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Ringer's Injection

DEFINITION

Change to read:

Ringer's Injection is a sterile solution of Sodium Chloride, Potassium Chloride, and Calcium Chloride in Water for Injection. It contains, in each 100 mL, NLT 323.0 mg and NMT 354.0 mg of sodium (Na) [equivalent to NLT 820.0 mg and NMT 900.0 mg of sodium chloride (NaCl)]; NLT 14.9 mg and NMT 16.5 mg of potassium (K) [equivalent to NLT 28.5 mg and NMT 31.5 mg of potassium chloride (KCl)]; NLT 8.20 mg and NMT 9.80 mg of calcium (Ca) [equivalent to NLT 30.0 mg and NMT 36.0 mg of calcium chloride ($CaCl_2 \cdot 2H_2O$)]; and NLT 523.0 mg and NMT 580.0 mg of chloride (Cl) as sodium chloride (NaCl), potassium chloride (KCl), and calcium chloride ($CaCl_2 \cdot 2H_2O$). It contains no antimicrobial agents.

[Note—The potassium, calcium, sodium ion, and chloride contents of Ringer's Injection are approximately 4, 4.5, 147.5, and 156 mEq/L, respectively.]

▲▲ (USP 1-Dec-2021)

IDENTIFICATION

• **A. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Calcium* and *Chloride*:** Meets the requirements of test *A* for *Calcium*, and test *A* for *Chloride*

• **B. Sodium:** A sample imparts an intense yellow color to a nonluminous flame.

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

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.]

Lanthanum chloride solution: Transfer 17.69 g of lanthanum chloride to a 200-mL volumetric flask, add 100 mL of water, and carefully add 50 mL of hydrochloric acid. Mix, and allow to cool. Dilute with water to volume.

Calcium stock solution: 1 mg/mL of calcium (Ca) 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 (Ca) 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, respectively, of *Calcium stock solution*. Dilute the contents of each flask with water to volume.

Sample solution: Transfer 20.0 mL of Injection, equivalent to 1.8 mg of calcium (Ca), 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▲ (USP 1-Dec-2021) wavelength: Calcium emission line, 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, determine the concentration (*C*), in mg/mL, of calcium in the *Sample solution.*

Calculate the quantity, in 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 of the *Sample solution,* 5

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

Acceptance criteria: 8.20–9.80 mg

Change to read:

• **Potassium**

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

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

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

Standard solutions: 0.005, 0.01, 0.015, and 0.020 mg/mL of potassium prepared as follows. Transfer 10 mL of *Solution B* to each of four separate 100-mL volumetric flasks each containing 10.0 mL of *Solution A*. To each flask add 5.0, 10.0, 15.0, and 20.0 mL of *Standard stock solution*, respectively, and dilute with water to volume.

Sample solution: Transfer 10 mL of Injection to a 100-mL volumetric flask. Add 10.0 mL of *Solution A*. Dilute with water to volume.

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

Instrumental conditions

Mode: ▲Flame photometry▲ (USP 1-Dec-2021)

▲**Analytical**▲ (USP 1-Dec-2021) **wavelength:** Maximum transmittance at 766 nm

Analysis

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

Set the instrument for maximum transmittance and adjust 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. ▲Draw the straight line best fitting the four plotted points. From the graph, calculate the concentration of potassium in the *Sample solution.*

Calculate the quantity, in mg, of potassium (K) in each 100 mL of Injection taken:

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

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

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

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

Acceptance criteria: 14.9–16.5 mg

Change to read:

• **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 separate 100-mL volumetric flasks. To each flask add 5.0, 10.0, 15.0, and 20.0 mL of *Standard stock solution*, respectively, and dilute with water to volume.

Sample solution: Transfer 5 mL of Injection into 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: ▲Flame photometry▲ (USP 1-Dec-2021)

▲**Analytical**▲ (USP 1-Dec-2021) **wavelength:** Maximum transmittance at 589 nm

Analysis

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

Set the instrument for maximum transmittance and adjust 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. ▲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, in mg, of sodium (Na) in each 100 mL of Injection:

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

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

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

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

Acceptance criteria: 323.0–354.0 mg

Change to read:

• **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 quantity, in mg, of chloride (Cl) in 100 mL of Injection:

$$\text{Result} = V \times N_A \times F_e \times F_c$$

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

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

F_e = equivalency factor, 35.45 mg/mEq

F_c = conversion factor for each 100 mL of Injection, 10▲ (USP 1-Dec-2021)

Acceptance criteria: 523.0–580.0 mg

SPECIFIC TESTS

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

Add the following:

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

• **pH ⟨791⟩:** 5.0–7.5

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Package 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.

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

Topic/Question	Contact	Expert Committee
RINGER'S INJECTION	Documentary Standards Support	SM52020 Small Molecules 5

Topic/Question	Contact	Expert Committee
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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