Status: Currently Official on 13-Feb-2025
Official Date: Official as of 01-May-2019
Document Type: USP Monographs
DocId: GUID-C9C847AC-195F-430D-A18C-21F7A8CDC08E_3_en-US
DOI: https://doi.org/10.31003/USPNF_M5130_03_01
DOI Ref: oyp5n

Anticoagulant Citrate Phosphate Dextrose Solution

DEFINITION

Anticoagulant Citrate Phosphate Dextrose Solution is a sterile solution of Citric Acid, Sodium Citrate, Monobasic Sodium Phosphate, and Dextrose in Water for Injection. It contains, in each 1000 mL, NLT 2.11 g and NMT 2.33 g of monobasic sodium phosphate ($NaH_2PO_4 \cdot H_2O$); NLT 24.22 g and NMT 26.78 g of dextrose ($C_6H_{12}O_6 \cdot H_2O$); NLT 19.16 g and NMT 21.18 g of total citrate, expressed as anhydrous citric acid ($C_6H_8O_7$); and NLT 6.21 g and NMT 6.86 g of Sodium (Na). It contains no antimicrobial agents.

Prepare Anticoagulant Citrate Phosphate Dextrose Solution as follows.

Citric Acid (anhydrous)	2.99 g
Sodium Citrate (dihydrate)	26.3 g
Monobasic Sodium Phosphate (monohydrate; $NaH_2PO_4 \cdot H_2O$)	2.22 g
Dextrose ($C_6H_{12}O_6 \cdot H_2O$)	25.5 g
Water for Injection, a sufficient quantity to make	1000 mL

Dissolve the ingredients, and mix. Filter the solution until clear, place immediately in suitable containers, and sterilize.

If desired, 3.27 g of monohydrated citric acid may be used instead of the indicated amount of anhydrous citric acid; 23.06 g of anhydrous sodium citrate may be used instead of the indicated amount of dihydrated sodium citrate; 1.93 g of anhydrous monobasic sodium phosphate may be used instead of the indicated amount of monohydrated monobasic sodium phosphate; and 23.2 g of anhydrous dextrose may be used instead of the indicated amount of monohydrated dextrose.

IDENTIFICATION

- **A. Dextrose**

  Analysis: Add a few drops of solution (1 in 20) to 5 mL of hot alkaline cupric tartrate TS.

  Acceptance criteria: A copious red precipitate of cuprous oxide is formed.
- **B. Identification Tests—General, *Phosphate*⟨191⟩:** Meets the requirements
- **C. Identification Tests—General, *Citrate*⟨191⟩:** Meets the requirements when concentrated to one-half its volume
- **D. Identification Tests—General, *Sodium*⟨191⟩:** Meets the requirements when concentrated to one-half its volume

ASSAY

- **Total Citrate and Total Phosphate**

  Mobile phase, Standard preparation 2, and **Chromatographic system:** Proceed as directed in *Assay for Citric Acid/Citrate and Phosphate ⟨345⟩*.

  Sample solution for total citrate: Pipet 10 mL of Solution into a suitable volumetric flask, and proceed as directed in *Assay for Citric Acid/Citrate and Phosphate ⟨345⟩, Sample solution (for the assay of citric acid/citrate)*.

  Sample solution for total phosphate: Pipet 5 mL of Solution into a suitable volumetric flask, and proceed as directed in *Assay for Citric Acid/Citrate and Phosphate ⟨345⟩, Sample solution (for the assay of phosphate)*.

  Analysis: Proceed as directed in *Assay for Citric Acid/Citrate and Phosphate ⟨345⟩, Procedure*.

  Calculate the quantity, in g, of anhydrous citric acid ($C_6H_8O_7$) in the volume of Solution taken:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times F \times D$$

  r_U = peak area of citrate from the *Sample solution for total citrate*

  r_S = peak area of citrate from *Standard preparation 2*

  C_S = concentration of citrate in *Standard preparation 2* (µg/mL)

  M_{r1} = molecular weight of anhydrous citric acid ($C_6H_8O_7$), 192.12

M_{r2} = molecular weight of citrate ($C_6H_5O_7$), 189.10

F = conversion factor, 0.000001 g/µg

D = dilution factor

Acceptance criteria: Each 1000 mL of Solution should contain 19.16 g–21.18 g of total citrate expressed as anhydrous citric acid.

Analysis: Proceed as directed in *Assay for Citric Acid/Citrate and Phosphate ⟨345⟩, Procedure*.

Calculate the quantity of phosphate, in g, expressed as monobasic sodium phosphate ($NaH_2PO_4 \cdot H_2O$), in the volume of Solution taken:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times F \times D$$

r_U = peak area of phosphate from the *Sample solution for total phosphate*

r_S = peak area of phosphate from *Standard preparation 2*

C_S = concentration of phosphate in *Standard preparation 2* (µg/mL)

M_{r1} = molecular weight of monobasic sodium phosphate monohydrate ($NaH_2PO_4 \cdot H_2O$), 137.99

M_{r2} = molecular weight of phosphate (PO_4), 94.97

F = conversion factor, 0.000001 g/µg

D = dilution factor

Acceptance criteria: Each 1000 mL of Solution should contain 2.11–2.33 g of monobasic sodium phosphate ($NaH_2PO_4 \cdot H_2O$).

- **Dextrose**

Sample: 5.0 mL of Solution

Analysis: Tare a clean, medium-porosity filtering crucible containing several carborundum boiling chips or glass beads. Pipet 50 mL of freshly mixed alkaline cupric tartrate TS into a 400-mL beaker. Add the boiling chips or glass beads from the tared crucible, 45 mL of water, and 5.0 mL of Solution to the beaker. Heat the beaker and contents over a burner that has been adjusted to cause boiling of the solution to start in 3.5–4 min. Boil the solution for 2 min, accurately timed, and filter immediately through the tared crucible, taking care to transfer all of the boiling chips or glass beads to the crucible. Wash the precipitate with hot water and 10 mL of alcohol. Dry the crucible and contents at 110° to constant weight. Perform a blank determination, and correct the weight of the precipitate from the sample for any precipitate obtained in the blank.

Each mg of cuprous oxide precipitate of the substance under assay is equivalent to 0.496 mg of dextrose ($C_6H_{12}O_6 \cdot H_2O$).

Acceptance criteria: Each 1000 mL of Solution should contain 24.22–26.78 g of dextrose ($C_6H_{12}O_6 \cdot H_2O$).

- **Sodium**

Solution A: Transfer 1.04 g of lithium nitrate to a 1000-mL volumetric flask, add a suitable nonionic surfactant, add water to volume, and mix. This solution contains 15 mEq/1000 mL of lithium.

Standard solution: Transfer 8.18 g of sodium chloride, previously dried at 105° for 2 h to a 1000-mL volumetric flask, dilute with water to volume, and mix. This solution contains 140 mEq/1000 mL of sodium. Transfer 50 µL of this solution to a 10-mL volumetric flask, dilute with *Solution A* to volume, and mix.

Sample solution: Transfer 25 mL of Solution to a 50-mL volumetric flask, and dilute with water to volume. Transfer 50 µL of this solution to a 10-mL volumetric flask, dilute with *Solution A* to volume, and mix.

Analysis

Samples: *Standard solution* and *Sample solution*

Using a suitable flame photometer, adjusted to read zero with *Solution A*, concomitantly determine the sodium flame emission readings for the *Standard solution* and the *Sample solution* at the wavelength of maximum emission at 589 nm.

Calculate the quantity, in g, of sodium (Na) in 1000 mL of Solution taken:

$$\text{Result} = (r_U/r_S) \times (A_r/M_r) \times W \times F$$

r_U = sodium emission readings from the *Sample solution*

r_S = sodium emission readings from the *Standard solution*

A_r = atomic weight of sodium, 22.99

M_r = molecular weight of sodium chloride, 58.44

W = weight of sodium chloride taken to make the *Standard solution*, 8.18 g

F = conversion factor, 2

Acceptance criteria: Each 1000 mL of Solution should contain 6.21–6.86 g of sodium.

IMPURITIES

• **Chloride and Sulfate,** *Chloride*⟨221⟩**:** A 10-mL portion shows no more chloride than corresponds to 0.50 mL of 0.020 N hydrochloric acid (0.0035%).

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 5.0–6.0

• **Bacterial Endotoxins Test** ⟨85⟩**:** It contains NMT 5.56 USP Endotoxin Units/mL.

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

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in single-dose containers of colorless, transparent Type I or Type II glass, or of a suitable plastic material (see ▲*Medical Devices—Bacterial Endotoxin and Pyrogen Tests* ⟨161⟩).▲ (CN 1-May-2019)

• **Labeling:** Label it to indicate the number of mL of Solution required per 100 mL of whole blood or the number of mL of Solution required per volume of whole blood to be collected.

• **USP Reference Standards** ⟨11⟩

USP Citric Acid RS

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

Topic/Question	Contact	Expert Committee
ANTICOAGULANT CITRATE PHOSPHATE DEXTROSE SOLUTION	Rebecca C. Potts Associate Scientific Liaison	BIO32020 Biologics Monographs 3 - Complex Biologics and Vaccines

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 31(3)

Current DocID: GUID-C9C847AC-195F-430D-A18C-21F7A8CDC08E_3_en-US

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