

Triethyl Citrate

1 Nonproprietary Names

BP: Triethyl citrate
PhEur: Triethylis citras
USPNE: Triethyl citrate

2 Synonyms

Citric acid, ethyl ester; *Citroflex 2*; *Citrofol AI*; E1505; *Hydagen CAT*; TEC.

3 Chemical Name and CAS Registry Number

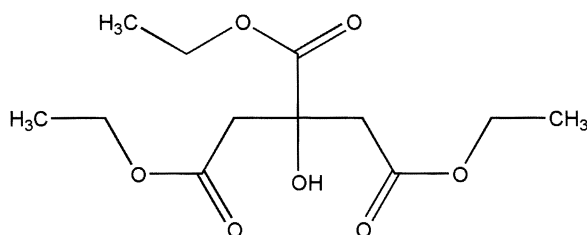
2-Hydroxy-1,2,3-propanetricarboxylic acid, triethyl ester [77-93-0]

4 Empirical Formula Molecular Weight

$C_{12}H_{20}O_7$

276.29

5 Structural Formula



6 Functional Category

Plasticizer.

7 Applications in Pharmaceutical Formulation or Technology

Triethyl citrate and the related esters acetyltriethyl citrate, tributyl citrate, and acetyltributyl are used to plasticize polymers in formulated pharmaceutical coatings.⁽¹⁻⁵⁾ The coating applications include capsules, tablets, beads, and granules for taste masking, immediate release, sustained-release, and enteric formulations.

Triethyl citrate is also used as a direct food additive for flavoring, for solvency, and as a surface active agent.

8 Description

Triethyl citrate is a clear, odorless, practically colorless, oily liquid.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for triethyl citrate.

Test	PhEur 2002	USPNE 20
Identification	+	+
Characters	+	—
Appearance	+	—
Specific gravity	—	1.135–1.139
Refractive index	1.440–1.446	1.439–1.441
Acidity	+	+
Related substances	+	—
Sulfated ash	≤0.1%	—
Heavy metals	≤5 ppm	≤0.001%
Water	≤0.25%	≤0.25%
Assay (anhydrous basis)	98.5–101.0%	99.0–100.5%

10 Typical Properties

Acid value: 0.02

Boiling point: 288°C (decomposes)

Flash point: 155°C

Pour point: –45°C

Solubility: soluble 1 in 125 of peanut oil, 1 in 15 of water.

Miscible with ethanol (95%), acetone, and propan-2-ol.

Viscosity (dynamic): 35.2 mPa s (35.2 cP) at 25°C

11 Stability and Storage Conditions

Triethyl citrate should be stored in a closed container in a cool, dry location. When stored in accordance with these conditions, triethyl citrate is a stable product.

12 Incompatibilities

Triethyl citrate is incompatible with strong alkalis and oxidizing materials.

13 Method of Manufacture

Triethyl citrate is prepared by the esterification of citric acid and ethanol in the presence of a catalyst.

14 Safety

Triethyl citrate is used in oral pharmaceutical formulations and as a direct food additive. It is generally regarded as a nontoxic and nonirritant material. However, ingestion of large quantities may be harmful.

LD₅₀ (cat, oral): 35 g/kg⁽⁶⁾

LD₅₀ (mouse, IP): 1.75 g/kg

LD₅₀ (rat, IP): 4 g/kg

LD₅₀ (rat, oral): 5.9 g/kg

LD₅₀ (rat, SC): 6.6 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Triethyl citrate is irritating to the eyes and may irritate the skin. Irritating to the respiratory system as a mist or at elevated temperatures. Gloves, eye protection, and a respirator are recommended.

16 Regulatory Status

GRAS listed. Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (oral capsules and tablets).

17 Related Substances

Acetyltributyl citrate; acetyltriethyl citrate; tributyl citrate.

18 Comments

The EINECS number for triethyl citrate is 201-070-7.

19 Specific References

- 1 Gutierrez-Rocca JC, McGinity JW. Influence of water soluble and insoluble plasticizers on the physical and mechanical properties of acrylic resin copolymers. *Int J Pharm* 1994; 103: 293-301.

- 2 Lehmann K. Chemistry and application properties of polymethacrylate coating systems. In: McGinity JW, ed. *Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms*. New York: Marcel Dekker, 1989: 153-245.
- 3 Steurnagel CR. Latex emulsions for controlled drug delivery. In: McGinity JW, ed. *Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms*. New York: Marcel Dekker, 1989: 1-61.
- 4 Gutierrez-Rocca JC, McGinity JW. Influence of aging on the physical-mechanical properties of acrylic resin films cast from aqueous dispersions and organic solutions. *Drug Dev Ind Pharm* 1993; 19(3): 315-332.
- 5 Liu J, Williams R. Properties of heat-humidity cured cellulose acetate phthalate free films. *Eur J Pharm Sci* 2002; 17(1-2): 31-41.
- 6 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 3547-3548.

20 General References

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21 Author

SW Kennedy.

22 Date of Revision

17 October 2002.