

Acetyltributyl Citrate

1 Nonproprietary Names

USPNF: Acetyltributyl citrate

2 Synonyms

Acetylbutyl citrate; acetylcitric acid, tributyl ester; ATBC; *Citroflex A-4*; tributyl acetylcitrate; tributyl *O*-acetylcitrate; tributyl citrate acetate.

3 Chemical Name and CAS Registry Number

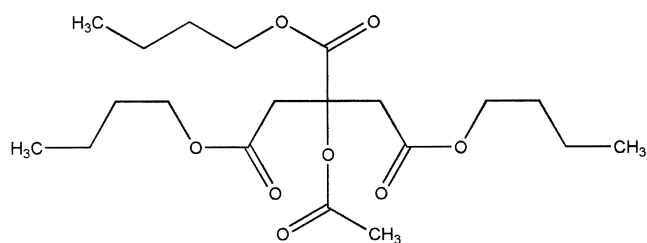
1,2,3-Propanetricarboxylic acid, 2-acetyloxy, tributyl ester [77-90-7]

4 Empirical Formula Molecular Weight

$C_{20}H_{34}O_8$

402.5

5 Structural Formula



6 Functional Category

Plasticizer.

7 Applications in Pharmaceutical Formulation or Technology

Acetyltributyl citrate is used to plasticize polymers in formulated pharmaceutical coatings,⁽¹⁻⁵⁾ including capsules, tablets, beads, and granules for taste masking, immediate release, sustained-release and enteric formulations.

8 Description

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

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for acetyltributyl citrate.

Test	USPNF 20
Identification	+
Specific gravity	1.045–1.055
Refractive index	1.4410–1.4425
Acidity	+
Water	≤0.25%
Heavy metals	≤0.001%
Assay (anhydrous basis)	≥99.0%

10 Typical Properties

Acid value: 0.02

Boiling point: 326 °C (decomposes)

Flash point: 204 °C

Pour point: –59 °C

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

Viscosity (dynamic): 33 mPa s (33 cP) at 25 °C

11 Stability and Storage Conditions

Acetyltributyl citrate should be stored in a well-closed container in a cool, dry location at temperatures not exceeding 38 °C. When stored in accordance with these conditions, acetyltributyl citrate is a stable product.

12 Incompatibilities

Acetyltributyl citrate is incompatible with strong alkalis and oxidizing materials.

13 Method of Manufacture

Acetyltributyl citrate is prepared by the esterification of citric acid with butanol followed by acylation with acetic anhydride.

14 Safety

Acetyltributyl citrate is used in oral pharmaceutical formulations and films intended for direct food contact. It is also used in self-adhesive thin films used for topical delivery systems.⁽⁶⁾ It is generally regarded as a relatively nontoxic and nonirritating material. However, ingestion of large quantities may be harmful.

LD₅₀ (cat, oral): >50 mL/kg⁽⁷⁾

LD₅₀ (mouse, IP): >4 g/kg

LD₅₀ (rat, oral): >31.5 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Acetyltributyl citrate is slightly irritating to the eyes and may be irritating to the respiratory system as a mist or at elevated temperatures. Gloves and eye protection are recommended for normal

handling, and a respirator is recommended when using acetyltributyl citrate at elevated temperatures.

16 Regulatory Status

Included in FDA Inactive Ingredients Guide (oral capsules and tablets). Included in nonparenteral medicines licensed in the UK. Approved in the USA for direct food contact in food films.

17 Related Substances

Acetyltriethyl citrate; tributyl citrate; triethyl citrate.

18 Comments

Acetyltributyl citrate is used as a plasticizer in food contact films, although it has been known to migrate from food-grade PVC films into high-fat foods such as olive oil.⁽⁸⁾

Poly lactide acetyltributyl citrate has been investigated as a biodegradable barrier for use in guided-tissue regeneration therapy.⁽⁹⁾

The EINECS number for acetyltributyl citrate is 201-067-0.

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 Repka MA, Gerding TG, Repka SL. Influence of plasticisers and drugs on the physical-mechanical properties of hydroxypropylcellulose films prepared by hot melt extrusion. *Drug Dev Ind Pharm* 1999; 25(5): 625–633.
- 6 Lieb S, Szeimies RM, Lee G. Self-adhesive thin films for topical delivery of 5-aminolevulinic acid. *Eur J Pharm Biopharm* 2002; 53(1): 99–106.
- 7 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 3512.
- 8 Goulas AE, Riganakos KA, Ehlermann DA, et al. Effect of high-dose electron beam irradiation on the migration of DOA and ATBC plasticizers from food-grade PVC and PVDC/PVC films, respectively, into olive oil. *J Food Prot* 1998; 61(6): 720–724.
- 9 Dorfer CE, Kim TS, Steinbrenner H, et al. Regenerative periodontal surgery in interproximal intrabony defects with biodegradable barriers. *J Clin Periodontol* 2000; 27(3): 162–168.

20 General References

—

21 Authors

SW Kennedy.

22 Date of Revision

28 May 2002.