ASSAY

Dissolve 0.800 g in a mixture of 150 ml of *water R* and 2 ml of *3 M hydrochloric acid R*. While stirring, add 12.5 ml of *0.1 M sodium edetate*, 15 ml of *1 M sodium hydroxide* and 0.3 g of *hydroxynaphthol blue, sodium salt R*. Titrate with *0.1 M sodium edetate* until the colour changes from violet to pure blue.

1 ml of *0.1 M sodium edetate* is equivalent to 49.04 mg of $C_{14}H_{26}CaO_{16}$.

STORAGE

In an airtight container. If the substance is sterile, store in a sterile, airtight, tamper-proof container.

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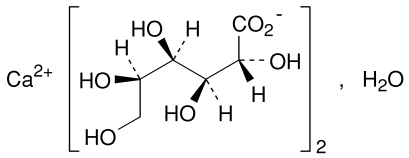
corrected 6.0

CALCIUM GLUCONATE

Calcii gluconas



$C_{12}H_{22}CaO_{14},H_2O$ M_r 448.4

DEFINITION

Calcium D-gluconate monohydrate.

Content: 98.5 per cent to 102.0 per cent of $C_{12}H_{22}CaO_{14},H_2O$.

CHARACTERS

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

Solubility: sparingly soluble in water, freely soluble in boiling water.

IDENTIFICATION

A. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 20 mg of the substance to be examined in 1 ml of *water R*, heating if necessary in a water-bath at 60 °C.

Reference solution. Dissolve 20 mg of *calcium gluconate CRS* in 1 ml of *water R*, heating if necessary in a water-bath at 60 °C.

Plate: *TLC silica gel G plate R*.

Mobile phase: *ethyl acetate R, concentrated ammonia R, water R, ethanol (96 per cent) R* (10:10:30:50 *V/V/V/V*).

Application: 5 µl.

Development: over a path of 10 cm.

Drying: at 100 °C for 20 min. Allow to cool.

Detection: spray with a 50 g/l solution of *potassium dichromate R* in a 40 per cent *m/m* solution of *sulphuric acid R*.

Results: after 5 min, the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

B. Solution S (see Tests) gives the reactions of calcium (*2.3.1*).

TESTS

Solution S. Dissolve 1.0 g in *water R* heated to 60 °C and dilute to 50 ml with the same solvent.

Appearance of solution. At 60 °C, solution S is not more intensely coloured than reference solution Y_6 (*2.2.2, Method II*). After cooling, it is not more opalescent than reference suspension II (*2.2.1*).

Organic impurities and boric acid. Introduce 0.5 g into a porcelain dish previously rinsed with *sulphuric acid R* and placed in a bath of iced water. Add 2 ml of cooled *sulphuric acid R* and mix. No yellow or brown colour develops. Add 1 ml of *chromotrope II B solution R*. A violet colour develops and does not become dark blue. The solution is not more intensely coloured than that of a mixture of 1 ml of *chromotrope II B solution R* and 2 ml of cooled *sulphuric acid R*.

Sucrose and reducing sugars. Dissolve 0.5 g in a mixture of 2 ml of *hydrochloric acid R1* and 10 ml of *water R*. Boil for 5 min, allow to cool, add 10 ml of *sodium carbonate solution R* and allow to stand. Dilute to 25 ml with *water R* and filter. To 5 ml of the filtrate add 2 ml of *cupri-tartaric solution R* and boil for 1 min. Allow to stand for 2 min. No red precipitate is formed.

Chlorides (*2.4.4*): maximum 200 ppm.

Dilute 12.5 ml of solution S to 15 ml with *water R*.

Sulphates (*2.4.13*): maximum 100 ppm.

Dissolve 10.0 g with heating in a mixture of 10 ml of *acetic acid R* and 90 ml of *distilled water R*.

Magnesium and alkali metals: maximum 0.4 per cent.

Dissolve 1.00 g in 100 ml of boiling *water R*, add 10 ml of *ammonium chloride solution R*, 1 ml of *ammonia R* and, dropwise, 50 ml of hot *ammonium oxalate solution R*. Allow to stand for 4 h, dilute to 200 ml with *water R* and filter. Evaporate 100 ml of the filtrate to dryness and ignite. The residue weighs a maximum of 2 mg.

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

2.0 g complies with test D. Heat the substance to be examined gradually and with care until it is almost completely transformed into a white mass and then ignite. Prepare the reference solution using 2 ml of *lead standard solution (10 ppm Pb) R*.

Microbial contamination. Total viable aerobic count (*2.6.12*) not more than 10^3 micro-organisms per gram, determined by plate count.

ASSAY

Dissolve 0.8000 g in 20 ml of hot *water R*, allow to cool and dilute to 300 ml with *water R*. Carry out the complexometric titration of calcium (*2.5.11*).

1 ml of *0.1 M sodium edetate* is equivalent to 44.84 mg of $C_{12}H_{22}CaO_{14},H_2O$.

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corrected 6.0

CALCIUM GLUCONATE FOR INJECTION

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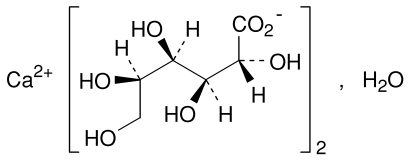

$C_{12}H_{22}CaO_{14},H_2O$ M_r 448.4

DEFINITION

Calcium D-gluconate monohydrate.

Content: 99.0 per cent to 101.0 per cent of $C_{12}H_{22}CaO_{14},H_2O$.

CHARACTERS

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

Solubility: sparingly soluble in water, freely soluble in boiling water.

IDENTIFICATION

A. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 20 mg of the substance to be examined in 1 ml of *water R*, heating if necessary in a water-bath at 60 °C.

Reference solution. Dissolve 20 mg of *calcium gluconate CRS* in 1 ml of *water R*, heating if necessary in a water-bath at 60 °C.

Plate: *TLC silica gel G plate R*.

Mobile phase: *concentrated ammonia R, ethyl acetate R, water R, ethanol (96 per cent) R* (10:10:30:50 *V/V/V/V*).

Application: 5 µl.

Development: over a path of 10 cm.

Drying: at 100 °C for 20 min and allow to cool.

Detection: spray with a 50 g/l solution of *potassium dichromate R* in a 40 per cent *m/m* solution of *sulphuric acid R*.

Results: after 5 min, the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

B. About 20 mg gives reaction (b) of calcium (*2.3.1*).

TESTS

Solution S. To 10.0 g add 90 ml of boiling *distilled water R* and boil with stirring, for not more than 10 s, until completely dissolved, then dilute to 100.0 ml with the same solvent.

Appearance of solution. At 60 °C, solution S is not more intensely coloured than reference solution B_7 (*2.2.2, Method II*). After cooling to 20 °C, it is not more opalescent than reference suspension II (*2.2.1*).

pH (*2.2.3*): 6.4 to 8.3.

Dissolve 1.0 g in 20 ml of *carbon dioxide-free water R*, heating on a water-bath.

Organic impurities and boric acid. Introduce 0.5 g into a porcelain dish previously rinsed with *sulphuric acid R* and placed in a bath of iced water. Add 2 ml of cooled *sulphuric acid R* and mix. No yellow or brown colour develops. Add 1 ml of *chromotrope II B solution R*. A violet colour develops and does not become dark blue. The solution is not more intensely coloured than that of a mixture of 1 ml of *chromotrope II B solution R* and 2 ml of cooled *sulphuric acid R*.

Oxalates. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 1.00 g of the substance to be examined in *water for chromatography R* and dilute to 100.0 ml with the same solvent.

Reference solution. Dissolve 1.00 g of the substance to be examined in *water for chromatography R*, add 0.5 ml of a 0.152 g/l solution of *sodium oxalate R* in *water for chromatography R* and dilute to 100.0 ml with the same solvent.

Guard column:

– *size*: *l* = 30 mm, Ø = 4 mm;

– *stationary phase*: suitable strong anion exchange resin (30-50 µm).

Columns 1 and 2:

– *size*: *l* = 0.25 m, Ø = 4 mm;

– *stationary phase*: suitable strong anion exchange resin (30-50 µm).

Anion-suppresser column: connected in series with the guard and analytical columns and equipped with a micromembrane that separates the mobile phase from the suppressor regeneration solution, flowing countercurrent to the mobile phase.

Mobile phase: dissolve 0.212 g of *anhydrous sodium carbonate R* and 63 mg of *sodium hydrogen carbonate R* in *water for chromatography R* and dilute to 1000.0 ml with the same solvent.

Flow rate of the mobile phase: 2 ml/min.

Suppressor regeneration solution: 1.23 g/l solution of *sulphuric acid R* in *water for chromatography R*.

Flow rate of the suppressor regeneration solution: 4 ml/min.

Detection: conductance.

Injection: 50 µl.

System suitability: reference solution:

– *repeatability*: maximum relative standard deviation of the area of the peak due to oxalate of 2.0 per cent after 5 injections.

Inject 50 µl of each solution 3 times. Calculate the content of oxalates in parts per million using the following expression:

$$\frac{S_T \times 50}{S_R - S_T}$$

S_T = area of the peak due to oxalate in the chromatogram obtained with the test solution;

S_R = area of the peak due to oxalate in the chromatogram obtained with the reference solution.

Limit:

– *oxalates*: maximum 100 ppm.