Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: USP Monographs
DocId: GUID-69228677-0289-4202-AD0F-DCF02750847B_3_en-US
DOI: https://doi.org/10.31003/USPNF_M73720_03_01
DOI Ref: at9f4

Lactated Ringer's Injection

DEFINITION

Lactated Ringer's 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 sodium lactate ($C_3H_5NaO_3$)], NLT 14.2 and NMT 17.3 mg of potassium (K) [equivalent to NLT 27.0 and NMT 33.0 mg of potassium chloride (KCl)], NLT 4.90 and NMT 6.00 mg of calcium (Ca) [equivalent to NLT 18.0 and NMT 22.0 mg of calcium chloride ($CaCl_2 \cdot 2H_2O$)], NLT 368.0 and NMT 428.0 mg of chloride (Cl) [as sodium chloride (NaCl), potassium chloride (KCl), and 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 sodium lactate ($C_3H_5NaO_3$)]. It contains no antimicrobial agents.

[Note—The calcium, potassium, and sodium contents of Lactated Ringer's Injection are approximately 2.7, 4, and 130 mEq/L, respectively.]

IDENTIFICATION

Change to read:

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

• **B. 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.]

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

• **D.** 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 solutions* and the *Sample solution* may be modified to fit the linear or working range of the atomic absorption spectrophotometer.]

Solution A: Transfer 17.69 g of lanthanum chloride to a 200-mL volumetric flask, add 100 mL of water, carefully add 50 mL of hydrochloric acid, 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 dilute 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 *Solution A*, add 1.0, 1.5, and 2.0 mL, respectively, of *Calcium stock solution*. Dilute the contents of each flask with water to volume.

Sample solution: Dilute with water, 20.0 mL of Injection, equivalent to 1 mg of calcium, in a 100-mL volumetric flask containing 5.0 mL of *Solution A* to volume, and mix.

Blank: 5.0 mL of *Solution A* diluted with water to 100.0 mL

Instrumental conditions

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

Mode: Atomic absorption spectrophotometer

Analytical wavelength: Calcium emission line at 422.7 nm

Lamp: Calcium hollow-cathode

Flame: Air–acetylene

Analysis

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

Concomitantly determine the absorbances of the *Standard solutions* and the *Sample solution*. 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 this graph, calculate the concentration (*C*) in mg/mL, of calcium in the *Sample solution*.

Calculate the quantity of calcium in each 100 mL of Injection taken:

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

C = concentration of calcium in the *Sample solution* (mg/mL)

D = dilution factor for the *Sample solution*, 5

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

Acceptance criteria: 4.90–6.00 mg of calcium per 100 mL of Injection

- **Potassium**

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

Solution B: 10.93 mg/mL of sodium chloride in water

Standard stock solution: 0.100 mg/mL of potassium, prepared as follows. Transfer 190.7 mg of potassium chloride, previously dried at 105° for 2 h, 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 potassium, prepared as follows. To four separate 100-mL volumetric flasks, each containing 10.0 mL of *Solution A* and 10 mL of *Solution B*, add 5.0, 10.0, 15.0, and 20.0 mL, respectively, of *Standard stock solution*. Dilute the contents of each flask with water to volume.

Sample solution: Pipet 10 mL of Injection to a 100-mL volumetric flask containing 10 mL of *Solution A*, dilute with water to volume, and mix.

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

Instrumental conditions

Mode: Flame photometry

Analytical wavelength: Maximum transmittance at 766 nm

Analysis

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

Set the flame photometer for maximum transmittance. 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 of the *Standard solutions* versus the concentration, in mg/mL, of potassium. Draw the straight line best fitting the four plotted points. From this graph, calculate the concentration of potassium in the *Sample solution*.

Calculate the quantity, in milligrams, of potassium in each 100 mL of Injection taken:

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

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

D = dilution factor for the *Sample solution*, 10

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

Acceptance criteria: 14.2–17.3 mg of potassium per 100 mL of Injection

- **Sodium**

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

Standard stock solution: 0.100 mg/mL of sodium, prepared as follows. Dissolve 254.2 mg of sodium chloride, previously dried at 105° for 2 h, in 50 mL of water. Transfer this 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. To four separate 100-mL volumetric flasks, each containing 10.0 mL of *Solution A*, add 5.0, 10.0, 15.0, and 20.0 mL, respectively, of *Standard stock solution*. Dilute the contents of each flask with water to volume.

Sample solution: Transfer 5 mL of Injection to a 1-L volumetric flask containing 100.0 mL of *Solution A* and dilute with water to volume.

Blank: Transfer 10.0 mL of *Solution A* to a 100-mL volumetric flask. Dilute with water to volume.

Instrumental conditions

Mode: Flame photometry

Analytical wavelength: Maximum transmittance at 589 nm

Analysis

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

Set the flame photometer for maximum transmittance. 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 of the *Standard solutions* versus concentration, in mg/mL, of sodium, and draw the straight line best fitting the four plotted points. From this graph, calculate the concentration of sodium in the *Sample solution*.

Calculate the quantity of sodium in each 100 mL of Injection taken:

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

C = concentration of sodium in the *Sample solution* (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 per 100 mL of Injection

Change to read:

- **Chloride**

Sample solution: Transfer 10 mL of Injection into a conical flask, and add 10 mL of glacial acetic acid and 75 mL of methanol.

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: 0.1 N silver nitrate VS

Endpoint detection: Visual

Analysis

Sample: *Sample solution*

Titrate the *Sample solution*, with shaking, with *Titrant* to a pink endpoint using 3 drops of eosin Y TS, as an indicator.

Calculate the labeled amount of chloride (Cl) in 100 mL of Injection taken:

$$\blacktriangle\text{Result} = V \times N_A \times F_e \times F_c\blacktriangle \text{ (USP 1-May-2021)}$$

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

$\blacktriangle N_A\blacktriangle$ (USP 1-May-2021) = actual normality of the *Titrant* (mEq/mL)

$\blacktriangle F_e\blacktriangle$ (USP 1-May-2021) = equivalency factor, 35.45 mg/mEq

$\blacktriangle F_c$ = conversion factor for each 100 mL of Injection, $10\blacktriangle$ (USP 1-May-2021)

Acceptance criteria: 368.0–428.0 mg of chloride per 100 mL of Injection

- **Lactate**

Mobile phase: Dicyclohexylamine, formic acid, and water (1:1:998)

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 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 the acetate and lactate peaks, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response from the *Sample solution*

r_S = peak response 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

Acceptance criteria: 231.0–261.0 mg of lactate ($C_3H_5O_3$) per 100 mL of Injection

SPECIFIC TESTS

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

Add the following:

▲• **Sterility Tests ⟨71⟩:** Meets the requirements▲ (USP 1-May-2021)

• **pH ⟨791⟩:** 6.0–7.5

• **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 also includes 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
LACTATED RINGER'S 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-69228677-0289-4202-AD0F-DCF02750847B_3_en-US

DOI: https://doi.org/10.31003/USPNF_M73720_03_01

DOI ref: at9f4