Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: USP Monographs
DocId: GUID-0A83D713-83B4-4194-AF49-12B7F426D345_3_en-US
DOI: https://doi.org/10.31003/USPNF_M67440_03_01
DOI Ref: hr1jw

Potassium Chloride in Lactated Ringer's and Dextrose Injection

DEFINITION

Potassium Chloride in Lactated Ringer's and Dextrose Injection is a sterile solution of Calcium Chloride, Potassium Chloride, Sodium Chloride, and Sodium Lactate in Water for Injection. It contains, in each 100 mL, NLT 285.0 and NMT 315.0 mg of sodium (Na) [as sodium chloride (NaCl) and anhydrous sodium lactate ($C_3H_5NaO_3$)], NLT 4.90 and NMT 6.00 mg of calcium (Ca) [equivalent to NLT 18.0 and NMT 22.0 mg of calcium chloride ($CaCl_2 \cdot 2H_2O$)], and NLT 231.0 and NMT 261.0 mg of lactate ($C_3H_5O_3$) [equivalent to NLT 290.0 and NMT 330.0 mg of anhydrous sodium lactate ($C_3H_5NaO_3$)]. It contains NLT 95.0% and NMT 105.0% of the labeled amount of potassium chloride (KCl), NLT 90.0% and NMT 105.0% of the labeled amount of dextrose ($C_6H_{12}O_6 \cdot H_2O$), and NLT 90.0% and NMT 110.0% of the labeled amount of chloride (Cl) [as sodium chloride (NaCl), potassium chloride (KCl), and calcium chloride ($CaCl_2 \cdot 2H_2O$)]. It contains no antimicrobial agents.

IDENTIFICATION

• **A.**

Sample solution: Nominally 50 mg/mL of dextrose from a suitable volume of Injection in water

Analysis: Add a few drops of *Sample solution* to 5 mL of hot alkaline cupric tartrate TS.

Acceptance criteria: A copious red precipitate of cuprous oxide is formed.

Change to read:

• **B. Identification Tests—General** ⟨191⟩**,** *Chemical Identification Tests, Chloride* and *Calcium***:** Meets the requirements of ▲the▲ (USP 1-May-2021) test ▲▲ (USP 1-May-2021) under *Chloride* and test *A* under *Calcium*

• **C. Sodium:** The sample imparts an intense yellow color to a nonluminous flame.

• **D. Potassium:** The sample imparts a violet color to a nonluminous flame. Because the presence of small quantities of sodium masks the color, screen out the yellow color produced by sodium by viewing through a blue filter that blocks the emission at 589 nm (sodium), but is transparent to emission at 404 nm (potassium). [Note—Traditionally, cobalt glass has been used, but other suitable filters are commercially available.]

• **E.** The retention time of the lactate peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Lactate*.

ASSAY

• **Calcium**

[Note—Concentrations of the *Standard solution* and the *Sample solution* may be modified to fit the linear or working range of the atomic absorption spectrophotometer.]

Lanthanum chloride solution: 88.45 g/L of lanthanum chloride prepared as follows. Transfer a suitable quantity of lanthanum chloride to an appropriate volumetric flask. Add 50% of the final flask volume of water. Carefully add 25% of the final flask volume of hydrochloric acid. Mix, and allow to cool. Dilute with water to volume.

Calcium stock solution: 1 mg/mL of calcium prepared as follows. Transfer 499.5 mg of primary standard calcium carbonate to a 200-mL volumetric flask, and add 10 mL of water. Carefully add 5 mL of diluted hydrochloric acid, and swirl to dissolve the calcium carbonate. Dilute with water to volume.

Standard solutions: 0.010, 0.015, and 0.020 mg/mL of calcium prepared as follows. To three separate 100-mL volumetric flasks, each containing 5.0 mL of *Lanthanum chloride solution*, add 1.0, 1.5, and 2.0 mL of *Calcium stock solution*, respectively. Dilute the contents of each flask with water to volume.

Sample solution: Transfer 30.0 mL of Injection to a 100-mL volumetric flask containing 5.0 mL of *Lanthanum chloride solution*. Dilute with water to volume.

Blank: Transfer 5.0 mL of *Lanthanum chloride solution* to a 100-mL volumetric flask and dilute with water to volume.

Instrumental conditions

(See *Atomic Absorption Spectroscopy* ⟨852⟩.)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: Calcium emission line at 422.7 nm

Lamp: Calcium hollow-cathode

Flame: Air–acetylene

Analysis

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

Plot the absorbances of the *Standard solutions* versus the concentration, in mg/mL, of calcium, and draw the straight line best fitting the three plotted points. From the graph so obtained, determine the concentration (*C*), in mg/mL, of calcium in the *Sample solution*.

Calculate the quantity (mg) of calcium (Ca) in each 100 mL of Injection taken:

$$\text{Result} = C \times D \times F$$

C = concentration of calcium in the *Sample solution*, as determined from the graph (mg/mL)

D = dilution factor for the *Sample solution*, 3.3

F = conversion factor for each 100 mL of Injection, 100 mL

Acceptance criteria: 4.90–6.00 mg of calcium (Ca) in each 100 mL

- **Chloride**

Sample solution: Transfer 10 mL of Injection into a conical flask. Add 10 mL of glacial acetic acid, 75 mL of methanol, and 3 drops of eosin Y TS.

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N silver nitrate VS

Endpoint detection: Visual

Analysis

Sample: *Sample solution*

Titrate, with shaking, with *Titrant* to a pink endpoint.

Calculate the percentage of the labeled amount of chloride (Cl) in the portion of Injection taken:

$$\text{Result} = V \times N \times (F/W) \times 100$$

V = volume of *Titrant* consumed by the *Sample solution* (mL)

N = actual normality of the *Titrant* (mEq/mL)

F = equivalency factor, 35.45 mg/mEq

W = nominal amount of chloride in the *Sample solution* (mg)

Acceptance criteria: 90.0%–110.0%

- **Dextrose**

Sample solution: Transfer a volume of Injection containing 2–5 g of dextrose to a 100-mL volumetric flask. Add 0.2 mL of 6 N ammonium hydroxide, and dilute with water to volume.

Analysis

Sample: *Sample solution*

Determine the angular rotation in a suitable polarimeter tube (see *Optical Rotation* ⟨781⟩).

Calculate the percentage of the labeled amount of dextrose ($C_6H_{12}O_6 \cdot H_2O$) in the portion of Injection taken:

$$\text{Result} = [(100 \times a)/(l \times \alpha)] \times (1/C_U) \times (M_{r1}/M_{r2}) \times 100$$

a = observed angular rotation of the *Sample solution* (°)

l = length of the polarimeter tube (dm)

α = midpoint of the specific rotation range for anhydrous dextrose, 52.9°

C_U = nominal concentration of dextrose in the *Sample solution* (g/100 mL)

M_{r1} = molecular weight of dextrose monohydrate, 198.17

M_{r2} = molecular weight of anhydrous dextrose, 180.16

Acceptance criteria: 90.0%–105.0%

Change to read:

- **Lactate**

Mobile phase: Add 1 mL of formic acid and 1 mL of dicyclohexylamine per liter of water.

System suitability solution: 3 mg/mL each of anhydrous sodium acetate and USP Sodium Lactate RS in water

Standard solution: 3 mg/mL of USP Sodium Lactate RS in water

Sample solution: Use the undiluted Injection.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 10-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2 between acetate and lactate, *System suitability solution*

Tailing factor: NMT 2.0▲ (USP 1-May-2021) , *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the quantity (mg) of lactate ($C_3H_5O_3$) in each 100 mL of Injection taken:

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

r_U = peak response of lactate from the *Sample solution*

r_S = peak response of lactate from the *Standard solution*

C_S = concentration of USP Sodium Lactate RS in the *Standard solution* (mg/mL)

M_{r1} = molecular weight of lactate, 89.07

M_{r2} = molecular weight of anhydrous sodium lactate, 112.06

V = volume of the Injection, 100 mL

Acceptance criteria: 231.0–261.0 mg of lactate ($C_3H_5O_3$) in each 100 mL

- **Potassium**

Solution A: Suitable nonionic wetting agent (1 in 500)

Standard stock solution A: 100 µg/mL of potassium in water prepared as follows. Dissolve 190.7 mg of potassium chloride, previously dried at 105° for 2 h, in 50 mL of water. Transfer the resulting solution to a 1-L volumetric flask, and dilute with water to volume.

Standard stock solution B: 10.93 mg/mL of sodium chloride in water

Standard solutions: 0.005, 0.010, 0.015, and 0.020 mg/mL of potassium prepared as follows. Transfer 10 mL of *Standard stock solution B* to each of four 100-mL volumetric flasks containing 10.0 mL of *Solution A*. To each flask add, respectively, 5.0, 10.0, 15.0, and 20.0 mL of *Standard stock solution A*, and dilute with water to volume.

Sample solution: Nominally 0.015 mg/mL of potassium prepared as follows. Transfer a suitable portion of Injection into an appropriate volumetric flask. Add 10% of the final flask volume of *Solution A*. Dilute with water to volume.

Blank: Transfer 10 mL of *Standard stock solution B* to a 100-mL volumetric flask containing 10.0 mL of *Solution A*. Dilute with water to volume.

Instrumental conditions

Mode: Atomic emission spectrophotometry

Emission wavelength: 766 nm

Analysis

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

Set a suitable flame photometer for maximum transmittance at a wavelength of 766 nm. Adjust the instrument to zero transmittance with the *Blank*. Adjust the instrument to 100% transmittance with the most concentrated of the *Standard solutions*. Read the percentage

transmittance of the other *Standard solutions*, and plot transmittances versus concentration of potassium. From the graph so obtained, read the percentage transmittance of the *Sample solution*.

Calculate the percentage of the labeled amount of potassium chloride (KCl) in the portion of Injection taken:

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

C = concentration of potassium in the *Sample solution*, as determined from the graph (mg/mL)

C_U = nominal concentration of potassium in the *Sample solution* (mg/mL)

M_r = molecular weight of potassium chloride, 74.55

A_r = atomic weight of potassium, 39.10

Acceptance criteria: 95.0%–105.0%

• **Sodium**

Solution A: Suitable nonionic wetting agent (1 in 500)

Standard stock solution: 100 µg/mL of sodium in water prepared as follows. Dissolve 254.2 mg of sodium chloride, previously dried at 105° for 2 h, in 50 mL of water. Transfer the resulting solution to a 1-L volumetric flask, and dilute with water to volume.

Standard solutions: 0.005, 0.010, 0.015, and 0.020 mg/mL of sodium prepared as follows. Transfer 10 mL of *Solution A* to each of four 100-mL volumetric flasks. To each flask add, respectively, 5.0, 10.0, 15.0, and 20.0 mL of *Standard stock solution*, and dilute with water to volume.

Sample solution: Transfer 5 mL of Injection to a 1-L volumetric flask containing 100 mL of *Solution A*. Dilute with water to volume.

Blank: Transfer 10 mL of *Solution A* to a 100-mL volumetric flask. Dilute with water to volume.

Instrumental conditions

Mode: Atomic emission spectrophotometry

Emission wavelength: 589 nm

Analysis

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

Set a suitable flame photometer for maximum transmittance at a wavelength of 589 nm. Adjust the instrument to zero transmittance with the *Blank*. Adjust the instrument to 100% transmittance with the most concentrated of the *Standard solutions*. Read the percentage transmittance of the other *Standard solutions*, and plot transmittances versus concentration of sodium. From the graph so obtained, read the percentage transmittance of the *Sample solution*.

Calculate the quantity (mg) of sodium (Na) in each 100 mL of Injection taken:

$$\text{Result} = C \times D \times F$$

C = concentration of sodium in the *Sample solution*, as determined from the graph (mg/mL)

D = dilution factor for the *Sample solution*, 200

F = conversion factor for each 100 mL of Injection, 100 mL

Acceptance criteria: 285.0–315.0 mg of sodium (Na) in each 100 mL

IMPURITIES

Change to read:

• **Limit of 5-Hydroxymethylfurfural and Related Substances**

Sample solution: Nominally 2.0 mg/mL of dextrose ($C_6H_{12}O_6 \cdot H_2O$) from Injection in water

Instrumental conditions

Mode: UV▲ (USP 1-May-2021)

Analytical wavelength: 284 nm

Cell: 1 cm

Blank: Water

Analysis

Samples: *Sample solution* and *Blank*

Determine the absorbance of the *Sample solution* with a suitable spectrophotometer.

Acceptance criteria: The absorbance is NMT 0.25.

SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** NMT 0.5 USP Endotoxin Units/mL

• **pH ⟨791⟩:** 3.5–6.5

• **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose glass or plastic containers. Glass containers are preferably of Type I or Type II glass.

• **Labeling:** The label states the total osmolar concentration in mOsmol/L. Where the contents are less than 100 mL, the label alternatively may state the total osmolar concentration in mOsmol/mL. The label includes also the warning: "Not for use in the treatment of lactic acidosis."

• **USP Reference Standards ⟨11⟩**
USP Sodium Lactate RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
POTASSIUM CHLORIDE IN LACTATED RINGER'S AND DEXTROSE INJECTION	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(2)

Current DocID: GUID-0A83D713-83B4-4194-AF49-12B7F426D345_3_en-US

DOI: https://doi.org/10.31003/USPNF_M67440_03_01

DOI ref: hr1jw