**Sodium Citrate**

C₆H₅Na₃O₇ 258.07
1,2,3-Propanetricarboxylic acid, 2-hydroxy-, trisodium salt; Trisodium citrate (anhydrous) [68-04-2].

C₆H₅Na₃O₇ · 2H₂O 294.10
Trisodium citrate dihydrate [6132-04-3].

**DEFINITION**
Sodium Citrate is anhydrous or contains two molecules of water of hydration. It contains NLT 99.0% and NMT 100.5% of C₆H₅Na₃O₇, calculated on the anhydrous basis.

**IDENTIFICATION**

- **A. IDENTIFICATION TESTS—GENERAL, Sodium (191)**
  - Sample solution: 50 mg/mL
  - Acceptance criteria: Meets the requirements

- **B. IDENTIFICATION TESTS—GENERAL, Citrate (191)**
  - Sample solution: 50 mg/mL
  - Acceptance criteria: Meets the requirements

- **C.**
  - Upon ignition, it yields an alkaline residue that effervesces with treatment with 3 N hydrochloric acid.

**ASSAY**

- **PROCEDURE**
  - Sample: Add 100 mL of glacial acetic acid to 350 mg of Sodium Citrate (previously dried at 180°C for 18 h) in a 250-mL beaker. Stir until completely dissolved.
  - Analysis: Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction (see Titrimetry (541)). Each mL of 0.1 N perchloric acid is equivalent to 8.602 mg of C₆H₅Na₃O₇.
  - Acceptance criteria: 99.0%–100.5% on the anhydrous basis.

**IMPURITIES**

- **HEAVY METALS (231)**
  - [NOTE—Use 50-mL color comparison tubes for preparing the Standard preparation, Test preparation, and Monitor preparation.]
  - Standard preparation: 1.0 mL of Standard Lead Solution and 11 mL of water
  - Test stock preparation: 88 mg/mL of anhydrous sodium citrate in water
  - Test preparation: 12 mL of the Test stock preparation
  - Monitor preparation: 11 mL of the Test stock preparation and 1.0 mL of Standard Lead Solution
  - Analysis: Proceed as directed in the chapter for Procedure, omitting the dilution to 50 mL.
  - Acceptance criteria: NMT 10 ppm

- **TARTRATE**
  - Analysis: To a solution of 1 g in 2 mL of water in a test tube, add 1 mL of potassium acetate TS and 1 mL of 6 N acetic acid. Rub the wall of the tube with a glass rod. Acceptance criteria: No crystalline precipitate is formed.

**SPECIFIC TESTS**

- **ALKALINITY**
  - Sample solution: 1.0 g in 20 mL of water
  - Acceptance criteria: The Sample solution is alkaline to litmus paper, but after the addition of 0.20 mL of 0.10 N sulfuric acid, no pink color is produced by 1 drop of phenolphthalein TS.

- **WATER DETERMINATION, Method III (921)**: Dry a sample at 180°C for 18 h; the anhydrous form loses NMT 1.0% of its weight; the hydrous form loses 10.0%–13.0% of its weight.

**ADDITIONAL REQUIREMENTS**

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **LABELING:** Label it to indicate whether it is anhydrous or hydrous.

**Sodium Citrate and Citric Acid Oral Solution**

- 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, not less than 2.23 g and not more than 2.46 g of sodium (Na), and not less than 6.11 g and not more than 6.75 g of citrate (C₆H₅O₇), equivalent to not less than 9.5 g and not more than 10.5 g of sodium citrate dihydrate (C₆H₅Na₃O₇ · 2H₂O) and not less than 6.34 g and not more than 7.02 g of citric acid monohydrate (C₆H₈O₇ · H₂O).

**Packaging and storage**—Preserve in tight containers.

**Identification**—

- A: It meets the requirements of the flame test for Sodium (191).
- B: Add 2 mL of 15% potassium carbonate TS to 2 mL of Oral Solution, boil, and cool. Add 4 mL of potassium pyroantimonate TS: a dense precipitate is formed (presence of sodium).
- C: To 2 mL of a dilution of Oral Solution (1 in 20) add 5 mL of sodium cobaltinitrite TS: a yellow precipitate is not formed immediately (absence of potassium).
- D: It meets the requirements of the tests for Citrate (191), 3 to 5 drops of Oral Solution and 20 mL of the mixture of pyridine and acetic anhydride being used.

**Uniformity of dosage units (905)**—

- FOR ORAL SOLUTION PACKAGED IN SINGLE-UNIT CONTAINERS: meets the requirements.

**Deliverable volume (698)**—

- FOR ORAL SOLUTION PACKAGED IN MULTIPLE-UNIT CONTAINERS: meets the requirements.

**pH (791)**: between 4.0 and 4.4.

**Assay for sodium**—

- Potassium stock solution, Sodium stock solution, Lithium diluent solution, and Standard preparation—Prepare as directed in the Assay for sodium and potassium under Tricitrates Oral Solution.

- **Assay preparation**—Transfer an accurately measured volume of Oral Solution, equivalent to about 1 g of sodium citrate dihydrate, to a 100-mL volumetric flask, dilute with water to volume, and mix. Transfer 50 µL of this solution to a 10-mL volumetric flask, dilute with Lithium diluent solution to volume, and mix.

- **Procedure**—Using a suitable flame photometer, adjusted to read zero with Lithium diluent solution, concomitantly determine the sodium flame emission readings for the Standard preparation and the Assay preparation at the wavelength of maximum emission at about 589 nm. Calculate the quantity, in g, of Na in each mL of Oral Solution taken by the formula:

\[
14.61 (\text{VS}) (22.99/58.44) (R_{\text{USP}} / R_{\text{RU}})
\]

in which 14.61 is the weight, in g, of sodium chloride in the Sodium stock solution; V is the volume, in mL, of Oral Solution taken, 22.99 is the atomic weight of sodium; 58.44 is the molecular weight of sodium chloride; and R_{USP} and R_{RU} are the sodium emission readings obtained for the Assay preparation and the Standard preparation, respectively.
Assay for 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.

**Procedure**—Transfer an accurately measured volume of Oral Solution, equivalent to about 1 g of sodium citrate dihydrate, to a 100-mL volumetric flask; dilute with water to volume; and mix. Pipet 5 mL of this 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 per minute, collecting about 65 mL of the eluate. Add 5 drops of phenolphthalein TS to the eluate, swirl the flask, and titrate with 0.02 N sodium hydroxide VS. Record the buret reading, and calculate the volume (B) of 0.02 N sodium hydroxide used. Calculate the quantity, in mg, of sodium citrate dihydrate (C₆H₅Na₃O₇ · 2H₂O) in each mL of the Oral Solution taken by the formula:

\[
\text{Quantity} = \frac{\text{Volume} (A) \times \text{Volume} (B) \times \text{Equivalent}}{1000}
\]

where Quantity is the quantity, in mg, of citric acid monohydrate (C₆H₈O₇ · H₂O) in each mL of the Oral Solution taken by the formula:

\[
\text{Quantity} = \frac{1.401 \times \text{Volume} (V)}{1000}
\]

in which 1.401 is the equivalent, in mg, of C₆H₅Na₃O₇ · 2H₂O, of each mL of 0.02 N sodium hydroxide; and V is the volume, in mL, of Oral Solution taken.

**Assay for citric acid**—Transfer an accurately measured volume of Oral Solution, equivalent to about 0.67 g of citric acid monohydrate, to a 100-mL volumetric flask; dilute with water to volume; and mix. Pipet 5 mL of this solution into a suitable flask, add 25 mL of water and 5 drops of phenolphthalein TS, and titrate with 0.02 N sodium hydroxide VS to a pink endpoint. Record the buret reading, and calculate the volume (A) of 0.02 N sodium hydroxide consumed. Calculate the quantity, in mg, of citric acid monohydrate (C₆H₈O₇ · H₂O) in each mL of the Oral Solution taken by the formula:

\[
\text{Quantity} = \frac{1.961 \times \text{Volume} (V)}{1000}
\]

in which 1.961 is the equivalent, in mg, of C₆H₅Na₃O₇ · 2H₂O, of each mL of 0.02 N sodium hydroxide; and V is the volume, in mL, of Oral Solution taken.

**SAFETY PRECAUTIONS**

1. Sodium fluoride and sodium citrate are irritants and corrosives. Use appropriate personal protective equipment when handling these substances. Avoid direct skin contact and inhalation of dusts and vapors. Wash hands thoroughly after handling.

2. Sodium fluoride is highly flammable. Store in a cool, dry place away from heat and sources of ignition.

3. Sodium citrate is also flammable. Store in a cool, dry place away from heat and sources of ignition.

**REFERENCES**

- USP <4658> Sodium
- USP <331> Acidity or Alkalinity
- USP <731> Loss on Drying
- USP <541> Fluorosilicate

**ADDITIONAL REQUIREMENTS**

- **Combustion**
- **Sulfuric Acid Digestion**

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**Sodium Fluoride Gel**

**DEFINITION**

Sodium Fluoride Gel contains NLT 90.0% and NMT 110.0% of the labeled amount of NaF, in an aqueous medium contain-