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Anticoagulant Citrate Phosphate Dextrose Adenine Solution

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-anticoagulant-citrate-phosphate-dextrose-adenine-sol-20230331.

DEFINITION

Anticoagulant Citrate Phosphate Dextrose Adenine Solution is a sterile solution of Citric Acid, Sodium Citrate, Monobasic Sodium Phosphate,Dextrose, and Adenine 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 30.30 g and NMT 33.50 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 citric acid, anhydrous ($C_6H_8O_7$); NLT 6.21 g and NMT 6.86 g of sodium (Na); and NLT 0.247 g and NMT 0.303 g of adenine ($C_5H_5N_5$). It contains no antimicrobial agents.

Prepare Anticoagulant Citrate Phosphate Dextrose Adenine 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 (monohydrate)	31.9 g
Adenine ($C_5H_5N_5$)	0.275 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 Citric Acid (anhydrous); 23.06 g of anhydrous sodium citrate may be used instead of the indicated amount of Sodium Citrate (dihydrate); 1.93 g of anhydrous monobasic sodium phosphate may be used instead of the indicated amount of monohydrated monobasic sodium phosphate; and 29.0 g of anhydrous dextrose may be used instead of the indicated amount of Dextrose (monohydrate)

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 citric acid/citrate)*.

Analysis

Samples: *Standard preparation 2* and *Sample solution for total citrate*

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, 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 NLT 19.16 g and NMT 21.18 g of total citrate expressed as anhydrous citric acid ($C_6H_8O_7$).

Analysis

Samples: *Standard preparation 2* and *Sample solution for total phosphate*

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, 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 ($NaH_2PO_4 \cdot H_2O$).

- **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, dilute with water to volume, and mix. 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 g–6.86 g of sodium.

- **Dextrose**

Sample: 5 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 make any necessary correction.

Each mg of cuprous oxide precipitate obtained 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 30.30–33.50 g of dextrose ($C_6H_{12}O_6 \cdot H_2O$).

• **Adenine**

Mobile phase: Dissolve 3.45 g of ammonium dihydrogen phosphate in 950 mL of water, add 10 mL of glacial acetic acid, dilute with water to 1000 mL, and mix. Pass the solution through a membrane filter with a 1-µm or finer pore size, and degas.

System suitability solution: 0.275 mg/mL of each USP Adenine RS and purine in dilute hydrochloric acid (1 in 120)

Standard solutions: Place quantities of USP Adenine RS in dilute hydrochloric acid (1 in 120) in three separate volumetric flasks, and dilute with the dilute hydrochloric acid solution to volume to obtain *Standard solutions* having known concentrations of 0.25, 0.275, and 0.30 mg of adenine per mL, respectively. Protect from light.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 30-cm stainless steel; packing L9

Flow rate: 2.0 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution* (NLT four injections)

Suitability requirements

Resolution: NLT 3.0 between adenine and purine

Relative standard deviation: NMT 2.5% for adenine peak and NMT 2.0% for the retention time of adenine peak

Analysis

Samples: *Standard solutions* and Solution

Plot the responses against the concentrations, in mg, of USP Adenine RS per mL of the *Standard solutions*.

Calculate the quantity, in mg, of adenine ($C_5H_5N_5$) in each mL of the Solution taken as the value read directly from the Standard curve corresponding to the response obtained from the portion of the Solution chromatographed.

Acceptance criteria: Each 1000 mL of Solution should contain 0.247–0.303 g of adenine ($C_5H_5N_5$).

IMPURITIES

• **Chloride and Sulfate ⟨221⟩, *Chloride*:** 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, ▲preferably▲ (RB 1-Apr-2023) Type I or Type II glass, or of a suitable plastic material (see *Medical Devices—Bacterial Endotoxin and Pyrogen Tests ⟨161⟩*).

• **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 Adenine RS

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 ADENINE 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

Chromatographic Database Information: Chromatographic Database

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