

Benzyl Benzoate

1 Nonproprietary Names

BP: Benzyl benzoate
JP: Benzyl benzoate
PhEur: Benzylis benzoas
USP: Benzyl benzoate

2 Synonyms

Benzoic acid benzyl ester; benzylbenzenecarboxylate; benzyl phenylformate.

3 Chemical Name and CAS Registry Number

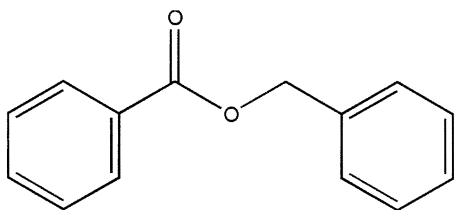
Benzoic acid phenylmethyl ester [120-51-4]

4 Empirical Formula Molecular Weight

C₁₄H₁₂O₂

212.24

5 Structural Formula



6 Functional Category

Plasticizer; solubilizing agent; solvent; therapeutic agent.

7 Applications in Pharmaceutical Formulation or Technology

Benzyl benzoate is used as a solubilizing agent and nonaqueous solvent in intramuscular injections at concentrations of 0.01–46.0% v/v,⁽¹⁾ and as a solvent and plasticizer for cellulose and nitrocellulose. It is also used in the preparation of spray-dried powders using nanocapsules.⁽²⁾

However, the most widespread pharmaceutical use of benzyl benzoate is as a topical therapeutic agent in the treatment of scabies. Benzyl benzoate is also used therapeutically as a parasiticide in veterinary medicine.⁽³⁾

Other applications of benzyl benzoate include its use as a pediculicide and as a solvent and fixative for flavors and perfumes in cosmetics and food products.

8 Description

Benzyl benzoate is a clear, colorless, oily liquid with a slightly aromatic odor. It produces a sharp, burning sensation on the tongue. At temperatures below 17°C it exists as clear, colorless crystals.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for benzyl benzoate.

Test	JP 2001	PhEur 2002	USP 25
Identification	+	+	+
Characters	+	+	—
Specific gravity	≈ 1.123	1.118–1.122	1.116–1.120
Congealing temperature	≈ 17°C	≥ 17.0°C	≥ 18.0°C
Boiling point	≈ 323°C	≈ 320°C	—
Refractive index	1.568–1.570	1.568–1.570	1.568–1.570
Aldehyde	—	—	≤ 0.05%
Acidity	+	+	+
Sulfated ash	≤ 0.05%	≤ 0.1%	—
Organic volatile impurities	—	—	+
Assay	≥ 99.0%	99.0–100.5%	99.0–100.5%

10 Typical Properties

Autoignition temperature: 481°C

Boiling point: 323°C

Flash point: 148°C

Freezing point: 17°C

Refractive index: $n_D^{21} = 1.5681$

Solubility: practically insoluble in glycerin and water; miscible with chloroform, ethanol (95%), ether, and oils.

Specific gravity: 1.12

Vapor density (relative): 7.3 (air = 1)

11 Stability and Storage Conditions

Benzyl benzoate is stable when stored in tight, well-filled, light-resistant containers. Exposure to excessive heat should be avoided.

12 Incompatibilities

Benzyl benzoate is incompatible with alkalis and oxidizing agents.

13 Method of Manufacture

Benzyl benzoate is a constituent of Peru balsam and occurs naturally in certain plant species. Commercially, benzyl benzoate is produced synthetically by the dry esterification of sodium benzoate and benzoyl chloride in the presence of triethylamine or by the reaction of sodium benzoate with benzaldehyde.

14 Safety

Benzyl benzoate is metabolized by rapid hydrolysis to benzoic acid and benzyl alcohol. Benzyl alcohol is then further metabolized to hippuric acid, which is excreted in the urine.

Benzyl benzoate is widely used as a 25% v/v topical application in the treatment of scabies and as an excipient in intramuscular injections and oral products. Adverse reactions to benzyl benzoate include skin irritation and hypersensitivity reactions. Oral ingestion may cause harmful stimulation of the CNS and convulsions.

LD₅₀ (cat, oral): 2.24 g/kg⁽⁴⁻⁶⁾
 LD₅₀ (guinea pig, oral): 1.0 g/kg
 LD₅₀ (mouse, oral): 1.4 g/kg
 LD₅₀ (rabbit, oral): 1.68 g/kg
 LD₅₀ (rabbit, skin): 4.0 g/kg
 LD₅₀ (rat, oral): 0.5 g/kg
 LD₅₀ (rat, skin): 4.0 g/kg

15 Handling Precautions

Benzyl benzoate may be harmful if ingested and is irritating to the skin, eyes, and mucous membranes. Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection, gloves, and a respirator are recommended. It is recommended that benzyl benzoate is handled in a fume cupboard. Benzyl benzoate is flammable.

16 Regulatory Status

Included in the FDA Inactive Ingredients Guide (IM injections and oral capsules). Included, as an active ingredient, in non-parenteral medicines licensed in the UK.

17 Related Substances

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18 Comments

The EINECS number for benzyl benzoate is 204-402-9.

19 Specific References

- 1 Spiegel AJ, Noseworthy MM. Use of nonaqueous solvents in parenteral products. *J Pharm Sci* 1963; **52**: 917-927.
- 2 Guterres SS, Weiss V, de Lucca Freitas L, Pohlmann AR. Influence of benzyl benzoate as oil core on the physicochemical properties of spray-dried powders from polymeric nanocapsules containing indomethacin. *Drug Deliv* 2000; **7**(4): 195-199.
- 3 Bishop Y, ed. *The Veterinary Formulary*, 5th edn. London: Pharmaceutical Press, 2001: 297.
- 4 Graham BE, Kuizenga MH. Toxicity studies on benzyl benzoate and related benzyl compounds. *J Pharmacol Exp Ther* 1945; **84**: 358-362.
- 5 Draize JH, Alvarez E, Whitesell MF, *et al.* Toxicological investigations of compounds proposed for use as insect repellents. *J Pharmacol Exp Ther* 1948; **93**: 26-39.
- 6 Sweet DV, ed. *Registry of Toxic Effects of Chemical Substances*. Cincinnati: US Department of Health, 1987: 965.

20 General References

- Gupta VD, Ho HW. Quantitative determination of benzyl benzoate in benzyl benzoate lotion NF. *Am J Hosp Pharm* 1976; **33**: 665-666.
- Hassan MMA, Mossa JS. Benzyl benzoate. In: Florey K, ed. *Analytical Profiles of Drug Substances*, volume 10. New York: Academic Press, 1981: 55-74.

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22 Date of Revision

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