Potassium Chloride Extended-Release Capsules

Type of Posting	Revision Bulletin
Posting Date	31–Aug–2018
Official Date	01–Sep–2018
Expert Committee	Chemical Medicines Monographs 5
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 5 Expert Committee has revised the Potassium Chloride Extended-Release Capsules monograph. The purpose for the revision is to add *Dissolution Test 2* to accommodate FDA-approved drug products with different tolerances than the existing dissolution test. *Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

Additionally, minor editorial changes have been made to update the monograph to current *USP* style.

The Potassium Chloride Extended-Release Capsules Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Ren-Hwa Yeh, Ph.D., Senior Scientific Liaison (301-998-6818 or rhy@usp.org).

Potassium Chloride Extended-Release Capsules

DEFINITION

Potassium Chloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of potassium chloride (KCl).

IDENTIFICATION

• **A. IDENTIFICATION TESTS—GENERAL** ⟨191⟩**,** *Chemical Identification Tests, Potassium*

Sample solution: A portion of the filtrate, obtained as directed for *Sample stock solution* in the *Assay*

Acceptance criteria: Meet the requirements

• **B. IDENTIFICATION TESTS—GENERAL** ⟨191⟩**,** *Chemical Identification Tests, Chloride*

Sample solution: A portion of the filtrate, obtained as directed for *Sample stock solution* in the *Assay*

Acceptance criteria: Meet the requirements

ASSAY

• **PROCEDURE**

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: To separate 100-mL volumetric flasks transfer 10.0, 15.0, and 20.0 mL, respectively, 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, respectively, 1.0, 1.5, and 2.0 µg/mL of potassium.

Sample stock solution: Place NLT 20 Capsules in a suitable container with 400 mL of water, heat to boiling, and boil for 20 min. Allow to cool, transfer the solution to a 1000-mL volumetric flask, and dilute with water to volume. Filter, discarding the first 20 mL of the filtrate. Transfer a measured volume of the subsequent filtrate, equivalent to 60 mg of potassium chloride, to a 1000-mL volumetric flask, and dilute with water to volume. [NOTE—Retain a portion of the filtrate for use in the *Identification* tests.]

Sample solution: Transfer 5.0 mL of *Sample stock solution* to a 100-mL volumetric 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.

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, determine the concentration of potassium in the *Sample solution* (µg/mL).

Calculate the percentage of the labeled amount of potassium chloride (KCl) in each Capsule taken:

$$\text{Result} = (C/C_U) \times (M_r/A_r) \times 100$$

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

C_U = concentration of potassium chloride in the *Sample solution* (µg/mL)

M_r = molecular weight of potassium chloride, 74.55

A_r = atomic weight of potassium, 39.10

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION** ⟨711⟩

▲**Test 1**▲ (RB 1-Sep-2018)

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Time: 2 h

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: To separate 100-mL volumetric flasks transfer 10.0, 15.0, and 20.0 mL, respectively, 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, respectively, 1.0, 1.5, and 2.0 µg/mL of potassium.

Sample stock solution: Filter the solution under test, and dilute quantitatively with *Medium* to obtain a solution containing 60 µg/mL of potassium chloride.

Sample solution: Add 5.0 mL of the *Sample stock solution* to a 100-mL volumetric 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.

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, determine the concentration of potassium in the *Sample solution* (µg/mL).

Calculate the percentage of the labeled amount of potassium chloride (KCl) dissolved:

$$\text{Result} = [C \times D \times (V/L)] \times (M_r/A_r) \times 100$$

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

D = dilution factor of the *Sample solution*

V = volume of *Medium*, 900 mL

L = labeled amount of potassium chloride (µg/Capsule)

M_r = molecular weight of potassium chloride, 74.55

A_r = atomic weight of potassium, 39.10

Tolerances: NMT 35% (Q) of the labeled amount of potassium chloride (KCl) is dissolved in 2 h. The requirements are met if the quantities dissolved from the Capsules tested conform to *Table 1* instead of to the table shown in *Dissolution* ⟨711⟩.

Table 1

Stage	Number Tested	Acceptance Criteria
S_1	6	Each unit is within the range $Q \pm 30\%$.
S_2	6	Average of 12 units ($S_1 + S_2$) is within the range between $Q - 30\%$ and $Q + 35\%$, and no unit is outside the range $Q \pm 40\%$.
S_3	12	Average of 24 units ($S_1 + S_2 + S_3$) is within the range between $Q - 30\%$ and $Q + 35\%$, and NMT 2 units are outside the range $Q \pm 40\%$.

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

Standard stock solution and **Standard solutions:** Prepare as directed in *Test 1*.

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Times: 1, 2, 4, and 6 h

Sample stock solution: Transfer 4.0 mL of the solution under test into a 50-mL volumetric flask, dilute with water to volume, and filter.

Sample solution: Transfer 4.0 mL of the *Sample stock solution* to a 100-mL volumetric 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.

Blank solution: To a 100-mL volumetric 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.

Instrumental conditions: Proceed as directed in *Test 1*, except do not use the *Blank*.

System sutability

Samples: *Standard solutions*

Suitability requirements

Linearity: Correlation coefficient NLT 0.99

Relative standard deviation: NMT 5.0% from 5 replicate analyses of the 1.5-µg/mL *Standard solution*

Analysis

Samples: 1.5-µg/mL *Standard solution*, *Sample solution*, and *Blank solution*

Calculate the percentage of the labeled amount of potassium chloride (KCl) dissolved:

$$\text{Result}_i = [(A_U/A_S) \times C_S \times D \times (V/L)] \times (M_r/A_r) \times 100$$

A_U = absorbance of potassium in the *Sample solution*

A_S = absorbance of potassium in the *Standard solution*

C_S = concentration of potassium in the *Standard solution* (µg/mL)

D = dilution factor of the *Sample solution*

V = volume of *Medium*, 900 mL

L = labeled amount of potassium chloride (µg/Capsule)

M_r = molecular weight of potassium chloride, 74.55

A_r = atomic weight of potassium, 39.10

Tolerances: See *Table 2*.

Table 2

Time Point (*i*)	Time (h)	Amount Dissolved (%) 750 mg/Capsule
1	1	25–45
2	2	45–65
3	4	70–90
4	6	NLT 85

The percentages of the labeled amount of potassium chloride (KCl), dissolved at the times specified, conform to *Dissolution* ⟨711⟩, *Acceptance Table 2*.▲ (RB 1-Sep-2018)

• **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers, and store at a temperature not exceeding 30°.

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-Sep-2018)