

Dibasic Calcium Phosphate Dihydrate

Pharmacopeial Discussion Group Sign-Off Document

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Legend: +, will adopt and implement; −, will not stipulate.

Nonharmonized attributes: Packaging and Storage, Heavy Metals, Limit of Fluoride, Iron

Specific local attributes: Identification C (EP), Lead (USP), Description (JP)

CaHPO₄ · 2H₂O 172.09
Phosphoric acid, calcium salt (1:1);
Calcium phosphate, dihydrate (1:1) [7789-77-7].

DEFINITION
Dibasic Calcium Phosphate Dihydrate contains two molecules of water of hydration. It contains NL T 98.0% and NMT 105.0% of dibasic calcium phosphate dihydrate (CaHPO₄ · 2H₂O).

IDENTIFICATION
A. Sample: 0.1 g of Dibasic Calcium Phosphate Dihydrate
Analysis: Dissolve the Sample by warming in 10 mL of 2 N hydrochloric acid. Add 2.5 mL of ammonia TS dropwise, with shaking, and then add 5 mL of ammonium oxalate solution (freshly prepared).
Acceptance criteria: A white precipitate is formed.

B. Sample: 0.1 g of Dibasic Calcium Phosphate Dihydrate
Analysis: Dissolve the Sample in 5 mL of dilute nitric acid. Warm the solution to 70 °C, and add 2 mL of 10% ammonium molybdate solution (freshly prepared).
Acceptance criteria: A yellow precipitate of ammonium phosphomolybdate is formed.

ASSAY

Buffer: Dissolve 53.5 g of ammonium chloride with sufficient water in a 1000-mL volumetric flask. Add 570 mL of ammonia water, stronger, and dilute with water to volume. The pH of this solution is 10.7.

Sample solution: Transfer 400 mg of Dibasic Calcium Phosphate Dihydrate to a 200-mL volumetric flask. Dissolve in 12 mL of diluted hydrochloric acid with the aid of gentle heat, if necessary, and dilute with water to volume.

Blank: 20 mL of water containing 1.2 mL of diluted hydrochloric acid

Titrmetric system
(See Titrimetry (541).)
Mode: Residual titration
Titrant: 0.02 M edetate disodium VS
Back-titrant: 0.02 M zinc sulfate VS
Endpoint detection: Visual
Analysis: To 20.0 mL of the Sample solution add 25.0 mL of Titrant, 50 mL of water, and 5 mL of Buffer. Add 25 mg of eriochrome black T–sodium chloride indicator. Titrate with the Back-titrant. Perform a Blank determination in the same manner.
Calculate the percentage of dibasic calcium phosphate dihydrate (CaHPO₄ · 2H₂O) in the sample taken:

\[
\text{Result} = \left(\frac{V_B - V_S}{V_S} \times M \times f \times W\right) \times 100
\]

\[
V_B = \text{Back-titrant volume consumed by the Blank (mL)}
\]

\[
V_S = \text{Back-titrant volume consumed by the Sample (mL)}
\]

\[
M = \text{actual molarity of the Back-titrant (mM/mL)}
\]

\[
F = \text{equivocality factor, 172.1 mg/mM}
\]

\[
W = \text{Sample weight (mg)}
\]

Acceptance criteria: 98.0%–105.0%

IMPURITIES

• CARBONATE
Sample: 1.0 g of Dibasic Calcium Phosphate Dihydrate
Analysis: Mix the Sample with 5 mL of carbon dioxide-free water, and immediately add 2 mL of hydrochloric acid.
Acceptance criteria: No effervescence occurs.

• CHLORIDE AND SULFATE, Chloride (221)
Standard: 0.70 mL of 0.010 N hydrochloric acid
Sample: 0.2 g of Dibasic Calcium Phosphate Dihydrate
Analysis: To the Sample add 20 mL of water and 13 mL of dilute nitric acid, and warm gently, if necessary, to completely dissolve. Dilute with water to 100 mL, and filter if necessary. To 50 mL of the filtrate add 1 mL of silver nitrate TS.
Acceptance criteria: The turbidity of the Sample does not exceed that of the Standard (NMT 0.25%).

• CHLORIDE AND SULFATE, Sulfate (221)
Standard: 1.0 mL of 0.010 N sulfuric acid
Sample: 0.5 g of Dibasic Calcium Phosphate Dihydrate
Analysis: To the Sample add 5 mL of water and 5 mL of dilute hydrochloric acid, and warm gently, if necessary, to completely dissolve. Dilute with water to 100 mL, and filter if necessary. To 20 mL of the filtrate add 1 mL of dilute hydrochloric acid, and dilute with water to 50 mL. Add 1 mL of barium chloride TS.
Acceptance criteria: The turbidity of the Sample does not exceed that of the Standard (NMT 0.5%).

• ARSENIC, Method I (211)
Test preparation: 1.0 g in 25 mL of 3 N hydrochloric acid, diluted with water to 55 mL. Omit the addition of 20 mL of 7 N sulfuric acid specified in Procedure.
Acceptance criteria: NMT 3 µg/g

• BARIUM
Sample: 0.5 g Dibasic Calcium Phosphate Dihydrate
Analysis: Heat the Sample to boiling with 10 mL of water, and add 1 mL of hydrochloric acid dropwise, stirring after each addition. Allow to cool, and filter, if necessary. To the filtrate add 2 mL of potassium sulfate TS.
Acceptance criteria: No turbidity is produced within 10 min.

• HEAVY METALS, Method I (231)
Test preparation: Warm 1.3 g with 3 mL of 3 N hydrochloric acid to completely dissolve. Cool, dilute with water to 50 mL, and filter.
Acceptance criteria: NMT 30 ppm

• LIMIT OF ACID-INSOLUBLE SUBSTANCES
Sample solution: Dissolve 5.0 g in a mixture of 40 mL of water and 10 mL of hydrochloric acid by boiling gently for 5 min.
Analysis: After cooling, collect the insoluble substance on ashless filter paper, and wash with water until the last washing does not give a reaction for chloride (no turbidity results from the addition of silver nitrate TS). Ignite to completely incinerate the residue and the ashless filter paper at 600 ± 50 °C.
Acceptance criteria: The weight of the residue does not exceed 10 mg (NMT 0.2%).
• **LIMIT OF FLUORIDE**

**DEFINITION**
Anhydrous Dibasic Calcium Phosphate contains NLT 98.0% and NMT 103.0% of anhydrous dibasic calcium phosphate (CaHPO₄).

**IDENTIFICATION**
- **A.**
  - Sample: 0.1 g of Anhydrous Dibasic Calcium Phosphate
  - Analysis: Dissolve the Sample by warming in 10 mL of 2 N hydrochloric acid. Add 2.5 mL of ammonia TS dropwise, with shaking, and then add 5 mL of ammonium oxalate TS.
  - Acceptance criteria: A white precipitate is formed.

- **B.**
  - Sample: 0.1 g of Anhydrous Dibasic Calcium Phosphate
  - Analysis: Dissolve the Sample in 5 mL of diluted nitric acid. Warm the solution to 70 °C and add 2 mL of 10% ammonium molybdate solution (freshly prepared).
  - Acceptance criteria: A yellow precipitate of ammonium phosphomolybdate is formed.

**ASSAY**
- **PROCEDURE**
  - Buffer: Dissolve 53.5 g of ammonium chloride with sufficient water in a 1000-mL volumetric flask. Add 570 mL of ammonia water, stronger, and dilute with water to volume. The pH of this solution is 10.7.

  - Sample solution: Transfer 400 mg of Anhydrous Dibasic Calcium Phosphate to a 200-mL volumetric flask. Dissolve in 12 mL of diluted hydrochloric acid with the aid of gentle heat, if necessary, and dilute with water to volume.

  - Blank: 20 mL of water containing 1.2 mL of diluted hydrochloric acid

  - Titrimetric system
    - (See Titrimetry (541).)
  - Mode: Residual titration
  - Titrant: 0.02 M edetate disodium VS
  - Back-titrant: 0.02 M zinc sulfate VS
  - Endpoint detection: Visual

  - Analysis: To 20.0 mL of the Sample solution add 25.0 mL of Titrant, 50 mL of water, and 5 mL of Buffer. Add 25 mg of eriochrome black T-sodium chloride indicator. Titrate the excess Titrant with the Back-titrant. Perform a Blank determination in the same manner.

  - Calculate the percentage of anhydrous dibasic calcium phosphate (CaHPO₄) in the sample taken:
    
    \[
    \text{Result} = 100 \times \left( \frac{\left( V_b - V_s \right) \times M \times F}{W} \right)
    \]

  - \( V_s \) = Back-titrant volume consumed by the Blank (mL)
  - \( V_b \) = Back-titrant volume consumed by the Sample (mL)
  - \( M \) = actual molarity of the Back-titrant (mM/mL)
  - \( F \) = equivalency factor, 136.06 mg/mM
  - \( W \) = Sample weight (mg)

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**SPECIFIC TESTS**
- **Loss on Ignition (733)**
  - Sample: 1 g of Dibasic Calcium Phosphate Dihydrate
  - Analysis: Ignite the Sample at 800–825 °C to constant weight.
  - Acceptance criteria: 24.5%–26.5%

**ADDITIONAL REQUIREMENTS**
- **Packaging and Storage:** Preserve in well-closed containers. No storage requirements specified.
- **USP Reference Standards (11)**
  - USP Sodium Fluoride RS

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**Pharmacopeial Discussion Group Sign-Off Document**

**Attribute**
- JP
- EP
- USP

**Anhydrous Dibasic Calcium Phosphate**

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**Legend:** + will adopt and implement; - will not stipulate.