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Anticoagulant Citrate Dextrose Solution

DEFINITION

Anticoagulant Citrate Dextrose Solution is a sterile solution of Citric Acid, Sodium Citrate, and Dextrose in Water for Injection. It contains no antimicrobial agents, and in each 1000 mL it contains:

	Solution A	Solution B
Total Citrate, expressed as anhydrous citric acid ($C_6H_8O_7$)	NLT 20.59 g	NLT 12.37 g
	NMT 22.75 g	NMT 13.67 g
Dextrose ($C_6H_{12}O_6 \cdot H_2O$)	NLT 23.28 g	NLT 13.96 g
	NMT 25.73 g	NMT 15.44 g
Sodium (Na)	NLT 4.90 g	NLT 2.94 g
	NMT 5.42 g	NMT 3.25 g

Prepare Anticoagulant Citrate Dextrose Solution as follows.

	Solution A	Solution B
Citric Acid (anhydrous)	7.3 g	4.4 g
Sodium Citrate (dihydrate)	22.0 g	13.2 g
Dextrose (monohydrate)	24.5 g	14.7 g
Water for Injection, a sufficient quantity to make	1000 mL	1000 mL

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

If desired, 8 g and 4.8 g of monohydrated citric acid may be used instead of the indicated, respective amounts of anhydrous citric acid; 19.3 g and 11.6 g of anhydrous sodium citrate may be used instead of the indicated, respective amounts of dihydrated sodium citrate; and 22.3 g and 13.4 g of anhydrous dextrose may be used instead of the indicated, respective amounts 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, *Citrate*⟨191⟩:** Meets the requirements when concentrated to one-half its volume

- **C. Identification Tests—General, *Sodium*⟨191⟩:** Meets the requirements when concentrated to one-half its volume

ASSAY

- **Total Citrate**

  Mobile phase, Standard preparation 1, and **Chromatographic system:** Proceed as directed in *Assay for Citric Acid/Citrate and Phosphate ⟨345⟩*.

  Sample solution: 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 citric acid/citrate)*.

  Analysis

  Samples: *Standard preparation 1* and *Sample solution*

  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*

r_S = peak area of citrate from *Standard preparation 1*

C_S = concentration of citrate in *Standard preparation 1* (µg/mL)

M_{r1} = molecular weight of anhydrous citric acid, 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 should contain 20.59–22.75 g in Solution A and 12.37–13.67 g in Solution B of total citrate expressed as anhydrous citric acid.

- **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 should contain 4.90–5.42 g in Solution A and 2.94–3.25 g in Solution B of sodium.

- **Dextrose**

Analysis: Determine the angular rotation of Solution in a suitable polarimeter tube (see *Optical Rotation* ⟨781⟩).

Where Solution is labeled to contain anhydrous dextrose, calculate the percentage, in g/100 mL, of anhydrous dextrose ($C_6H_{12}O_6$) in the portion of Solution taken:

$$\text{Result} = (100/F) \times A \times R$$

F = midpoint of the specific rotation range for anhydrous dextrose, 52.9°

A = 100 mm divided by the length of the polarimeter tube (mm)

R = observed rotation (°)

Where Solution is labeled to contain dextrose monohydrate, calculate the percentage, in g/100 mL, of dextrose ($C_6H_{12}O_6 \cdot H_2O$) in the portion of Solution taken:

$$\text{Result} = (100/F) \times (M_{r1}/M_{r2}) \times A \times R$$

F = midpoint of the specific rotation range for anhydrous dextrose, 52.9°

M_{r1} = molecular weight for dextrose monohydrate, 198.17

M_{r2} = molecular weight for anhydrous dextrose, 180.16

A = 100 mm divided by the length of the polarimeter tube (mm)

R = observed rotation (°)

Acceptance criteria: Each 1000 mL should contain 23.28–25.73 g in Solution A and 13.96–15.44 g in Solution B of dextrose monohydrate.

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⟩**:** 4.5–5.5

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

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

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 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 DEXTROSE SOLUTION	Rebecca C. Potts Associate Scientific Liaison	BIO32020 Biologics Monographs 3 - Complex Biologics and Vaccines
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	BIO32020 Biologics Monographs 3 - Complex Biologics and Vaccines

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