S is 6.8 to 8.0.

Specific optical rotation (*2.2.7*): + 25.5 to + 27.5, determined on solution S and calculated with reference to the dried substance.

3-Aminopropionic acid. Examine by thin-layer chromatography (*2.2.27*), using *silica gel G R* as the coating substance.

Test solution (a). Dissolve 0.2 g of the substance to be examined in *water R* and dilute to 5 mL with the same solvent.

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

Reference solution (a). Dissolve 20 mg of *calcium pantothenate CRS* in *water R* and dilute to 5 mL with the same solvent.

Reference solution (b). Dissolve 10 mg of *3-aminopropionic acid R* in *water R* and dilute to 50 mL with the same solvent.

Apply separately to the plate 5 µL of each solution. Develop over a path of 12 cm using a mixture of 35 volumes of *water R* and 65 volumes of *ethanol R*. Dry the plate in a current of air and spray with *ninhydrin solution R1*. Heat at 110 °C for 10 min. Any spot corresponding to 3-aminopropionic acid in the chromatogram obtained with test solution (a) is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.5 per cent).

Chlorides (*2.4.4*). 5 mL of solution S diluted to 15 mL with *water R* complies with the limit test for chlorides (200 ppm).

Heavy metals (*2.4.8*). 12 mL of solution S complies with limit test A for heavy metals (20 ppm). Prepare the standard using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*). Not more than 3.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

ASSAY

Dissolve 0.180 g in 50 mL of *anhydrous acetic acid 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 23.83 mg of $C_{18}H_{32}CaN_2O_{10}$.

STORAGE

Store in an airtight container.

04/2009:1052

CALCIUM PHOSPHATE

Tricalcii phosphas

DEFINITION

Mixture of calcium phosphates.

Content: 35.0 per cent to 40.0 per cent of Ca (A_r 40.08).

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water. It dissolves in dilute hydrochloric acid and in dilute nitric acid.

IDENTIFICATION

A. Dissolve 0.1 g in 5 mL of a 25 per cent *V/V* solution of *nitric acid R*. The solution gives reaction (b) of phosphates (*2.3.1*).

B. It gives reaction (b) of calcium (*2.3.1*). Filter before adding *potassium ferrocyanide solution R*.

C. It complies with the limits of the assay.

TESTS

Solution S. Dissolve 2.50 g in 20 mL of *dilute hydrochloric acid R*. If the solution is not clear, filter it. Add *dilute ammonia R1* dropwise until a precipitate is formed. Dissolve the precipitate by adding *dilute hydrochloric acid R* and dilute to 50 mL with *distilled water R*.

Chlorides (*2.4.4*): maximum 0.15 per cent.

Dissolve 0.22 g in a mixture of 1 mL of *nitric acid R* and 10 mL of *water R* and dilute to 100 mL with *water R*.

Fluorides: maximum 75 ppm.

Potentiometry (*2.2.36, Method II*).

Test solution. Dissolve 0.250 g in *0.1 M hydrochloric acid,* add 5.0 mL of *fluoride standard solution (1 ppm F) R* and dilute to 50.0 mL with *0.1 M hydrochloric acid.* To 20.0 mL of this solution add 20.0 mL of *total-ionic-strength-adjustment buffer R* and 3 mL of an 82 g/L solution of *anhydrous sodium acetate R*. Adjust to pH 5.2 with *ammonia R* and dilute to 50.0 mL with *distilled water R*.

Reference solution. Fluoride standard solution (10 ppm F) R.

Indicator electrode: fluoride-selective.

Reference electrode: silver-silver chloride.

Carry out the measurements on the test solution, then add at least 3 quantities, each of 0.5 mL, of the reference solution, carrying out a measurement after each addition. Calculate the concentration of fluorides using the calibration curve, taking into account the addition of fluoride to the test solution.

Sulfates (*2.4.13*): maximum 0.5 per cent.

Dilute 1 mL of solution S to 25 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 400 ppm.

Dilute 0.5 mL of solution S to 10 mL with *water R*.

Heavy metals (*2.4.8*): maximum 30 ppm.

Dilute 13 mL of solution S to 20 mL with *water R*. 12 mL of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Acid-insoluble matter: maximum 0.2 per cent.

Dissolve 5.0 g in a mixture of 10 mL of *hydrochloric acid R* and 30 mL of *water R*. Filter, wash the residue with *water R* and dry to constant mass at 100-105 °C. The residue weighs a maximum of 10 mg.

Loss on ignition: maximum 8.0 per cent, determined on 1.000 g by ignition at 800 ± 50 °C for 30 min.

ASSAY

Dissolve 0.200 g in a mixture of 1 mL of *hydrochloric acid R1* and 5 mL of *water R*. Add 25.0 mL of *0.1 M sodium edetate* and dilute to 200 mL with *water R*. Adjust to about pH 10 with *concentrated ammonia R*. Add 10 mL of *ammonium chloride buffer solution pH 10.0 R* and a few milligrams of *mordant black 11 triturate R*. Titrate the excess sodium edetate with *0.1 M zinc sulfate* until the colour changes from blue to violet.

1 mL of *0.1 M sodium edetate* is equivalent to 4.008 mg of Ca.

FUNCTIONALITY-RELATED CHARACTERISTICS

This section provides information on characteristics that are recognised as being relevant control parameters for one or more functions of the substance when used as an excipient (see chapter 5.15). This section is a non-mandatory part of the monograph and it is not necessary to verify the characteristics to demonstrate compliance. Control of these characteristics can however contribute to the quality of a medicinal product by improving the consistency of the manufacturing process and the performance of the medicinal product during use. Where control methods are cited, they are recognised as being suitable for the purpose, but other methods can also be used. Wherever results for a particular characteristic are reported, the control method must be indicated.

The following characteristics may be relevant for calcium phosphate is used as a filler in tablets and capsules.

Particle-size distribution (*2.9.31* or *2.9.38*).

Bulk and tapped density (*2.9.34*).

Powder flow (*2.9.36*).

07/2010:0882
corrected 7.0

CALCIUM STEARATE

Calcii stearas

[1592-23-0]

DEFINITION

Mixture of calcium salts of different fatty acids consisting mainly of stearic (octadecanoic) acid [$(C_{17}H_{35}COO)_2Ca$; M_r 607] and palmitic (hexadecanoic) acid [$(C_{15}H_{31}COO)_2Ca$; M_r 550.9] with minor proportions of other fatty acids.

Content:

– *calcium*: 6.4 per cent to 7.4 per cent (A_r 40.08) (dried substance);

– *stearic acid in the fatty acid fraction*: minimum 40.0 per cent;

– *sum of stearic acid and palmitic acid in the fatty acid fraction*: minimum 90.0 per cent.

CHARACTERS

Appearance: fine, white or almost white, crystalline powder.

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

IDENTIFICATION

First identification: C, D.

Second identification: A, B, D.

A. Freezing point (*2.2.18*): minimum 53 °C, for the residue obtained in the preparation of solution S (see Tests).

B. Acid value (*2.5.1*): 195 to 210.

Dissolve 0.200 g of the residue obtained in the preparation of solution S in 25 mL of the prescribed mixture of solvents.

C. Examine the chromatograms obtained in the test for fatty acid composition.