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Multiple Electrolytes Injection Type 1

DEFINITION

Multiple Electrolytes Injection Type 1 is a sterile solution of suitable salts in Water for Injection to provide sodium, potassium, magnesium, and chloride ions. In addition, the salts provide ions of acetate, acetate and gluconate, or acetate, gluconate, and phosphate. It contains NLT 90.0% and NMT 110.0% of the labeled amounts of sodium (Na), potassium (K), magnesium (Mg), chloride (Cl), acetate ($C_2H_3O_2$), gluconate ($C_6H_{11}O_7$), and phosphate (PO_4). It may contain Hydrochloric Acid or Sodium Hydroxide used to adjust the pH. It contains no antimicrobial agents.

IDENTIFICATION

• **A. Identification Tests—General ⟨191⟩, *Magnesium* and *Chloride*:** Meets the requirements

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

• **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.** The retention time of the acetate peak of the *Sample solution* corresponds to that of the *Standard solution*, obtained as directed in the *Assay* for *Acetate*.

• **E.** Where gluconate is purported to be present, the retention time of the gluconate peak of the *Sample solution* corresponds to that of the *Standard solution*, obtained as directed in the *Assay* for *Gluconate*.

• **F.** Where phosphate is purported to be present, proceed as follows.

Sample solution: Add 5 mL of Injection and 1 mL of ammonium molybdate TS to a test tube and mix.

Acceptance criteria: A yellow precipitate, which is soluble in 6 N ammonium hydroxide, is formed.

ASSAY

• **Acetate**

Mobile phase: 0.05 N sulfuric acid

Standard solution: 1.2 mg/mL of sodium acetate trihydrate (0.0088 mEq/mL of acetate) in water

Sample solution: Nominally 0.0088 mEq/mL of acetate from a volume of Injection in water

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Columns

Guard: 4.6-mm × 3-cm; packing L17

Analytical: 7.8-mm × 30-cm; packing L17

Column temperature: 60°

Flow rate: 0.8 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acetate ($C_2H_3O_2$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

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

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

C_S = concentration of acetate in the *Standard solution* (mEq/mL)

C_U = nominal concentration of acetate in the *Sample solution* (mEq/mL)

Acceptance criteria: 90.0%–110.0%

- **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

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 = *Titrant* volume 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%

- **Gluconate** (if present)

Mobile phase: 0.05 N sulfuric acid

Standard solution: 1 mg/mL of USP Potassium Gluconate RS (0.0043 mEq/mL of gluconate) in water

Sample solution: Nominally 0.004 mEq/mL of gluconate from a volume of Injection in water

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Columns

Guard: 4.6-mm × 3-cm; packing L17

Analytical: 7.8-mm × 30-cm; packing L17

Flow rate: 0.8 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of gluconate ($C_6H_{11}O_7$) in the portion of Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

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

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

C_S = concentration of USP Potassium Gluconate RS in the *Standard solution* (mEq/mL)

C_U = nominal concentration of gluconate in the *Sample solution* (mEq/mL)

Acceptance criteria: 90.0%–110.0%

- **Magnesium**

[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.

Solution B: Mix 678 mL of hydrochloric acid with water to make 3000 mL.

Standard stock solution A: 1.00 mg/mL of magnesium (Mg) prepared as follows. Transfer 1.00 g of magnesium metal to a 1000-mL volumetric flask containing 10 mL of water. Slowly add 10 mL of hydrochloric acid, and swirl to dissolve the metal. Dilute with *Solution B* to volume.

Standard stock solution B: 100 µg/mL of magnesium (Mg) prepared as follows. Transfer 10.0 mL of *Standard stock solution A* to a 100-mL volumetric flask, and dilute with *Solution B* to volume.

Standard solutions: 10.0, 15.0, and 20.0 µg/mL of magnesium (Mg) prepared as follows. To three separate 100-mL volumetric flasks, each containing 5.0 mL of *Solution A*, add 10.0, 15.0, and 20.0 mL, respectively, of *Standard stock solution B.* Dilute the contents of each flask with *Solution B* to volume.

Sample solution: Nominally 20.0 µg/mL of magnesium from Injection prepared as follows. Transfer a volume of Injection, equivalent to 20 mg of magnesium (Mg) to a 1000-mL volumetric flask containing 50.0 mL of *Solution A*. Dilute with *Solution B* to volume.

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

Instrumental conditions

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

Mode: Atomic absorption spectrophotometry

Analytical wavelength: Magnesium emission line at 285.2 nm

Lamp: Magnesium hollow-cathode

Flame: Air–acetylene

Analysis

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

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

Calculate the percentage of the labeled amount of magnesium (Mg) in the portion of Injection taken:

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

C = concentration of magnesium (Mg) in the *Sample solution* (µg/mL), interpolated from the graph obtained

C_U = nominal concentration of magnesium (Mg) in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

- **Phosphate** (if present)

Solution A: 50 g/L of ammonium molybdate prepared as follows. Transfer a suitable amount of ammonium molybdate to an appropriate volumetric flask. Add 60% of the final flask volume of water, and swirl to dissolve. Add 15% of the final flask volume of sulfuric acid, and swirl. Allow to cool, and dilute with water to volume.

Solution B: Dissolve 0.5 g of hydroquinone in 100 mL of water, and add 1 drop of sulfuric acid. Prepare this solution fresh daily.

Solution C: Dissolve 1 g of sodium sulfite in water to make 5 mL. Prepare this solution fresh daily.

Standard solution: 0.11 mg/mL of monobasic potassium phosphate (0.0008 mEq/mL of phosphate) in water

Sample solution: Nominally 0.0008 mEq/mL of phosphate from a volume of Injection in water

Blank: Water

Instrumental conditions

Mode: Vis

Analytical wavelength: 640 nm

Analysis

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

Use water to zero the instrument. Transfer 2.0 mL each of the *Standard solution*, *Sample solution*, and the *Blank* to separate test tubes. To each test tube add 1.0 mL of *Solution A*, mix, and allow to stand for 3 min. Add 1.0 mL of *Solution B*, and mix. Add 1.0 mL of *Solution C*, mix, and allow to stand for 30 min.

Calculate the percentage of the labeled amount of phosphate (PO_4) in the portion of Injection taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*, corrected for any absorbance of the solution from the *Blank*

A_S = absorbance of the *Standard solution*, corrected for any absorbance of the solution from the *Blank*

C_S = concentration of phosphate (PO_4) in the *Standard solution* (mEq/mL)

C_U = nominal concentration of phosphate (PO_4) in the *Sample solution* (mEq/mL)

Acceptance criteria: 90.0%–110.0%

- **Potassium and Sodium**

Internal standard solution: 1.04 mg/mL of lithium nitrate prepared as follows. Transfer 1.04 g of lithium nitrate to a 1000-mL volumetric flask. Add a suitable nonionic surfactant, and then dilute with water to volume.

Potassium stock solution: 74.56 mg/mL of potassium chloride (1 mEq/mL of potassium) prepared as follows. Transfer 18.64 g of potassium chloride, previously dried at 105° for 2 h, to a 250-mL volumetric flask, and dilute with water to volume.

Sodium stock solution: 58.44 mg/mL of sodium chloride (1 mEq/mL of sodium) prepared as follows. Transfer 14.61 g of sodium chloride, previously dried at 105° for 2 h, to a 250-mL volumetric flask, and dilute with water to volume.

Standard stock solution: 0.0391*J* mg/mL of potassium (K) from *Potassium stock solution* and 0.02299*J*' mg/mL of sodium (Na) from *Sodium stock solution* prepared as follows. Transfer 0.1*J* mL of *Potassium stock solution* and 0.1*J*' mL of *Sodium stock solution* to a 100-mL volumetric flask, where *J* and *J*' are the labeled amounts, in mEq/L, of potassium and sodium, respectively, in the Injection. Dilute with water to volume.

Standard solution: Dilute 5.0 mL of the *Standard stock solution* with *Internal standard solution* to 500.0 mL.

Sample solution: Dilute 5.0 mL of Injection with *Internal standard solution* to 500.0 mL.

Instrumental conditions

Mode: Flame photometer

Analytical wavelengths

Potassium: Maximum at 766 nm

Sodium: Maximum at 589 nm

Lithium: Maximum at 671 nm

Blank: *Internal standard solution*

Analysis

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

Use the *Blank* to zero the instrument. Concomitantly determine the flame emission readings for the *Standard solution* and *Sample solution*.

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

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = emission reading ratio of potassium to lithium from the *Sample solution*

R_S = emission reading ratio of potassium to lithium from the *Standardsolution*

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

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

[Note—Each mg of potassium (K) is equivalent to 0.02558 mEq of potassium (K).]

Calculate the percentage of the labeled amount of sodium (Na) in the portion of Injection taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = emission reading ratio of sodium to lithium from the *Sample solution*

R_S = emission reading ratio of sodium to lithium from the *Standard solution*

C_S = concentration of sodium (Na) in the *Standard solution* (mg/mL)

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

[NOTE—Each mg of sodium (Na) is equivalent to 0.04350 mEq of sodium (Na).]

Acceptance criteria

Potassium: 90.0%–110.0%

Sodium: 90.0%–110.0%

SPECIFIC TESTS

• **BACTERIAL ENDOTOXINS TEST ⟨85⟩:** NMT 0.5 USP Endotoxin Units/mL

• **pH ⟨791⟩:** 4.0–8.0

• **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 of Type I or Type II glass are preferable.

• **LABELING:** The label states the content of each electrolyte in terms of milliequivalents (mEq) in a given volume. The label states the total osmolar concentration in mOsmol/L. When the contents are less than 100 mL, the label alternatively may state the total osmolar concentration in mOsmol/mL.

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Potassium Gluconate RS

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

Topic/Question	Contact	Expert Committee
MULTIPLE ELECTROLYTES INJECTION TYPE 1	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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