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

Calcium Hydrogen Phosphate Dihydrate[1]

General Notices

Dibasic Calcium Phosphate

(Ph. Eur. monograph 0116)

NOTE: *The name Calcium Hydrogen Phosphate was formerly used in the United Kingdom.*

$CaHPO_4,2H_2O$ 172.1 *7789-77-7*

Ph Eur

DEFINITION

Content

98.0 per cent to 105.0 per cent.

♦ CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water and in ethanol (96 per cent). It dissolves in dilute hydrochloric acid and in dilute nitric acid.♦

IDENTIFICATION

A. Dissolve with heating 0.1 g in 10 mL of *dilute hydrochloric acid R*. Add 2.5 mL of *dilute ammonia R1*, shake and add 5 mL of a 35 g/L solution of *ammonium oxalate R*. A white precipitate is produced.
B. Dissolve 0.1 g in 5 mL of *dilute nitric acid R*, add 2 mL of *ammonium molybdate solution R* and heat at 70 °C for 2 min. A yellow precipitate is produced.
◊ C. It complies with the limits of the assay.◊

TESTS

Solution S

Dissolve 2.5 g in 20 mL of *dilute hydrochloric acid R*, filter if necessary and add *dilute ammonia R1* until a precipitate is formed. Add just sufficient *dilute hydrochloric acid R* to dissolve the precipitate and dilute to 50 mL with *distilled water R*.

Acid-insoluble substances

Maximum 0.2 per cent.

Dissolve 5.0 g in 40 mL of *water R*, add 10 mL of *hydrochloric acid R* and heat to boiling for 5 min. Cool, then collect the insoluble substances using ashless filter paper. Wash with *water R* until turbidity is no longer produced when *silver nitrate solution R2* is added to the filtrate. Ignite at 600 ± 50 °C. The residue weighs not more than 10 mg.

Carbonates

Shake 0.5 g with 5 mL of *carbon dioxide-free water R* and add 1 mL of *hydrochloric acid R*. No effervescence is produced.

Chlorides

Maximum 0.25 per cent.

Test solution Dissolve 0.20 g in a mixture of 20 mL of *water R* and 13 mL of *dilute nitric acid R* by warming if necessary, dilute to 100 mL with *water R* and filter if necessary. Use 50 mL of this solution.

Reference solution To 0.70 mL of *0.01 M hydrochloric acid*, add 6 mL of *dilute nitric acid R* and dilute to 50 mL with *water R*.

Add 1 mL of *silver nitrate solution R2* to the test solution and to the reference solution and mix. After standing for 5 min protected from light, any opalescence in the test solution is not more intense than that in the reference solution.

♦ **Fluorides**

Maximum 100 ppm.

Potentiometry (*2.2.36, Method II*).

Chelating solution Dissolve 45 g of *cyclohexylenedinitrilotetra-acetic acid R* in 75 mL of *sodium hydroxide solution R* and dilute to 250 mL with *water R*.

Test solution Dissolve 1.000 g in 4 mL of *hydrochloric acid R1*, add 20 mL of chelating solution, 2.7 mL of *glacial acetic acid R* and 2.8 g of *sodium chloride R*, adjust to pH 5-6 with *sodium hydroxide solution R* and dilute to 50.0 mL with *water R*.

Reference solution Dissolve 4.42 g of *sodium fluoride R*, previously dried at 300 °C for 12 h, in *water R* and dilute to 1000.0 mL with the same solvent. Dilute 50.0 mL of this solution to 500.0 mL with *total-ionic-strength-adjustment buffer R* (200 ppm F).

Indicator electrode Fluoride-selective.

Reference electrode Silver-silver chloride.

Carry out the measurement on 20.0 mL of the test solution. Add at least 3 times 0.10 mL of the reference solution and carry out the measurement after each addition. Calculate the concentration of fluorides using the calibration curve.♦

Sulfates

Maximum 0.5 per cent.

Test solution Dissolve 0.5 g in a mixture of 5 mL of *water R* and 5 mL of *dilute hydrochloric acid R* and dilute to 100 mL with *water R*. Filter if necessary. To 20 mL of this solution, add 1 mL of *dilute hydrochloric acid R* and dilute to 50 mL with *water R*.

Reference solution To 1.0 mL of *0.005 M sulfuric acid*, add 1 mL of *dilute hydrochloric acid R* and dilute to 50 mL with *water R*. Filter if necessary.

To the test solution and to the reference solution, add 2 mL of a 120 g/L solution of *barium chloride R* and allow to stand for 10 min. Any opalescence in the test solution is not more intense than that in the reference solution.

♦ **Arsenic** (*2.4.2, Method A*)

Maximum 10 ppm, determined on 2 mL of solution S.♦

Barium

To 0.5 g, add 10 mL of *water R* and heat to boiling. While stirring, add 1 mL of *hydrochloric acid R* dropwise. Allow to cool and filter if necessary. Add 2 mL of a 10 g/L solution of *dipotassium sulfate R* and allow to stand for 10 min. No turbidity is produced.

♦ **Iron** (*2.4.9*)

Maximum 400 ppm.

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

Loss on ignition

24.5 per cent to 26.5 per cent, determined on 1.000 g by ignition to constant mass at 800-825 °C.

ASSAY

Dissolve 0.4 g in 12 mL of *dilute hydrochloric acid R* by heating on a water bath if necessary and dilute to 200 mL with *water R*. To 20.0 mL of this solution add 25.0 mL of *0.02 M sodium edetate*, 50 mL of *water R*, 5 mL of *ammonium chloride buffer solution pH 10.7 R* and about 25 mg of *mordant black 11 triturate R*. Titrate the excess of sodium edetate with *0.02 M zinc sulfate*. Carry out a blank titration.

1 mL of *0.02 M sodium edetate* is equivalent to 3.44 mg of $CaHPO_4,2H_2O$.

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). Some of the characteristics described in the Functionality-related characteristics section may also be present in the mandatory part of the monograph since they also represent mandatory quality criteria. In such cases, a cross-reference to the tests described in the mandatory part is included in the Functionality-related characteristics section. Control of the characteristics can 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 hydrogen phosphate dihydrate used as filler in tablets and capsules.

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

Bulk density of powders (*2.9.34*)

Powder flow (*2.9.36*).◊

Ph Eur

[1] This monograph has undergone pharmacopoeial harmonisation. See chapter *5.8. Pharmacopoeial harmonisation*.