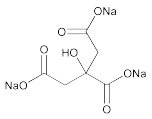
Sodium Citrate



$C_6H_5Na_3O_7$ 258.07
1,2,3-Propanetricarboxylic acid, 2-hydroxy-, trisodium salt; Trisodium citrate (anhydrous) [68-04-2].

$C_6H_5Na_3O_7 \cdot 2H_2O$ 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 $C_6H_5Na_3O_7$, 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 when treated 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° 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 $C_6H_5Na_3O_7$.
  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° 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 ($C_6H_5O_7$), equivalent to not less than 9.5 g and not more than 10.5 g of sodium citrate dihydrate ($C_6H_5Na_3O_7 \cdot 2H_2O$); and not less than 6.34 g and not more than 7.02 g of citric acid monohydrate ($C_6H_8O_7 \cdot H_2O$).

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:

$$(14.61/25V)(22.99/58.44)(R_{U,Na} / R_{S,Na})$$

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 $R_{U,Na}$ and $R_{S,Na}$ 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 consumed. Calculate the quantity, in mg, of sodium citrate dihydrate ($C_6H_5Na_3O_7 \cdot 2H_2O$) in each mL of the Oral Solution taken by the formula:

$$[1.961B(20/V)] - [(294.10/210.14)C]$$

in which 1.961 is the equivalent, in mg, of $C_6H_5Na_3O_7 \cdot 2H_2O$, of each mL of 0.02 N sodium hydroxide; *V* is the volume, in mL, of Oral Solution taken; 294.10 and 210.14 are the molecular weights of sodium citrate dihydrate and citric acid monohydrate, respectively; and *C* is the concentration, in mg per mL, of citric acid monohydrate in the Oral Suspension, as obtained in the *Assay for citric acid.*

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 ($C_6H_8O_7 \cdot H_2O$) in each mL of the Oral Solution taken by the formula:

$$1.401A(20/V)$$

in which 1.401 is the equivalent, in mg, of $C_6H_8O_7 \cdot H_2O$, of each mL of 0.02 N sodium hydroxide; and *V* is the volume, in mL, of Oral Solution taken.

Sodium Fluoride

NaF 41.99
Sodium fluoride [7681-49-4].

DEFINITION
Sodium Fluoride contains NLT 98.0% and NMT 102.0% of NaF, calculated on the dried basis.

IDENTIFICATION
- **A. Fluoride**
  Sample: 1 g
  Analysis: Place the *Sample* in a platinum crucible in a well-ventilated hood, add 15 mL of sulfuric acid, and cover the crucible with a piece of clear, polished glass. Heat the crucible on a steam bath for 1 h, remove the glass cover, rinse it in water, and wipe dry.
  Acceptance criteria: The surface of the glass is etched.
- **B. Identification Tests—General,** *Sodium* ⟨**191**⟩
  Sample solution: 1 in 25
  Acceptance criteria: Meets the requirements

ASSAY
- **Procedure**
  Sample solution: To 80.0 mg add a mixture of 5 mL of acetic anhydride and 20 mL of glacial acetic acid, and heat to dissolve. Allow to cool. [Note—The heating step to dissolve the sodium fluoride in the acetic acid mixture is critical. It is recommended to heat for a minimum of 30 min and use sonication, if necessary, to make sure dissolution is complete prior to the titration step.]
  Analysis: Add 20 mL of dioxane to the *Sample solution*. Add 1 drop of crystal violet TS, and titrate with 0.1 N perchloric acid VS to a green endpoint. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 4.199 mg of NaF.
  Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES
- **Chloride**
  Sample solution: 300 mg in 20 mL of water
  Analysis: To the *Sample solution* add 200 mg of boric acid, 1 mL of nitric acid, and 1 mL of 0.1 N silver nitrate.
  Acceptance criteria: Any turbidity produced is NMT that of a blank to which has been added 1.0 mL of 0.0010 N hydrochloric acid (NMT 0.012%).
- **Heavy Metals** ⟨**231**⟩
  Test preparation: Place 1 g in a platinum dish or crucible, under a hood. Add 1 mL of water and 3 mL of sulfuric acid, and heat at as low a temperature as practicable until all of the sulfuric acid has been expelled. Dissolve the residue in 20 mL of water, and neutralize the solution to phenolphthalein TS with ammonium hydroxide. Add 1 mL of glacial acetic acid, dilute with water to 45 mL, and filter. Use 30 mL of the filtrate for the test.
  Acceptance criteria: NMT 30 ppm

SPECIFIC TESTS
- **Acidity or Alkalinity**
  Sample: 2.0 g
  Analysis: Dissolve the *Sample* in 40 mL of water in a platinum dish. Add 10 mL of a saturated solution of potassium nitrate, cool the solution to 0°, and add 3 drops of phenolphthalein TS.
  Acceptance criteria: If no color appears, a pink color persisting for 15 s is produced by NMT 2.0 mL of 0.10 N sodium hydroxide. If the solution is colored pink by the addition of phenolphthalein TS, it is rendered colorless by NMT 0.50 mL of 0.10 N sulfuric acid. [Note—Save the neutralized solution for the test for *Fluosilicate*.]
- **Loss on Drying** ⟨**731**⟩**:** Dry a sample at 150° for 4 h: it loses NMT 1.0% of its weight.
- **Fluosilicate**
  Analysis: After the solution from the test for *Acidity or Alkalinity* has been neutralized, heat to boiling, and titrate while hot with 0.10 N sodium hydroxide until a permanent pink color is obtained.
  Acceptance criteria: NMT 1.5 mL of 0.10 N sodium hydroxide is required.

ADDITIONAL REQUIREMENTS
- **Packaging and Storage:** Preserve in well-closed containers.

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-