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Modified Lactated Ringer's and Dextrose Injection

DEFINITION

Modified Lactated Ringer's and Dextrose Injection is a sterile solution of Calcium Chloride, Potassium Chloride, Sodium Chloride, Sodium Lactate, and Dextrose in Water for Injection. It contains, in each 100 mL, NLT 57.0 and NMT 63.0 mg of sodium (Na) [as sodium chloride (NaCl) and sodium lactate, ($C_3H_5NaO_3$)], NLT 2.82 and NMT 3.46 mg of potassium (K) [equivalent to NLT 5.4 and NMT 6.6 mg of potassium chloride (KCl)], NLT 0.98 and NMT 1.20 mg of calcium (Ca) [equivalent to NLT 3.6 and NMT 4.4 mg of calcium chloride ($CaCl_2 \cdot 2H_2O$)], NLT 73.6 and NMT 85.6 mg of chloride (Cl) [as sodium chloride (NaCl), potassium chloride (KCl), and calcium chloride ($CaCl_2 \cdot 2H_2O$)], and NLT 46.2 and NMT 52.20 mg of lactate ($C_3H_5O_3$) [equivalent to NLT 58.0 and NMT 66.0 mg of sodium lactate ($C_3H_5NaO_3$)]. It contains NLT 90.0% and NMT 105.0% of the labeled amount of dextrose ($C_6H_{12}O_6 \cdot H_2O$). It contains no antimicrobial agents.

[Note—The calcium, potassium, and sodium contents of Modified Lactated Ringer's and Dextrose Injection are approximately 0.5, 0.8, and 26 mEq/L, respectively.]

IDENTIFICATION

• **A.**

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

Analysis: Add a few drops of the *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 test ▲▲ (USP 1-May-2021) under *Chloride* and test *A* under *Calcium*

• **C. 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.]

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

• **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

Change to read:

• **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: 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 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: Add 5.0 mL of *Solution A* to a 100-mL volumetric flask, and dilute with Injection to volume.

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

Blank: *Blank*

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 of calcium, in mg/mL, and draw the straight line best fitting the three plotted points. From this graph, calculate the concentration of calcium in the *Sample solution*.

Calculate the quantity, in mg, 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*, 1.055

F = conversion factor for each 100 mL of Injection, 100 ▲mL▲ (USP 1-May-2021)

Acceptance criteria: 0.98 mg–1.20 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: Transfer 50.0 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 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*, 2

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

Acceptance criteria: 2.82–3.46 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 25.0 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 the 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*, 40

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

Acceptance criteria: 57.0–63.0 mg of sodium per 100 mL of Injection

Change to read:

• **Chloride**

Sample solution: Transfer a volume of Injection equivalent to 55 mg of chloride (1.55 mEq) to a suitable conical flask, and add water, if necessary, to bring the volume to 10 mL. Add 10 mL of glacial acetic acid, 75 mL of methanol, and 0.5 mL of eosin Y TS.

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.

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

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

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

$\blacktriangle V_s$ = volume of the sample (mL)

F_c = conversion factor for each 100 mL of Injection, 100 mL▲ (USP 1-May-2021)

Acceptance criteria: 73.6–85.6 mg of chloride per 100 mL

• **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: 0.6 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:

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

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: 46.2–52.20 mg of lactate ($C_3H_5O_3$) per 100 mL of Injection

Change to read:

• **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*▲ (USP 1-May-2021)

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%

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 a suitable volume of Injection, in water

Instrumental conditions

▲Mode: UV▲ (USP 1-May-2021)

Analytical wavelength: Maximum transmittance at 284 nm

Cell: 1 cm

Blank: Water

Analysis

Samples: *Sample solution* and *Blank*

Acceptance criteria: The absorbance is NMT 0.25.

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⟩:** 4.0–6.5

• **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 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
MODIFIED 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

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