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Potassium Citrate Extended-Release Tablets

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DEFINITION

Potassium Citrate Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of potassium citrate as monohydrate ($C_6H_5K_3O_7 \cdot H_2O$).

IDENTIFICATION

- **A. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Potassium**

Sample solution: Powder 5 Tablets, mix with 20 mL of [water](#), and filter.

Acceptance criteria: The filtrate meets the requirements.

- **B. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Citrate**

Sample: A portion of powdered Tablets containing about 50 mg of potassium citrate

Acceptance criteria: Meet the requirements

ASSAY

- **PROCEDURE**

Buffer: 3.4 g/L of [monobasic potassium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 2.2.

Mobile phase: *Buffer*

Standard solution: 0.4 mg/mL of [USP Citric Acid RS](#) in *Mobile phase*

Sample stock solution: Weigh and finely powder NLT 20 Tablets. Transfer a portion of the powder, equivalent to 2000 mg of potassium citrate monohydrate, to a 250-mL volumetric flask, and add 150 mL of hot [water](#) (60°–70°). Sonicate for 20 min with occasional shaking. Allow to cool to room temperature, dilute with [water](#) to volume, and mix.

Sample solution: Pass a portion of the *Sample stock solution* through a suitable filter of 0.45-μm pore size, discarding the first 5 mL of filtrate. Transfer 4 mL of the filtrate to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. [NOTE—Reserve the remaining filtrate for use in the *Content of Potassium* test.]

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 5-μm packing L1

Column temperature: 55°

Flow rate: 1 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of potassium citrate monohydrate ($C_6H_5K_3O_7 \cdot H_2O$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = citric acid peak area from the *Sample solution*

r_s = citric acid peak area from the *Standard solution*

C_s = concentration of [USP Citric Acid RS](#) in the *Standard solution* (mg/mL)

C_u = nominal concentration of potassium citrate monohydrate in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of potassium citrate monohydrate, 324.41

M_{r2} = molecular weight of citric acid ($C_6H_8O_7$), 192.13

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

• CONTENT OF POTASSIUM

Standard stock solution: 19.07 µg/mL of potassium chloride, previously dried at 105° for 2 h, in [water](#). This solution contains 10 µg/mL of potassium.

Standard solutions: Transfer 10.0, 15.0, and 20.0 mL, respectively, to separate 100-mL volumetric flasks of the *Standard stock solution*. To each flask, add 2.0 mL of sodium chloride solution (200 mg/mL) and 1.0 mL of hydrochloric acid, and dilute with [water](#) to volume. The *Standard solutions* contain 1.0, 1.5, and 2.0 µg/mL of potassium, respectively.

Sample stock solution: Dilute the clear filtrate, reserved from the Assay, with [water](#) to obtain a solution containing about 160 µg/mL of potassium citrate monohydrate.

Sample solution: Transfer 3.0 mL of the *Sample stock solution* to a 100-mL volumetric flask.

Instrumental conditions

(See [Atomic Absorption Spectroscopy \(852\)](#).)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: Potassium emission line at 766.5 nm

Lamp: Potassium hollow-cathode

Flame: Air–acetylene

Blank: [Water](#)

Analysis

Samples: *Standard solutions*, *Sample solution*, and *Blank*

Plot the absorbance of the *Standard solutions* versus the concentration of potassium, in µg/mL, and draw the straight line best fitting the three plotted points. From the graph obtained, determine the concentration of potassium in the *Sample solution* (µg/mL).

Calculate the percentage of potassium (K) in the portion of Tablets taken:

$$\text{Result} = C \times 100/C_u$$

C = concentration of potassium in the *Sample solution* as determined in this test (µg/mL)

C_u = concentration of potassium citrate anhydrous ($C_6H_5K_3O_7$) in the *Sample solution* calculated from the Assay value of potassium citrate monohydrate ($C_6H_5K_3O_7 \cdot H_2O$) (µg/mL)

Acceptance criteria: 36.4%–40.2%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#)

Test 1

Medium: [Water](#); 900 mL

Apparatus 2: 50 rpm

Times: 0.5, 1, and 3 h; without *Medium* replacement

[NOTE—Withdraw the same volume at each time point.]

Standard stock solution and **Standard solutions:** Prepare as directed in the *Content of Potassium* test.

Sample solution: Filter the solution under test and dilute quantitatively with *Medium* to obtain a solution containing about 60 µg of potassium citrate per mL. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, add 2.0 mL of [sodium chloride](#) solution (1 in 5) and 1.0 mL of [hydrochloric acid](#). Dilute with [water](#) to volume, and mix.

Instrumental conditions

(See [Atomic Absorption Spectroscopy \(852\)](#).)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: Potassium emission line at 766.5 nm

Lamp: Potassium hollow-cathode

Flame: Air–acetylene

Blank: [Water](#)

Analysis

Samples: *Standard solutions, Sample solution, and Blank*

Determine the concentration, in µg/mL, of potassium in the *Sample solution* at each time point.

Calculate the percentage of the labeled amount of potassium citrate monohydrate ($C_6H_5K_3O_7 \cdot H_2O$) dissolved at each time point:

At 0.5 h:

$$\text{Result}_1 = C_1 \times V \times R \times F \times 100/L$$

At 1 h:

$$\text{Result}_2 = [C_2 \times (V - V_s) + C_1 \times V_s] \times R \times F \times 100/L$$

At 3 h:

$$\text{Result}_3 = \{C_3 \times [V - 2 \times V_s] + (C_1 + C_2) \times V_s\} \times R \times F \times 100/L$$

C = as C_1, C_2, C_3 , concentration of potassium in the *Sample solution* at each time point (µg/mL)

V = volume of *Medium*, 900 mL

R = ratio of the molecular weight of potassium citrate monohydrate to 3 times the atomic weight of potassium, 2.765

F = dilution factor of the *Sample solution*

L = label claim (mg/Tablet)

V_s = volume of sample withdrawn at each time point (mL)

Tolerances: The percentages of the labeled amount of potassium citrate monohydrate ($C_6H_5K_3O_7 \cdot H_2O$) dissolved from the Tablets are NMT 45% (Q) in 30 min, NMT 60% (Q') in 1 h, and NLT 80% (Q'') in 3 h. The requirements are met if the quantities dissolved from the Tablets tested conform to [Table 1](#) instead of the table shown under [Dissolution \(711\)](#).

Table 1

Stage	Number Tested	Acceptance Criteria
S_1	6	Each unit is within the range between $Q \pm 10\%$ and $Q' \pm 10\%$, and is NLT $Q'' + 5\%$ at the stated times.
S_2	6	Average of 12 units ($S_1 + S_2$) is within the range between $Q \pm 10\%$ and $Q' \pm 10\%$ and is NLT Q'' ; no unit is outside the range between $Q \pm 15\%$ and $Q' \pm 15\%$, and no unit is less than $Q'' - 5\%$ at the stated times.
S_3	12	Average of 24 units ($S_1 + S_2 + S_3$) is within the range between $Q \pm 10\%$ and $Q' \pm 10\%$ and is NLT Q'' ; NMT 1 unit is outside the range between $Q \pm 15\%$, NMT 1 unit is outside the range between $Q' \pm 15\%$, and NMT 1 unit is less than $Q'' - 5\%$ at the stated times.

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

Medium: [Water](#); 900 mL

Apparatus 2: 50 rpm

Times: 0.5, 1, 4, and 6 h. Replace the volume withdrawn with the equal volume of *Medium* preheated to $37 \pm 0.5^\circ$.

Buffer: 3.4 g/L of [monobasic potassium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 2.2.

Mobile phase: *Buffer*

Standard solution: Prepare a solution of [USP Citric Acid RS](#) in *Medium* as directed in [Table 2](#).

Table 2

Tablet Strength (mg, as potassium citrate monohydrate)	Concentration of Citric Acid (mg/mL)
540	0.35
1080	0.70
1620	1.05

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 5 mL of filtrate.

Chromatographic system
(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 55°

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the concentration, in mg/mL, of potassium citrate monohydrate ($C_6H_5K_3O_7 \cdot H_2O$) in the sample withdrawn from the vessel at each time point:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

- r_U = citric acid peak area from the *Sample solution*
- r_S = citric acid peak area from the *Standard solution*
- C_S = concentration of [USP Citric Acid RS](#) in the *Standard solution* (mg/mL)
- M_{r1} = molecular weight of potassium citrate monohydrate ($C_6H_5K_3O_7 \cdot H_2O$), 324.41
- M_{r2} = molecular weight of citric acid ($C_6H_8O_7$), 192.13

Calculate the percentage of the labeled amount of potassium citrate monohydrate ($C_6H_5K_3O_7 \cdot H_2O$) dissolved at each time point:

At 0.5 h:

$$\text{Result}_1 = C_1 \times V \times 100/L$$

At 1 h:

$$\text{Result}_2 = (C_2 \times V + C_1 \times V_S) \times 100/L$$

At 4 h:

$$\text{Result}_3 = [C_3 \times V + (C_1 + C_2) \times V_S] \times 100/L$$

At 6 h: