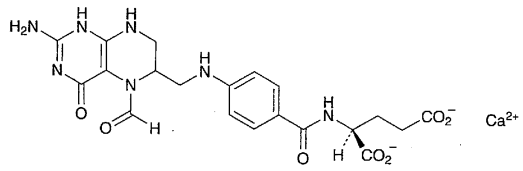
Calcium Folinate

Calcium Leucovorin

ホリナートカルシウム



$C_{20}H_{21}CaN_7O_7$: 511.50
Monocalcium *N*-{4-[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxopteridin-6-yl)methylamino]benzoyl}-L-glutamate [*1492-18-8*]

Calcium Folinate contains not less than 95.0% and not more than 102.0% of $C_{20}H_{21}CaN_7O_7$, calculated on the anhydrous basis.

Description Calcium Folinate occurs as a light yellow to yellow powder. It is odorless and tasteless.

It is very soluble in water, freely soluble in acetic acid (100), and practically insoluble in ethanol (95) and in diethyl ether.

It is gradually affected by light.

Identification **(1)** Determine the absorption spectrum of a solution of Calcium Folinate (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Calcium Folinate Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Calcium Folinate, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of previously dried Calcium Folinate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) A solution of Calcium Folinate (1 in 100) responds to the Qualitative Tests (2), (3) and (4) for calcium salt.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Calcium Folinate in 10 mL of water: the solution is clear and yellow.

(2) Heavy metals—Proceed with 0.40 g of Calcium Folinate according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 50 ppm).

Water Weigh accurately about 0.2 g of Calcium Folinate in a dried titration flask, and dissolve in 25 mL of acetic acid (100). Add 10.0 mL of Standard Water-Methanol Solution, titrate with Karl Fischer TS to the end point and perform the test: it is not more than 17.0%. Perform a blank determination, and make any necessary correction.

Assay Weigh accurately about 0.02 g of Calcium Folinate, dissolve in the mobile phase to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.0175 g of Calcium Folinate Reference Standard, calculated on the anhydrous basis, dissolve in the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine the peak areas, A_T and A_S, of folinate in each solution.

Amount (mg) of $C_{20}H_{21}CaN_7O_7$
= amount (mg) of Calcium Folinate Reference Standard, calculated on the anhydrous basis
$\times \frac{A_T}{A_S}$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 to 10 μm in particle diameter).

Column temperature: Room temperature.

Mobile phase: To 860 mL of water add 100 mL of acetonitrile and 15 mL of tetrabutylammonium hydroxide-methanol TS, adjust the pH to 7.5 with 2 mol/L sodium dihydrogenphosphate TS, and add water to make 1000 mL.

Flow rate: Adjust the flow rate so that the retention time of folinate is about 10 minutes.

Selection of column: Dissolve 0.0175 g of folic acid in 100 mL of the mobile phase, and to 5 mL of this solution add 20 mL of the standard solution. Proceed with 20 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of folinate and folic acid in this order with the resolution of these peaks being not less than 3.6.

System repeatability: When the test is repeated 6 times with the standard solution under the above operating conditions, the relative standard deviation of each peak area of folinate is not more than 2.0%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Calcium Gluconate

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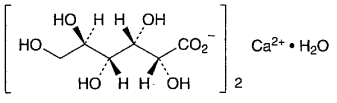

$C_{12}H_{22}CaO_{14}.H_2O$: 448.39
Monocalcium di-D-gluconate monohydrate [*299-28-5*]

Calcium Gluconate, when dried, contains not less than 99.0% and not more than 104.0% of $C_{12}H_{22}CaO_{14}.H_2O$.

Description Calcium Gluconate occurs as a white, crystalline powder or granules. It is odorless and tasteless.

It is freely soluble in hot water, soluble in water, and prac-

tically insoluble in ethanol (95) and in diethyl ether.

Identification (1) Dissolve 0.5 g of Calcium Gluconate in 5 mL of water by heating, add 0.65 mL of acetic acid (100) and 1 mL of freshly distilled phenylhydrazine, and heat on a water bath for 30 minutes. After cooling, scratch the inner surface of the vessel with a glass rod to induce crystallization. Collect the crystals, dissolve in 10 mL of hot water, add a small amount of activated charcoal, and filter. Cool the filtrate, scratch the inner surface of the vessel, filter the formed crystals by suction, wash with three 10 mL-portions of cold water, and dry: the crystals melt between 187°C and 199°C (with decomposition).

(2) A solution of Calcium Gluconate (1 in 40) responds to the Qualitative Tests for calcium salt.

Purity (1) Clarity of solution—Dissolve 1.0 g of Calcium Gluconate in 50 mL of water by warming: the solution is clear.

(2) Acid or alkali—Dissolve 0.50 g of Calcium Gluconate in 20 mL of water by warming. After cooling, add 0.10 mL of 0.01 mol/L hydrochloric acid VS and 2 drops of phenolphthalein TS: the solution remains colorless. To the solution add 0.30 mL of 0.01 mol/L sodium hydroxide VS: the solution turns red.

(3) Chloride—Take 0.40 g of Calcium Gluconate, and perform the test. Prepare the control solution with 0.80 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.071%).

(4) Sulfate—Take 1.0 g of Calcium Gluconate, and perform the test. Prepare the control solution with 1.0 mL of 0.005 mol/L sulfuric acid VS (not more than 0.048%).

(5) Heavy metals—Dissolve 1.0 g of Calcium Gluconate in 30 mL of water and 2 mL of dilute acetic acid by warming, cool, and add water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 2.0 mL of Standard Lead Solution, 2 mL of dilute acetic acid, and water to make 50 mL (not more than 20 ppm).

(6) Arsenic—Dissolve 0.6 g of Calcium Gluconate in 5 mL of water by warming, add 5 mL of dilute sulfuric acid and 1 mL of bromine TS, and concentrate on a water bath to 5 mL. Perform the test using Apparatus B with this solution as the test solution (not more than 3.3 ppm).

(7) Sucrose and reducing sugars—To 0.5 g of Calcium Gluconate add 10 mL of water and 2 mL of dilute hydrochloric acid, and boil the solution for 2 minutes. After cooling, add 5 mL of sodium carbonate TS, allow to stand for 5 minutes, add water to make 20 mL, and filter. To 5 mL of the filtrate add 2 mL of Fehling's TS, and boil for 1 minute: no orange-yellow to red precipitate is formed immediately.

Loss on drying Not more than 1.0% (1 g, 80°C, 2 hours).

Assay Weigh accurately about 0.4 g of Calcium Gluconate, previously dried, dissolve in 100 mL of water, add 2 mL of 8 mol/L potassium hydroxide TS and 0.1 g of NN indicator, and titrate immediately with 0.05 mol/L disodium dihydrogen ethylenediamine tetraacetate VS until the color of the solution changes from red-purple to blue.

Each mL of 0.05 mol/L disodium dihydrogen ethylenediamine tetraacetate VS
= 22.420 mg of $C_{12}H_{22}CaO_{14}.H_2O$

Containers and storage Containers—Well-closed containers.

Calcium Lactate

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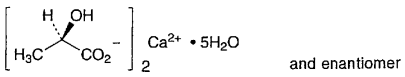

$C_6H_{10}CaO_6.5H_2O$: 308.29
Monocalcium bis[(*RS*)-2-hydroxypropanonate] pentahydrate [*63690-56-2*]

Calcium Lactate, when dried, contains not less than 97.0% of $C_6H_{10}CaO_6$ (mol. wt.: 218.22).

Description Calcium Lactate occurs as white powder or granules. It is odorless, and has a slightly acid taste.

A 1-g portion of it dissolves gradually in 20 mL of water, and it is slightly soluble in ethanol (95), and practically insoluble in diethyl ether.

It is partly efflorescent at ordinary temperature, and yields the anhydride at 120°C.

Identification A solution of Calcium Lactate (1 in 20) responds to the Qualitative Tests for calcium salt and for lactate.

Purity (1) Clarity of solution—Dissolve 1.0 g of Calcium Lactate in 20 mL of water by warming: the solution is clear.

(2) Acid or alkali—To the solution obtained in (1) add 2 drops of phenolphthalein TS: no red color is produced. Then add 0.50 mL of 0.1 mol/L sodium hydroxide VS: a red color develops.

(3) Heavy metals—Dissolve 1.0 g of Calcium Lactate in 30 mL of water and 5 mL of dilute acetic acid by warming, cool, add water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution from 2.0 mL of Standard Lead Solution and 2 mL of dilute acetic acid, and dilute with water to 50 mL (not more than 20 ppm).

(4) Magnesium or alkali metals—Dissolve 1.0 g of Calcium Lactate in 40 mL of water, add 0.5 g of ammonium chloride, boil, then add 20 mL of ammonium oxalate TS. Heat the mixture on a water bath for 1 hour, cool, dilute with water to 100 mL, and filter. To 50 mL of the filtrate add 0.5 mL of sulfuric acid, evaporate to dryness, and ignite between 450°C and 550°C to constant mass: the mass of the residue is not more than 5 mg.

(5) Arsenic—Dissolve 0.5 g of Calcium Lactate in 2 mL of water and 3 mL of hydrochloric acid, and perform the test with this solution as the test solution using Apparatus B (not more than 4 ppm).

(6) Volatile fatty acid—Warm 1.0 g of Calcium Lactate with 2 mL of sulfuric acid: an odor of acetic acid or butyric acid is not perceptible.

Loss on drying 25.0 - 30.0% (1 g, 80°C, 1 hour at first, then 120°C, 4 hours).

Assay Weigh accurately about 0.5 g of Calcium Lactate, previously dried, add water, dissolve by heating on a water