

Tributyl Citrate

1 Nonproprietary Names

USPNF: Tributyl citrate

2 Synonyms

Citric acid, tributyl ester; *Citroflex 4*; TBC; tri-*n*-butyl citrate; tributyl 2-hydroxy-1,2,3-propanetricarboxylate.

3 Chemical Name and CAS Registry Number

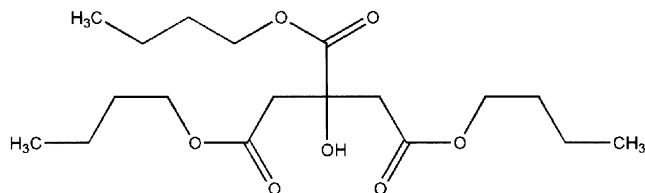
1,2,3-Propanetricarboxylic acid, 2-hydroxy, tributyl ester [77-94-1]

4 Empirical Formula Molecular Weight

$C_{18}H_{32}O_7$

360.5

5 Structural Formula



6 Functional Category

Plasticizer.

7 Applications in Pharmaceutical Formulation or Technology

Tributyl citrate is used to plasticize polymers in formulated pharmaceutical coatings. The coating applications include capsules, tablets, beads, and granules for taste masking, immediate release, sustained-release, and enteric formulations.⁽¹⁻⁶⁾

8 Description

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

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for tributyl citrate.

Test	USPNF 20
Identification	+
Specific gravity	1.037–1.045
Refractive index	1.443–1.445
Acidity	+
Water	≤0.2%
Heavy metals	≤0.001%
Assay (anhydrous basis)	≥99.0%

10 Typical Properties

Acid value: 0.02

Boiling point: 322°C (decomposes)

Flash point: 185°C

Pour point: –62°C

Solubility: miscible with acetone, ethanol, and vegetable oil; practically insoluble in water.

Viscosity: 32 mPa s (32 cP) at 25°C

11 Stability and Storage Conditions

Tributyl citrate should be stored in closed containers in a cool, dry location at temperatures not exceeding 38°C. When stored in accordance with these conditions, tributyl citrate is a stable material.

12 Incompatibilities

Tributyl citrate is incompatible with strong alkalis and oxidizing materials.

13 Method of Manufacture

Tributyl citrate is prepared by the esterification of citric acid with butanol.

14 Safety

Tributyl citrate is used in oral pharmaceutical formulations. It is generally regarded as an essentially nontoxic and nonirritating material. However, ingestion of large quantities may be harmful.

LD₅₀ (cat, oral): >50 mL/kg⁽⁷⁾

LD₅₀ (mouse, IP): 2.9 g/kg

LD₅₀ (rat, oral): >30 mL/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Tributyl citrate may be irritating to the eyes. It may also be irritating to the respiratory system at elevated temperatures.

Gloves and eye protection are recommended for normal handling, and a respirator is recommended for elevated temperatures.

16 Regulatory Status

Approved in the US for direct food contact in food films.

17 Related Substances

Acetyltributyl citrate; acetyltriethyl citrate; triethyl citrate.

18 Comments

The EINECS number for tributyl citrate is 201-071-2.

19 Specific References

- 1 Gutierrez-Rocca JC, McGinity JW. Influence of water soluble and insoluble plasticizer 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 Felton LA, McGinity JW. Influence of plasticisers on the adhesive properties of an acrylic resin copolymer to hydrophilic and hydrophobic tablet compacts. *Int J Pharm* 1997; **154**(2): 167–178.
- 6 Okarter TU, Singla K. The effects of plasticisers on the release of metoprolol tartrate from granules coated with a polymethacrylate film. *Drug Dev Ind Pharm* 2000; **26**(3): 323–329.
- 7 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 3513.

20 General References

Morflex Inc. Technical literature: *Citrate esters*, 2000.

21 Author

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22 Date of Revision

14 June 2002.