Potassium Citrate Extended-Release Tablets

**DEFINITION**

Potassium Citrate Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of potassium citrate as monohydrate (C₆H₅K₃O₇·H₂O). [RB 1-Feb-2015]

**IDENTIFICATION**

• **A. IDENTIFICATION TESTS—GENERAL, Potassium (191):**
  Sample solution: Powder 5 Tablets, mix with 20 mL of water, and filter.
  Acceptance criteria: The filtrate meets the requirements.

• **B. IDENTIFICATION TESTS—GENERAL, Citrate (191):**
  Sample: A portion of powdered Tablets containing about 50 mg of potassium citrate
  Acceptance criteria: Meet the requirements

**ASSAY**

**Change to read:**

- **PROCEDURE**
  Mobile phase, Standard solution 1, and Chromatographic system: Proceed as directed under Assay for Citric Acid/Citrate and Phosphate (345).
  Sample solution: Weigh and finely powder NLT 20 Tablets. Transfer a portion of the powder, equivalent to about 200 mg of potassium citrate monohydrate, to a 1000-mL volumetric flask, add about 300 mL of hot water, and shake by mechanical means for 15 min. Allow to cool, dilute with water to volume, and mix. Filter, discarding the first 30 mL of the filtrate. Transfer an aliquot of the clear filtrate to a suitable volumetric flask. Dilute with water and freshly prepared sodium hydroxide solution to obtain a solution containing about 20 µg/mL of citrate in 1 mM sodium hydroxide.
  [Note—Reserve the remaining filtrate for use in Content of Potassium.]

  Analysis
  Samples: Standard solution 1 and Sample solution
  Calculate the percentage of potassium citrate monohydrate (C₆H₅K₃O₇·H₂O) [RB 1-Feb-2015] in the portion of Tablets taken:

  \[
  \text{Result} = \left( \frac{r_0}{r_3} \right) \times \left( \frac{C_i}{C_o} \right) \times \left( \frac{M_1}{M_2} \right) \times 100
  \]

  \( r_0 \) = citrate peak area from the Sample solution
  \( r_3 \) = citrate peak area from Standard solution 1
  \( C_i \) = concentration of citrate in Standard solution 1 (µg/mL)
  \( C_o \) = nominal concentration of potassium citrate in the Sample solution (µg/mL)
  \( M_1 \) = molecular weight of potassium citrate monohydrate, 324.41 [RB 1-Feb-2015]
  \( M_2 \) = molecular weight of citrate (C₆H₅O₇), 189.10
  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°C 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 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 solution:** Transfer 3.0 mL of the clear filtrate, reserved from the Assay, 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 Spectrophotometry and Light-Scattering (851).)

**Mode:** Atomic absorption spectrophotometry

**Analytical wavelength:** Potassium emission line at 766.5 nm

**Performance Tests**

**Change to read:**

- **Dissolution (711)**
  Test 1: [RB 1-Feb-2015]
  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.

  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 Spectrophotometry and Light-Scattering (851).)

  **Mode:** Atomic absorption spectrophotometry

  **Analytical wavelength:** Potassium emission line at 766.5 nm

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**Potassium**

**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 (C₆H₅K₃O₇ · H₂O) dissolved at each time point.

At 0.5 h:

\[ \text{Result}_1 = (C_1 \times V/L) \times R \times F \times 100 \]

At 1 h:

\[ \text{Result}_2 = (C_2 \times (V - V_3) + C_1 \times V_3) \times R \times F \times 100/L \]

At 3 h:

\[ \text{Result}_3 = (C_1 \times [V - 2 \times V_3] + (C_1 + C_2) \times V_3) \times R \times F \times 100/L \]

\[ C = \text{as } C_1, C_2, C_3, \text{ concentration of potassium in the Sample solution at each time point (µg/mL)} \]

\[ V = \text{volume of Medium, } 900 \text{ mL} \]

\[ L = \text{label claim (mg/Tablet)} \]

\[ R = \text{ratio of the molecular weight of potassium citrate monohydrate to 3 times the atomic weight of potassium, } 2.765 \]

\[ F = \text{dilution factor of the Sample solution} \]

\[ V_i = \text{volume of sample withdrawn at each time point (mL)} \]

**Tolerances:** The percentages of the labeled amount of potassium citrate monohydrate (C₆H₅K₃O₇ · H₂O) dissolved from the Tablets are NMT 45% (Q₁) in 30 min, NMT 60% (Q₂) in 1 h, and NLT 80% (Q₃) 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>
<thead>
<tr>
<th>Stage</th>
<th>Number Tested</th>
<th>Acceptance Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>S₁</td>
<td>6</td>
<td>Each unit is within the range between Q ± 10% and Q ± 10%, and NLT Q’ + 5% at the stated times.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Average of 12 units (S₁ + S₂) is within the range between Q ± 10% and Q ± 10% and is NLT Q”; no unit is outside the range between Q ± 15% and Q’ ± 15%; and no unit is less than Q” – 5% at the stated times.</td>
</tr>
<tr>
<td>S₂</td>
<td>6</td>
<td>Average of 24 units (S₁ + S₂ + S₃) is within the range between Q ± 10% and Q ± 10% and is NLT Q”; no unit is outside the range between Q ± 15% and Q’ ± 15%, and NMT 1 unit is outside the range between Q’ ± 15% and NMT 1 unit is less than Q” – 5% at the stated times.</td>
</tr>
<tr>
<td>S₁</td>
<td>12</td>
<td>Test 2: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 2.</td>
</tr>
</tbody>
</table>

**Table 2**  
**Tablet Strength** (mg, as potassium citrate monohydrate)  
**Concentration of Citric Acid** (mg/mL)

<table>
<thead>
<tr>
<th>Tablet Strength</th>
<th>Concentration of Citric Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>540</td>
<td>0.35</td>
</tr>
<tr>
<td>1080</td>
<td>0.70</td>
</tr>
<tr>
<td>1620</td>
<td>1.05</td>
</tr>
</tbody>
</table>

**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 x 25-cm; 5-µm packing L1  
**Column temperature:** 55°C  
**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 (C₆H₅K₃O₇ · H₂O) in the sample withdrawn from the vessel at each time point:

\[ \text{Result} = \left( \frac{r_0}{r} \right) \times C_1 \times (M_{r1}/M_r) \]

\[ r_0 = \text{citric acid peak area from the Sample solution} \]

\[ r = \text{citric acid peak area from the Standard solution} \]

\[ C_1 = \text{concentration of USP Citric Acid RS in the Standard solution (mg/mL)} \]

\[ M_{r1} = \text{molecular weight of potassium citrate monohydrate (C₆H₅K₃O₇ · H₂O), } 324.41 \]

\[ M_r = \text{molecular weight of citric acid (C₆H₈O₇), } 192.13 \]

Calculate the percentage of the labeled amount of potassium citrate monohydrate (C₆H₅K₃O₇ · H₂O) dissolved at each time point:

At 0.5 h:

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

At 1 h:

\[ \text{Result}_2 = (C_2 \times V + C_1 \times V_2) \times 100/L \]

At 4 h:

\[ \text{Result}_3 = (C_1 \times V + C_1 \times V_3) \times 100/L \]

At 6 h:

\[ \text{Result}_4 = (C_1 \times V + C_1 \times C_2 \times V_4) \times 100/L \]
Uniformity of Dosage Units (905): Meet the requirements

Additional Requirements

Packaging and Storage: Preserve in tight containers.

Add the following:

Labeling: The label states the amount of potassium citrate as monohydrate (C₆H₅K₃O₇·H₂O) in mEq and in g/Tablet. The label indicates the Dissolution Test with which the product complies. • (RB 1-Feb-2015)

USP Reference Standards (11)

USP Citric Acid RS

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>25–50</td>
</tr>
<tr>
<td>1</td>
<td>40–65</td>
</tr>
<tr>
<td>4</td>
<td>NLT 70</td>
</tr>
<tr>
<td>6</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

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