Calcium Acetate Capsules

Type of Posting: Revision Bulletin
Posting Date: 26–Apr–2019
Official Date: 01–May–2019
Expert Committee: Chemical Medicines Monographs 6
Reason for Revision: Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 6 Expert Committee has revised the Calcium Acetate Capsules monograph. The purpose for the revision is to add Dissolution Test 2 and Dissolution Test 3 to accommodate FDA-approved drug products with different dissolution conditions and tolerances than the existing dissolution test. A Labeling section has also been incorporated to support the inclusion of Dissolution Test 2 and Dissolution Test 3.

The Calcium Acetate Capsules Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Michael Chang, Scientific Liason (301-230-3217 or mxc@usp.org).
Calcium 1

PERFORMANCE TESTS

Change to read:

▲ Dissolution (711)

▲ Test 1 (8B1-May-2019)

Medium: Water; 900 mL
Apparatus 2: 50 rpm, with sinkers
Time: 10 min

Mobile phase, Standard solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute with Medium to a concentration similar to the Standard solution, if necessary.

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of calcium acetate (C₆H₆CaO₄) dissolved at time point (t):

Result = \left( \frac{r_u}{r_S} \right) \times \left( \frac{C_i}{C_0} \right) \times V \times D \times (1/L) \times 100

r_u = peak response of calcium from the Sample solution
r_S = peak response of calcium from the Standard solution
C_i = concentration of USP Calcium Acetate RS in the Standard solution (mg/mL)
V = volume of Medium, 900 mL
D = dilution factor for the Sample solution, if needed
L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of calcium acetate (C₆H₆CaO₄) is dissolved.

▲ Test 2: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 2.

Medium: 0.1 N hydrochloric acid; 900 mL
Apparatus 1: 100 rpm
Time: 15 min
Blank: 0.2% (v/v) nitric acid

Standard solutions: 4.0, 5.0, 6.0, 7.0, and 8.0 µg/mL of calcium [from commercially available, National Institute of Standards and Technology (NIST) traceable standard solution for calcium] in Blank

Sample solution: Pass a portion of the solution under test through a suitable filter of 1.0-µm pore size. Dilute with Blank to a concentration similar to 6.0-µg/mL Standard solution, if necessary.

Instrumental conditions

(See Atomic Absorption Spectroscopy (852).)

Mode: Atomic absorption spectrometry

Analytical wavelength: 422.8 nm

Lamp: Calcium hollow-cathode

Flame: Air–acetylene oxidizing flame

System suitability

Samples: Blank and Standard solutions

Suitability requirements

Linearity: Use the Blank to set the instrument to zero. Concomitantly determine the responses for each of the Standard solutions. Construct a linear calibration curve by plotting the absorbance values of the Standard solutions versus their corresponding concentrations, in micrograms per milliliter.

Correlation coefficient: NLT 0.995
If the product complies with this test, the labeling=

Simulated gastric fluid TS; 900 mL

concentration of calcium acetate in the 4

15 min

2.4, 3.2, 4.0, 4.8, and 5.6 µg/mL

volume of Water; 900 mL

Calcium hollow-cathode

To an aliquot of the

label claim (mg/Capsule)  

dilution factor for the  

To an aliquot of the 100 rpm, with sinkers

Molecular weight of calcium, 40.08

Molecular weight of calcium acetate, 158.17

Dilution factor for the

Equivalency factor, 0.001 mg/µg

Pass a portion of the solution

Atomic absorption spectrometry

Equivalency factor, 0.001 mg/µg

15 min

Within ±5%, the absorbance value of 5.6

Tier 2

Tier 1

Tier 2

Medium 1: Water; 900 mL

Apparatus 2: 100 rpm, with sinkers

Dissolution procedure: Perform the test using the

cross-linking, repeat the test with a new set of Capsules using the

tier 2.

Analytical procedure 1

Blank: 0.02 N nitric acid

Standard solutions: 2.4, 3.2, 4.0, 4.8, and 5.6 µg/mL of USP Calcium Acetate RS in Blank

Sample solution: Nominally 3.7 µg/mL of calcium acetate from Sample stock solution, dilute with Blank if necessary

Instrumental conditions

(See Atomic Absorption Spectroscopy (852).)

Mode: Atomic absorption spectrometry

Analytical wavelength: 422.8 nm

Lamp: Calcium hollow-cathode

Flame: Nitrous oxide-acetylene

Replicates: 4

System suitability

Samples: Blank, Standard solutions, and Sample solution

Suitability requirements

Relative standard deviation: NMT 3.0% in 4 replicate measurements, Standard solutions and Sample solution

Correlation coefficient: NLT 0.995, use the Blank to set the instrument to zero. Concomitantly
determine the responses for each of the Standard solutions. Construct a quadratic calibration curve by plotting the absorbance values of the Standard solutions versus their corresponding concentrations, in micrograms per milliliter.

Drift: Within ±5%, the absorbance value of 5.6 µg/mL of USP Calcium Acetate RS from the Standard solutions. See Atomic Absorption Spectroscopy (852), Procedure, Analysis.

Analytical procedure 2

Titrimetric system

(See Titrimetry (541).)

Mode: Complexometric titration

Titrant: 0.005 M edetate acid (EDTA)

Endpoint detection: Photometric at 610 nm

Analysis: To an aliquot of the Sample stock solution equivalent to about 7.4 mg of calcium acetate, add 60 mL of 0.1 N sodium hydroxide and 0.2 g of hydroxynaphthol blue indicator. Titrate with Titrant, determining the endpoint photometrically using a suitable autotitrator.

Calculate the percentage of the labeled amount of calcium acetate (C₆H₆CaO₄) dissolved:

\[
\text{Result} = C \times V \times F \times D \times (1/L) \times 100
\]

C = concentration of calcium in the Sample solution determined (µg/mL)
V = volume of Medium, 900 mL
F = equivalency factor, 0.001 mg/µg
D = dilution factor for the Sample solution, if needed
M₁ = molecular weight of calcium acetate, 158.17
M₂ = molecular weight of calcium, 40.08
L = label claim (mg/Capsule)

Test 3: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 3.

Tier 1

Medium 1: Water; 900 mL

Apparatus 2: 100 rpm, with sinkers

Time: 15 min

Determine the amount of calcium acetate dissolved using Analytical procedure 1 or Analytical procedure 2 for Tier 1 and Analytical procedure 3 for Tier 2.

Sample stock solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size;

Dissolution procedure: Perform the test using the conditions under Tier 1. In the presence of cross-linking, repeat the test with a new set of Capsules using the conditions under Tier 2.

Analytical procedure 3

Blank: Medium

Titrimetric system

(See Titrimetry (541).)

Mode: Complexometric titration

Titrant: 0.005 M edetate acid (EDTA)

Endpoint detection: Visual

Analysis: To an aliquot of the Sample stock solution equivalent to about 7.4 mg of calcium acetate, add 50 mL of water, 10 mL of 0.1 N sodium hydroxide, and 0.2 g of hydroxynaphthol blue indicator. Titrate with Titrant to a blue endpoint while stirring using a

\[
\text{Result} = V_i \times M \times F \times (V_i/V_j) \times (1/L) \times 100
\]

V_i = volume of Titrant consumed by the aliquot of Sample stock solution (mL)
M = actual Titrant concentration, in molarity (mmol/mL)
F = equivalency factor of calcium acetate, 158.17 mg/mmol
V_j = volume of Medium, 900 mL
V_i = volume of the aliquot taken for Analysis (mL)
L = label claim (mg/Capsule)
magnetic stirring bar. Perform a Blank determination in the same manner.
Calculate the percentage of the labeled amount of calcium acetate \((\text{C}_4\text{H}_6\text{CaO}_4)\) dissolved:

\[
\text{Result} = \left( \frac{V_S - V_B}{V_M} \right) \times M \times F \times \left( \frac{V_A}{V_M} \right) \times \left( \frac{1}{L} \right) \times 100
\]

- \(V_S\) = volume of Titrant consumed by the aliquot of Sample stock solution (mL)
- \(V_B\) = volume of Titrant consumed by the Blank (mL)
- \(M\) = actual Titrant concentration, in molarity (mmol/mL)
- \(F\) = equivalency factor of calcium acetate, 158.17 mg/mmol
- \(V_M\) = volume of Medium, 900 mL
- \(V_A\) = volume of the aliquot taken for Analysis (mL)
- \(L\) = label claim (mg/Capsule)

**Tolerances:** NLT 85\% (Q) of the labeled amount of calcium acetate \((\text{C}_4\text{H}_6\text{CaO}_4)\) is dissolved. ▲ (RB 1-May-2019)

**Uniformity of Dosage Units** (905): Meet the requirements

**Specific Tests**
- **Microbial Enumeration Tests** (61) and **Tests for Specified Microorganisms** (62): The total aerobic microbial count does not exceed \(10^3\) cfu/g, and the total combined molds and yeast count does not exceed \(10^2\) cfu/g. It meets the requirements of the test for the absence of *Escherichia coli*.

**Additional Requirements**
- **Packaging and Storage:** Preserve in well-closed containers and store at controlled room temperature.

**Add the following:**

▲ **Labeling:** When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used. ▲ (RB 1-May-2019)

**USP Reference Standards** (11)
- USP Calcium Acetate RS ▲ USP 1-May-2019