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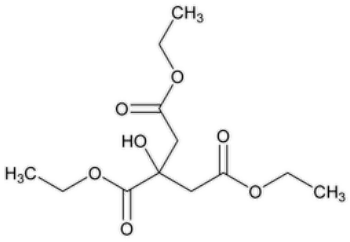
Triethyl Citrate



$C_{12}H_{20}O_7$ 276.29

1,2,3-Propanetricarboxylic acid, 2-hydroxy-, 1,2,3-triethyl ester;

Triethyl 2-hydroxypropane-1,2,3-tricarboxylate; CAS RN®: 77-93-0.

Change to read:

DEFINITION

Triethyl Citrate contains ▲NLT 97.0% and NMT 102.0%▲ (NF 1-May-2023) of triethyl citrate ($C_{12}H_{20}O_7$), calculated on the anhydrous basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197F

Change to read:

• **B. ▲Chromatographic Identity:▲** (NF 1-May-2023) The retention time of the major peak of the *Sample solution* corresponds to that of ▲the *Standard solution*,▲ (NF 1-May-2023) as obtained in the *Assay*.

ASSAY

Change to read:

• **Procedure**

▲Diluent: Methylene chloride

Internal standard solution: 1 mg/mL of trimethyl citrate in *Diluent*

Standard solution: 1 mg/mL of USP Triethyl Citrate RS in *Internal standard solution*

Sample solution: 1 mg/mL of Triethyl Citrate in *Internal standard solution*

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 30-m; 0.5-µm layer of phase G42

Temperatures

Injector: 225°

Detector: 275°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	—	50	5
50	20	220	15

Carrier gas: Helium

Flow rate: 2.3 mL/min

Injection volume: 1 µL

Injection type: Split, split ratio 30:1

System suitability

Sample: *Standard solution*

[NOTE—The retention time for triethyl citrate is about 14.6 min. The relative retention times for trimethyl citrate and triethyl citrate are 0.9 and 1.0, respectively.]

Suitability requirements

Tailing factor: NMT 1.5 for the triethyl citrate ▲and▲ (ERR 1-May-2023) trimethyl citrate peaks

Relative standard deviation: NMT 1.0% of the peak area ratio of triethyl citrate to trimethyl citrate

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of triethyl citrate ($C_{12}H_{20}O_7$) in the portion of Triethyl Citrate taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak area ratio of triethyl citrate to trimethyl citrate from the *Sample solution*

R_S = peak area ratio of triethyl citrate to trimethyl citrate from the *Standard solution*

C_S = concentration of USP Triethyl Citrate RS in the *Standard solution* (mg/mL)

C_U = concentration of Triethyl Citrate in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–102.0% on the anhydrous basis▲ (NF 1-May-2023)

Add the following:

▲IMPURITIES

• **ORGANIC IMPURITIES**

Diluent and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution A: 0.02 mg/mL of USP Triethyl Aconitate RS in *Diluent*

Standard solution B: 0.02 mg/mL of USP Triethyl Citrate RS in *Diluent*

Sample solution: 10 mg/mL of Triethyl Citrate in *Diluent*

System suitability

Samples: *Standard solution A* and *Standard solution B*

Suitability requirements

Relative standard deviation: NMT 3.0% for the triethyl aconitate peak, *Standard solution A*; NMT 3.0% for the triethyl citrate peak, *Standard solution B*

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

[NOTE—See *Table 2* for the relative retention times.]

Table 2

Compound Name	Relative Retention Time
Ethanol	0.11
Triethyl aconitate[a]	0.98
Triethyl citrate	1.0
Triethyl isocitrate	1.02
Any unidentified impurity	—

[a] Triethyl (*E*)-prop-1-ene-1,2,3-tricarboxylate.

Calculate the percentage of triethyl aconitate in the portion of Triethyl Citrate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area of triethyl aconitate from the *Sample solution*

r_S = peak area of triethyl aconitate from *Standard solution A*

C_S = concentration of USP Triethyl Aconitate RS in *Standard solution A* (mg/mL)

C_U = concentration of Triethyl Citrate in the *Sample solution* (mg/mL)

Calculate the percentage of each individual impurity, excluding any solvent peaks, in the portion of Triethyl Citrate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area of each individual impurity from the *Sample solution*

r_S = peak area of triethyl citrate from *Standard solution B*

C_S = concentration of USP Triethyl Citrate RS in *Standard solution B* (mg/mL)

C_U = concentration of Triethyl Citrate in the *Sample solution* (mg/mL)

Acceptance criteria

Triethyl aconitate: NMT 0.2%

Individual impurity: NMT 0.2%

Total impurities: NMT 0.5%▲ (NF 1-May-2023)

SPECIFIC TESTS

Delete the following:

▲• **Specific Gravity** ⟨841⟩▲ (NF 1-May-2023)

Delete the following:

▲• **Refractive Index** ⟨831⟩▲ (NF 1-May-2023)

• **Acidity**

Neutralized isopropyl alcohol: To a suitable quantity of isopropyl alcohol add 2–3 drops of bromothymol blue TS and just sufficient 0.10 N sodium hydroxide dropwise to produce a faint blue color. [Note—Prepare *Neutralized isopropyl alcohol* just prior to use.]

Sample solution: 32.0 g of Triethyl Citrate in 30 mL of *Neutralized isopropyl alcohol*

Analysis: Add bromothymol blue TS, and titrate with 0.10 N sodium hydroxide to a faint blue endpoint.

Acceptance criteria: NMT 1.0 mL of 0.10 N sodium hydroxide is required.

• **Water Determination** ⟨921⟩, *Method I*: NMT 0.25%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

Change to read:

• **USP Reference Standards ⟨11⟩**

▲ USP Triethyl Aconitate RS▲ (NF 1-May-2023)
USP Triethyl Citrate RS

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

Topic/Question	Contact	Expert Committee
TRIETHYL CITRATE	Documentary Standards Support	SE2020 Simple Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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