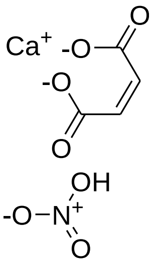
Calcium Citrate Malate



$Ca_3(C_6H_5O_7)_2,3CaC_4H_4O_5,6H_2O$ Mol. Wt.1123.0

Calcium Citrate Malate is 1,2,3-Propanetricarboxylic acid, 2-hydroxy- calcium salt mixture with 2-hydroxybutanedioic acid calcium salt (2:3:6),hexahydrate.

Calcium Citrate Malate is a complex of calcium, citrate and malate.

Calcium Citrate Malate contains not less than 23.0 per cent and not more than 24.2 per cent of calcium, calculated on the dried basis. The sum of citrate and malate is not less than 73.0 per cent, calculated on the dried basis.

Category. Calcium supplement

Description. A white or almost white powder.

Identification

A. Ignite completely 0.5 g at very low temperature, cool and dissolve the residue in *dilute glacial acetic acid*, filter. Add 10 ml of *ammonium oxalate* to the filtrate, a voluminous white precipitate is formed that is soluble in *hydrochloric acid*.

B. In the test for content of citrate, malate, and fumarate, the peaks due to citric acid and malic acid in the chromatogram obtained with the test solution corresponds to that in the chromatogram obtained with reference solution (d).

Tests

pH (2.4.24). 4.0 to 8.0, determined in 3.0 per cent w/v solution (*Note- The solution is slurry*).

Arsenic (2.3.10). Dissolve 3.3 g in 15 ml of *brominated hydrochloric acid* and 45 ml of *water* and remove the excess of bromine with a few drops of *stannous chloride solution AsT*. The resulting solution complies with the limit test for arsenic (3 ppm).

Lead (2.3.15). Not more than 0.0001 per cent.

Fluoride. Not more than 30 ppm.

NOTE-Prepare and store all solutions in plastic containers.

Buffer solution. A 29.4 per cent w/v solution of *sodium citrate dihydrate*.

Test solution. To 1.0 g of the substance under examination, add 10 ml of *water*, place on a hot plate stir with a magnetic stirrer. While stirring, add 10 ml of *1M hydrochloric acid* to dissolve. When dissolved, boil rapidly for 1 minute transfer to a 250-ml conical flask. Cool rapidly at room temperature in an ice bath, add 15 ml of buffer solution and 10 ml of *0.2 M EDTA* adjusted to pH 5.5 with *1 M hydrochloric acid* or *1 M sodium hydroxide*. Transfer the solution to a 100-ml volumetric flask and dilute to volume with *water*. Pour into 250-ml beaker for titration. Determine the end-point potentiometrically (2.4.25), using a suitable electrode system such as silver chloride reference electrode and fluoride specific ion indicating electrode.

Reference solution. A 0.11052 per cent w/v solution of *sodium fluoride* in *water.* Dilute 2.0 ml of the solution to 1000 ml with *water* (1µg per ml of fluoride ion).

Reference solution response line. Transfer 5.0 ml, 25.0 ml and 50 ml of the reference solution to three beakers containing plastic coated stirring bar, add 10 ml of *1 M hydrochloric acid*, 15 ml of buffer solution and *0.2 M EDTA* to each beaker, adjusted to pH 5.5 with *1M hydrochloric acid* or *1M sodium hydroxide*. Transfer the solution to individual 100-ml volumetric flask, dilute to volume with *water*. Pour the solutions back to 250-ml individual beakers for titration. Insert the electrode into solution and allow to stand for 15 minutes with constant stirring, determining the end point potentiometricaly (2.4.25). Plot the logarithms of the fluoride ion concentration (0.05,0.25 and 0.5 ppm) versus potential in milivolts. Rinse and dry the electrodes, insert them into the test solution, stir for 5 minutes and read the potential in milivolts.
Determine the concentration (in ppm) of fluoride ions in the test solution by measuring potential and the reference solution response line.

Content of Citrate, Malate, and Fumarate. Determine by liquid chromatography (2.4.14).

Solvent mixture. 0.2 *M hydrochloric acid*.

Test solution. Dissolve 0.5 g of the substance under examination in 100.0 ml of the solvent mixture.

Reference solution (a). A 0.18 per cent w/v solution of *citric acid RS* in the solvent mixture.

Reference solution (b). A 0.18 per cent w/v solution of *malic acid RS* in the solvent mixture.

Reference solution (c). A 0.002 per cent w/v solution of *fumaric acid RS* in the solvent mixture.

Reference solution (d). A 0.5 per cent w/v solution of *calcium citrate malate RS* in the solvent mixture.

Chromatographic system
- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- column temperature: 35°,
- mobile phase: A *0.05 M monobasic potassium phosphate* in *water*, adjusted to pH 2.5 with *orthophosphoric acid*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 226 nm,
- injection volume: 10µl.

Name	Relative retention time
Malic acid	0.6
Citric acid	1.0
Fumaric acid	1.4

Inject reference solution (a), (b), (c) and (d). The test is not valid unless the resolution between the peaks due to malic acid and citric acid is not less than 8.0 in the chromatogram obtained with reference solution (d), the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatograms obtained with reference solution (a),(b) and (c).

Inject reference solution (a), (b) (c) and the test solution.

Calculate the content of citric acid, malic acid and fumaric acid. Multiply by 0.98 to convert molecular weight of the acid form to the salt form.

Loss on drying (2.4.19). 8.0 per cent to 11.0 per cent, by drying in an oven at 150° for 4 hours.

Assay. Dissolve 0.35 g of the substance under examination in 10 ml of *water* and 3 ml of *3M hydrochloric acid* with swirling, add 90 ml of *water* and stir using a magnetic stirrer. While stirring, add 30.0 ml of *0.05 M disodium edetate* from the titration burette and 25 ml of *0.1 M sodium hydroxide,* and continue the titration with *0.05 M disodium edetate* using *hydroxyl naphthol blue* as indicator. Carry out a blank titration.

1 ml of *0.05 M disodium edetate* is equivalent to 0.002004 g of calcium.

Storage. Store protected from moisture.