

Propyl Gallate

1 Nonproprietary Names

BP: Propyl gallate
PhEur: Propylis gallas
USPNF: Propyl gallate

2 Synonyms

E310; gallic acid propyl ester; *n*-propyl gallate; *Progallin P*; propyl 3,4,5-trihydroxybenzoate; *Tenox PG*.

3 Chemical Name and CAS Registry Number

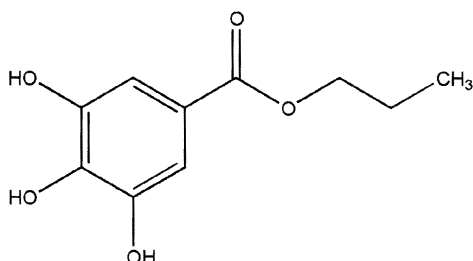
3,4,5-Trihydroxybenzoic acid propyl ester [121-79-9]

4 Empirical Formula Molecular Weight

C₁₀H₁₂O₅

212.20

5 Structural Formula



6 Functional Category

Antioxidant.

7 Applications in Pharmaceutical Formulation or Technology

Propyl gallate has become widely used as an antioxidant in cosmetics, perfumes, foods, and pharmaceuticals since its use in preventing autoxidation of oils was first described in 1943.^(1,2) It is primarily used, in concentrations up to 0.1% w/v, to prevent the rancidity of oils and fats;⁽³⁾ it may also be used at concentrations of 0.002% w/v to prevent peroxide formation in ether, and at 0.01% w/v to prevent the oxidation of paraldehyde. Synergistic effects with other antioxidants such as butylated hydroxyanisole and butylated hydroxytoluene have been reported. Propyl gallate is also said to possess some antimicrobial properties; see Section 10.

Studies have shown that, when added to powder blends containing ketorolac, propyl gallate significantly increases the drug stability in the preparation.⁽⁴⁾

Other alkyl gallates are also used as antioxidants and have approximately equivalent antioxidant properties when used in equimolar concentration; however, solubilities vary, see Section 17.

8 Description

Propyl gallate is a white, odorless or almost odorless crystalline powder, with a bitter astringent taste that is not normally noticeable at the concentrations employed as an antioxidant.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for propyl gallate.

Test	PhEur 2002	USPNF 20
Identification	+	+
Characters	+	—
Melting range	—	146–150°C
Appearance of solution	+	—
Gallic acid	+	—
Loss on drying	≤0.5%	≤0.5%
Residue on ignition	—	≤0.1%
Sulfated ash	≤0.1%	≤0.1%
Total chlorine	≤200 ppm	—
Chloride	≤100 ppm	—
Heavy metals	≤10 ppm	≤0.001%
Zinc	≤25 ppm	—
Organic volatile impurities	—	+
Assay (dried basis)	97.0–102.0%	98.0–102.0%

10 Typical Properties

Acidity/alkalinity: pH = 5.9 (0.1% w/v aqueous solution)

Antimicrobial activity: propyl gallate has been reported to possess some antimicrobial activity against Gram-negative, Gram-positive, and fungal species.⁽⁵⁾ Its effectiveness as a preservative may be improved when used in combination with zinc salts, such as zinc sulfate, owing to synergistic effects.⁽⁶⁾ For reported minimum inhibitory concentrations (MICs) for aqueous solutions containing 4% v/v ethanol as cosolvent, see Table II.⁽⁵⁾

Table II: Minimum inhibitory concentrations (MICs) for aqueous solutions containing propyl gallate and 4% v/v ethanol.

Microorganism	MIC (mg/mL)
<i>Candida albicans</i>	1500
<i>Escherichia coli</i>	330
<i>Staphylococcus aureus</i>	600

Dissociation constant: pK_a = 8.11

Melting point: 150°C

Partition coefficients:

Octanol : water = 32

Oleyl alcohol : water = 17

Solubility: see Table III.

Table III: Solubility of propyl gallate.

Solvent	Solubility at 20°C unless otherwise stated
Almond oil	1 in 44
Castor oil	1 in 4.5
Cottonseed oil	1 in 81 at 30°C
Ethanol (95%)	1 in 3
	1 in 0.98 at 25°C
Ether	1 in 3
	1 in 1.2 at 25°C
Lanolin	1 in 16.7 at 25°C
Lard	1 in 88 at 45°C
Mineral oil	1 in 200
Peanut oil	1 in 2000
Propylene glycol	1 in 2.5 at 25°C
Soybean oil	1 in 100 at 25°C
Water	1 in 1000
	1 in 286 at 25°C

11 Stability and Storage Conditions

Propyl gallate is unstable at high temperatures and is rapidly destroyed in oils that are used for frying purposes.

The bulk material should be stored in a well-closed, non-metallic container, protected from light, in a cool, dry place.

12 Incompatibilities

The alkyl gallates are incompatible with metals, e.g. sodium, potassium, and iron, forming intensely colored complexes. Complex formation may be prevented, under some circumstances, by the addition of a sequestering agent, typically citric acid. Propyl gallate may also react with oxidizing materials.

13 Method of Manufacture

Propyl gallate is prepared by the esterification of 3,4,5-trihydroxybenzoic acid (gallic acid) with *n*-propanol. Other alkyl gallates are prepared similarly using an appropriate alcohol of the desired alkyl chain length.

14 Safety

It has been reported, following animal studies, that propyl gallate has a strong contact sensitization potential.⁽⁷⁾ Propyl gallate has also produced cytogenic effects in CHO-K1 cells.⁽⁸⁾ However, despite this, there have been few reports of adverse reactions to propyl gallate.⁽⁹⁾ Those that have been described include contact dermatitis; allergic contact dermatitis;⁽⁹⁻¹¹⁾ and methemoglobinemia in neonates.⁽¹²⁾

The WHO has set an estimated acceptable daily intake for propyl gallate at up to 1.4 mg/kg body-weight.⁽¹³⁾

- LD₅₀ (cat, oral): 0.4 g/kg⁽¹⁴⁾
- LD₅₀ (mouse, oral): 1.7 g/kg
- LD₅₀ (rat, oral): 2.1 g/kg
- LD₅₀ (rat, IP): 0.38 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection and gloves are recommended. When heated to decomposition, propyl gallate may emit toxic fumes and smoke.

16 Regulatory Status

GRAS listed. Accepted for use as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (IM injections, oral, and topical preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Dodecyl gallate; ethyl gallate; octyl gallate.

Dodecyl gallate

Empirical formula: C₁₉H₃₀O₅

Molecular weight: 338.44

CAS number: [1166-52-5]

Synonyms: dodecyl 3,4,5-trihydroxybenzoate; dodecylis gal-las; E312; lauryl gallate.

Appearance: white, odorless or almost odorless, crystalline powder.

Melting point: 96–97.5°C

Solubility: *see* Table IV.

Table IV: Solubility of dodecyl gallate.

Solvent	Solubility at 20°C
Acetone	1 in 2
Chloroform	1 in 60
Ethanol (95%)	1 in 3.5
Ether	1 in 4
Methanol	1 in 1.5
Peanut oil	1 in 30
Propylene glycol	1 in 60
Water	Practically insoluble

Safety: the WHO has established a temporary estimated acceptable daily intake for dodecyl gallate at up to 0.05 mg/kg body-weight.⁽¹³⁾

Comments: the EINECS number for dodecyl gallate is 214-620-6.

Ethyl gallate

Empirical formula: C₉H₁₀O₅

Molecular weight: 198.17

CAS number: [831-61-8]

Synonyms: ethyl 3,4,5-trihydroxybenzoate.

Appearance: white, odorless or almost odorless, crystalline powder.

Melting point: 151–154°C

Solubility: *see* Table V.

Table V: Solubility of ethyl gallate.

Solvent	Solubility at 20°C
Ethanol (95%)	1 in 3
Ether	1 in 3
Peanut oil	Practically insoluble
Water	Slightly soluble

Octyl gallate

Empirical formula: C₁₅H₂₂O₅

Molecular weight: 282.34

CAS number: [1034-01-1]

Synonyms: E311; octyl 3,4,5-trihydroxybenzoate.

Appearance: white, odorless or almost odorless, crystalline powder.

Melting point: 100–102°C

Solubility: see Table VI.

Table VI: Solubility of octyl gallate.

Solvent	Solubility at 20°C
Acetone	1 in 1
Chloroform	1 in 30
Ethanol (95%)	1 in 2.5
Ether	1 in 3
Methanol	1 in 0.7
Peanut oil	1 in 33
Propylene glycol	1 in 7
Water	Practically insoluble

Safety: the WHO has established a temporary estimated acceptable daily intake for octyl gallate at up to 0.1 mg/kg body-weight.⁽¹³⁾

Comments: the EINECS number for octyl gallate is 252-073-5.

18 · Comments

Propyl gallate has been reported to impart an 'off' flavor to corn and cottonseed oils when used as an antioxidant.⁽¹⁵⁾ The EINECS number for propyl gallate is 204-498-2.

19 Specific References

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20 General References

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21 Authors

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22 Date of Revision

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