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Sodium Citrate and Citric Acid Oral Solution

DEFINITION

Sodium Citrate and Citric Acid Oral Solution is a solution of Sodium Citrate and Citric Acid in a suitable aqueous medium. It contains, in each 100 mL, NLT 2.23 g and NMT 2.46 g of sodium (Na), and NLT 6.11 g and NMT 6.75 g of citrate ($C_6H_5O_7$), equivalent to NLT 9.5 g and NMT 10.5 g of sodium citrate dihydrate ($C_6H_5Na_3O_7 \cdot 2H_2O$), and NLT 6.34 g and NMT 7.02 g of citric acid monohydrate ($C_6H_8O_7 \cdot H_2O$).

IDENTIFICATION

- **A.** Sodium Citrate and Citric Acid Oral Solution imparts an intense yellow color to a nonluminous flame.
- **B.**

  Sample solution: 2 mL of Oral Solution

  Analysis: Add 2 mL of 15% potassium carbonate TS to the *Sample solution*, boil, and cool. Add 4 mL of potassium pyroantimonate TS.

  Acceptance criteria: A dense precipitate is formed (indicates the presence of sodium).
- **C.**

  Sample solution: A dilution of Oral Solution (1 in 20)

  Analysis: Add 5 mL of sodium cobaltinitrite TS to 2 mL of *Sample solution*.

  Acceptance criteria: A yellow precipitate is not formed immediately (indicates the absence of potassium).
- **D.** Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Citrate*

  Sample solution: 3–5 drops of Oral Solution

  Analysis: Add 20 mL of a mixture of pyridine and acetic anhydride (3:1) to the *Sample solution*.

  Acceptance criteria: A light red color is produced.

ASSAY

- **Sodium**

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

  Diluent: 1.04 mg/mL of lithium nitrate in water (equivalent to 15 mEq per 1000 mL of lithium) with a suitable nonionic surfactant

  Standard stock solution: Pipet 50 mL of the *Sodium stock solution* into a 500-mL volumetric flask and dilute with water to volume.

  Standard solution: Dilute 50 µL of the *Standard stock solution* with *Diluent* to 10 mL.

  Sample stock solution: Transfer a volume of Oral Solution, equivalent to 1 g of sodium citrate dihydrate, to a 100-mL volumetric flask and dilute with water to volume.

  Sample solution: Dilute 50 µL of the *Sample stock solution* with *Diluent* to 10 mL.

  Blank: *Diluent*

  Instrumental conditions

  Mode: Flame photometry

  Analytical wavelength: Sodium emission line at 589 nm

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Adjust the flame photometer to read zero with the *Diluent*. Concomitantly determine the sodium flame emission readings for the *Standard solution* and the *Sample solution*.

  Calculate the quantity (g) of sodium (Na) in 100 mL of Oral Solution taken:

$$\text{Result} = (R_{U,Na}/R_{S,Na}) \times (W/V) \times F \times (A_r/M_r) \times F_1$$

  $R_{U,Na}$ = sodium emission reading of the *Sample solution*

  $R_{S,Na}$ = sodium emission reading of the *Standard solution*

W = weight of sodium chloride in the *Sodium stock solution* (g)

V = volume of Oral Solution taken (mL)

F = ratio of the dilution factor of the *Sample solution* to the *Standard solution*, 0.04

A_r = atomic weight of sodium, 22.99

M_r = molecular weight of sodium chloride, 58.44

F_1 = conversion factor for each 100 mL of Oral Solution, 100 mL

Acceptance criteria: 2.23–2.46 g of sodium (Na) in each 100 mL of Oral Solution

- **Sodium Citrate**

Cation-exchange column: Mix 10 g of styrene–divinylbenzene cation-exchange resin with 50 mL of water in a suitable beaker. Allow the resin to settle and decant the supernatant until a slurry of resin remains. Pour the slurry into a 15-mm × 30-cm glass chromatographic tube (having a sealed-in, coarse-porosity fritted disk and fitted with a stopcock), and allow to settle as a homogeneous bed. Wash the resin bed with about 100 mL of water, closing the stopcock when the water level is about 2 mm above the resin bed.

Sample solution: Transfer a volume of Oral Solution, equivalent to 1 g of sodium citrate dihydrate, to a 100-mL volumetric flask and dilute with water to volume.

Titrimetric system

Mode: Direct titration

Titrant: 0.02 N sodium hydroxide VS

Endpoint detection: Visual

Analysis

Sample: *Sample solution*

Pipet 5 mL of the *Sample solution* carefully onto the top of the resin bed in the *Cation-exchange column.* Place a 250-mL conical flask below the column, open the stopcock, and allow to flow until the solution has entered the resin bed. Elute the column with 60 mL of water at a flow rate of about 5 mL/min, collecting about 65 mL of the eluate. Add 5 drops of phenolphthalein TS to the eluate, swirl the flask, and titrate with *Titrant*. Record the buret reading and calculate the volume of *Titrant* consumed.

Calculate the quantity (g) of sodium citrate dihydrate ($C_6H_5Na_3O_7 \cdot 2H_2O$) in 100 mL of the Oral Solution taken:

$$\text{Result} = \{[V \times N \times F \times (D/V_S)] - [(M_{r1}/M_{r2}) \times C]\} \times F_1 \times F_2$$

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

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

F = equivalency factor, 98.05 mg/mEq for sodium citrate dihydrate

D = dilution factor of the *Sample solution*, 20

V_S = volume of Oral Solution taken (mL)

M_{r1} = molecular weight of sodium citrate dihydrate, 294.10

M_{r2} = molecular weight of citric acid monohydrate, 210.14

C = concentration of citric acid monohydrate in the *Sample solution*, as obtained in the *Assay* for *Citric Acid* (mg/mL)

F_1 = conversion factor from mg to g, 0.001

F_2 = conversion factor for each 100 mL of Oral Solution, 100 mL

Acceptance criteria: 9.5–10.5 g of sodium citrate dihydrate ($C_6H_5Na_3O_7 \cdot 2H_2O$) in each 100 mL of Oral Solution

- **Citric Acid**

Sample solution: Transfer a volume of Oral Solution, equivalent to 0.67 g of citric acid monohydrate, to a 100-mL volumetric flask and dilute with water to volume.

Titrimetric system

Mode: Direct titration

Titrant: 0.02 N sodium hydroxide VS

Endpoint detection: Visual

Analysis

Sample: *Sample solution*

Transfer 5 mL of the *Sample solution* to a suitable flask. Add 25 mL of water and 5 drops of phenolphthalein TS. Titrate with *Titrant* to a pink endpoint. Record the buret reading and calculate the volume of *Titrant* consumed.

Calculate the quantity (g) of citric acid monohydrate ($C_6H_8O_7 \cdot H_2O$) in 100 mL of Oral Solution taken:

$$\text{Result} = V \times N \times F \times (D/V_S) \times F_1 \times F_2$$

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

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

F = equivalency factor, 70.05 mg/mEq for citric acid monohydrate

D = dilution factor of the *Sample solution*, 20

V_S = volume of Oral Solution taken (mL)

F_1 = conversion factor from mg to g, 0.001

F_2 = conversion factor for each 100 mL of Oral Solution, 100 mL

Acceptance criteria: 6.34–7.02 g of citric acid monohydrate ($C_6H_8O_7 \cdot H_2O$) in each 100 mL of Oral Solution

PERFORMANCE TESTS

• **Deliverable Volume** ⟨698⟩

For multiple-unit containers

Acceptance criteria: Meets the requirements

• **Uniformity of Dosage Units** ⟨905⟩

For single-unit containers

Acceptance criteria: Meets the requirements

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 4.0–4.4

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

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

Topic/Question	Contact	Expert Committee
SODIUM CITRATE AND CITRIC ACID ORAL SOLUTION	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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