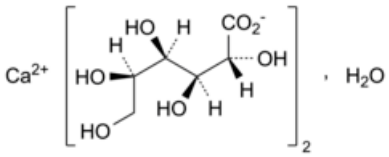
Edition: BP 2025 (Ph. Eur. 11.6 update)

Calcium Gluconate for Injection

General Notices

(Ph. Eur. monograph 0979)



$C_{12}H_{22}CaO_{14},H_2O$ 448.4 *18016-24-5*

Action and use

Used in treatment of calcium deficiency.

Preparation

Calcium Gluconate Injection

Ph Eur

DEFINITION

Calcium bis[(2*R*,3*S*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexanoate] monohydrate (calcium di(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 plate R* (5-40 µm) [or *TLC silica gel plate R* (2-10 µm)].

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

Application 1 µL.

Development Over 2/3 of the plate.

Drying At 100 °C for 20 min; allow to cool.

Detection Spray with a solution containing 10 g/L of *cerium sulfate R* and 25 g/L of *ammonium molybdate R* in *dilute sulfuric acid R* and heat at 105 °C for about 10 min.

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 *sulfuric acid R* and placed in a bath of iced water. Add 2 mL of cooled *sulfuric 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 *sulfuric acid R*.

Oxalates

Liquid chromatography (*2.2.29*).

Solvent mixture Dilute 1 mL of *hydrochloric acid R* to 1200 mL with *water for chromatography R*.

Test solution Dissolve 0.200 g of the substance to be examined in the solvent mixture using sonication and dilute to 10.0 mL with the solvent mixture.

Reference solution (a) Dilute 2.0 mL of a 0.152 g/L solution of *sodium oxalate R* to 100.0 mL with the solvent mixture.

Reference solution (b) Mix 2 mL of a 0.152 g/L solution of *sodium oxalate R*, 20 mL of *sulfate standard solution (10 ppm SO_4) R* and 50 mL of *water for chromatography R*, and dilute to 100 mL with *water for chromatography R*.

Precolumn:

— *size*: *l* = 50 mm, Ø = 4 mm;

— *stationary phase*: *strongly basic anion-exchange resin for chromatography R2* (13 µm).

Column:

— *size*: *l* = 0.25 m, Ø = 4 mm;

— *stationary phase*: *strongly basic anion-exchange resin for chromatography R2* (13 µm).

Mobile phase Dissolve 0.143 g of *sodium hydrogen carbonate R* and 0.191 g of *anhydrous sodium carbonate R* in *water for chromatography R* and dilute to 1000 mL with the same solvent.

Flow rate 2 mL/min.

Detection Conductivity detector equipped with a suitable ion suppressor.

Injection 50 µL.

Run time 1.5 times the retention time of oxalate.

Retention time Sulfate = about 8.1 min; oxalate = about 10.6 min.

System suitability Reference solution (b):

— *repeatability*: maximum relative standard deviation of 2.0 per cent for the area of the peak due to oxalate, determined on 5 injections;

— *resolution*: minimum 4.0 between the peaks due to sulfate and oxalate.

Calculation of content:

— for oxalates, use the concentration of sodium oxalate in reference solution (a).

Limit:

— *oxalates*: maximum 100 ppm.

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 for 10 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 boil for 1 min. Allow to stand for 2 min. No red precipitate is formed.

Chlorides (*2.4.4*)

Maximum 50 ppm.

To 10 mL of previously filtered solution S add 5 mL of *water R*.

Phosphates (*2.4.11*)

Maximum 100 ppm.

Dilute 1 mL of solution S to 100 mL with *water R*.

Sulfates (*2.4.13*)

Maximum 50 ppm, determined on previously filtered solution S.

Prepare the standard using a mixture of 7.5 mL of *sulfate standard solution (10 ppm SO_4) R* and 7.5 mL of *distilled water R*.

Iron

Maximum 5 ppm.

Atomic absorption spectrometry (2.2.23, Method I).

Test solution Introduce 2.0 g into a 100 mL polytetrafluoroethylene beaker and add 5 mL of *nitric acid R*. Boil, evaporating almost to dryness. Add 1 mL of *strong hydrogen peroxide solution R* and evaporate again almost to dryness. Repeat the hydrogen peroxide treatment until a clear solution is obtained. Using 2 mL of *nitric acid R*, transfer the solution into a 25 mL volumetric flask. Dilute to 25.0 mL with *dilute hydrochloric acid R*. In the same manner, prepare a compensation solution using 0.65 g of *calcium chloride R1* instead of the substance to be examined.

Reference solutions Prepare the reference solutions from *iron standard solution (20 ppm Fe) R*, diluting with *dilute hydrochloric acid R*.

Source Iron hollow-cathode lamp.

Wavelength 248.3 nm.

Atomisation device Air-acetylene flame.

Carry out a basic correction using a deuterium lamp.

Magnesium and alkali metals

Maximum 0.4 per cent.

To 0.50 g add a mixture of 1.0 mL of *dilute acetic acid R* and 10.0 mL of *water R* and rapidly boil, whilst shaking, until completely dissolved. To the boiling solution add 5.0 mL of *ammonium oxalate solution R* and allow to stand for at least 6 h. Filter through a sintered-glass filter (1.6) (2.1.2) into a porcelain crucible. Carefully evaporate the filtrate to dryness and ignite. The residue weighs not more than 2 mg.

Bacterial endotoxins (2.6.14)

Less than 167 IU/g.

Microbial contamination

TAMC: acceptance criterion 10^2 CFU/g (2.6.12).

ASSAY

Dissolve 0.350 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). Use 50 mg of *calconecarboxylic acid triturate R*.

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

Ph Eur