

Propylene Glycol

1 Nonproprietary Names

BP: Propylene glycol
JP: Propylene glycol
PhEur: Propylenglycolum
USP: Propylene glycol

2 Synonyms

1,2-Dihydroxypropane; E1520; 2-hydroxypropanol; methyl ethylene glycol; methyl glycol; propane-1,2-diol.

3 Chemical Name and CAS Registry Number

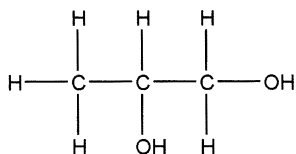
1,2-Propanediol [57-55-6]
(-)-1,2-Propanediol [4254-14-2]
(+)-1,2-Propanediol [4254-15-3]

4 Empirical Formula Molecular Weight

C₃H₈O₂

76.09

5 Structural Formula



6 Functional Category

Antimicrobial preservative; disinfectant; humectant; plasticizer; solvent; stabilizer for vitamins; water-miscible cosolvent.

7 Applications in Pharmaceutical Formulation or Technology

Propylene glycol has become widely used as a solvent, extractant, and preservative in a variety of parenteral and nonparenteral pharmaceutical formulations. It is a better general solvent than glycerin and dissolves a wide variety of materials, such as corticosteroids, phenols, sulfa drugs, barbiturates, vitamins (A and D), most alkaloids, and many local anesthetics.

As an antiseptic it is similar to ethanol, and against molds it is similar to glycerin and only slightly less effective than ethanol.

Propylene glycol is commonly used as a plastizer in aqueous film-coating formulations.

Propylene glycol is also used in cosmetics and in the food industry as a carrier for emulsifiers and as a vehicle for flavors in preference to ethanol, since its lack of volatility provides a more uniform flavor. See Table I.

Table I: Uses of propylene glycol.

Use	Dosage form	Concentration (%)
Humectant	Topicals	≈ 15
Preservative	Solutions, semisolids	15–30
Solvent or cosolvent	Aerosol solutions	10–30
	Oral solutions	10–25
	Parenterals	10–60
	Topicals	5–80

8 Description

Propylene glycol is a clear, colorless, viscous, practically odorless liquid with a sweet, slightly acrid taste resembling that of glycerin.

9 Pharmacopeial Specifications

See Table II.

Table II: Pharmacopeial specifications for propylene glycol.

Test	JP 2001	PhEur 2002	USP 25
Identification	+	+	+
Appearance	—	+	—
Specific gravity	1.035–1.040	1.035–1.040	1.035–1.037
Acidity	+	+	+
Water	≤ 0.5%	≤ 0.2%	≤ 0.2%
Residue on ignition	≤ 0.005%	—	≤ 0.007%
Sulfated ash	—	≤ 0.01%	—
Chloride	≤ 0.007%	—	≤ 0.007%
Sulfate	≤ 0.002%	—	≤ 0.006%
Heavy metals	≤ 5 ppm	≤ 5 ppm	≤ 5 ppm
Organic volatile impurities	—	—	+
Refractive index	—	1.431–1.433	—
Oxidizing substances	—	+	—
Reducing substances	—	+	—
Arsenic	≤ 2 ppm	—	—
Glycerin	+	—	—
Distilling range	184–189 °C	—	—
Assay	—	—	≥ 99.5%

10 Typical Properties

Autoignition temperature: 371 °C

Boiling point: 188 °C

Density: 1.038 g/cm³ at 20 °C

Flammability: upper limit, 12.6% v/v in air; lower limit, 2.6% v/v in air.

Flash point: 99 °C (open cup)

Heat of combustion: 1803.3 kJ/mol (431.0 kcal/mol)

Heat of vaporization: 705.4 J/g (168.6 cal/g) at b.p.

Melting point: –59 °C

Osmolarity: a 2.0% v/v aqueous solution is iso-osmotic with serum.

Refractive index: $n_D^{20} = 1.4324$

Specific rotation $[\alpha]_D^{20}$:

–15.0° (neat) for (R)-form

+15.8° (neat) for (S)-form

Solubility: miscible with acetone, chloroform, ethanol (95%), glycerin, and water; soluble at 1 in 6 parts of ether; not miscible with light mineral oil or fixed oils, but will dissolve some essential oils.

Specific heat: 2.47 J/g (0.590 cal/g) at 20 °C

Surface tension: 40.1 mN/m (40.1 dynes/cm) at 25 °C

Vapor density (relative): 2.62 (air = 1)

Vapor pressure: 9.33 Pa (0.07 mmHg) at 20 °C

Viscosity (dynamic): 58.1 mPa s (58.1 cP) at 20 °C

11 Stability and Storage Conditions

At cool temperatures, propylene glycol is stable in a well-closed container, but at high temperatures, in the open, it tends to oxidize, giving rise to products such as propionaldehyde, lactic acid, pyruvic acid, and acetic acid. Propylene glycol is chemically stable when mixed with ethanol (95%), glycerin, or water; aqueous solutions may be sterilized by autoclaving.

Propylene glycol is hygroscopic and should be stored in a well-closed container, protected from light, in a cool, dry place.

12 Incompatibilities

Propylene glycol is incompatible with oxidizing reagents such as potassium permanganate.

13 Method of Manufacture

Propylene is converted to chlorohydrin by chlorine water and hydrolyzed to 1,2-propylene oxide. With further hydrolysis, 1,2-propylene oxide is converted to propylene glycol.

14 Safety

Propylene glycol is used in a wide variety of pharmaceutical formulations and is generally regarded as a relatively nontoxic material. It is also used extensively in foods and cosmetics. Probably as a consequence of its metabolism and excretion, propylene glycol is less toxic than other glycols. Propylene glycol is rapidly absorbed from the gastrointestinal tract; there is also evidence that it is absorbed topically when applied to damaged skin. It is extensively metabolized in the liver, mainly to lactic and pyruvic acids and is also excreted unchanged in the urine.^(1,2)

In topical preparations, propylene glycol is regarded as minimally irritant, although it is more irritant than glycerin. Some local irritation is produced upon application to mucous membranes or when it is used under occlusive conditions.⁽³⁾ Parenteral administration may cause pain or irritation when used in high concentration.

Propylene glycol is estimated to be one-third as intoxicating as ethanol, with administration of large volumes being associated with adverse effects most commonly on the central nervous system, especially in neonates and children.⁽⁴⁻⁶⁾ Other adverse reactions reported, though generally isolated, include: ototoxicity,⁽⁷⁾ cardiovascular effects; seizures; and hyperosmolarity⁽⁸⁾ and lactic acidosis, both of which occur most frequently in patients with renal impairment. Adverse effects are more likely to occur following consumption of large

quantities of propylene glycol or on administration to neonates, children under 4 years of age, pregnant women, and patients with hepatic or renal failure. Adverse events may also occur in patients treated with disulfiram or metronidazole.⁽⁹⁾

On the basis of metabolic and toxicological data, the WHO has set an acceptable daily intake of propylene glycol at up to 25 mg/kg body-weight.⁽¹⁰⁾ Formulations containing 35% propylene glycol can cause hemolysis in humans.

In animal studies, there has been no evidence that propylene glycol is teratogenic or mutagenic. Rats can tolerate a repeated oral daily dose of up to 30 mL/kg in the diet over 6 months, while the dog is unaffected by a repeated oral daily dose of 2 g/kg in the diet for 2 years.⁽¹¹⁾

LD₅₀ (mouse, IP): 9.72 g/kg⁽¹²⁾

LD₅₀ (mouse, IV): 6.63 g/kg

LD₅₀ (mouse, oral): 22.0 g/kg

LD₅₀ (mouse, SC): 17.34 g/kg

LD₅₀ (rat, IM): 0.01 g/kg

LD₅₀ (rat, IP): 6.66 g/kg

LD₅₀ (rat, IV): 6.42 g/kg

LD₅₀ (rat, oral): 0.02 g/kg

LD₅₀ (rat, SC): 22.5 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Propylene glycol should be handled in a well-ventilated environment; eye protection is recommended. In the UK, the long-term (8-hour TWA) occupational exposure limit for propylene glycol vapor and particulates is 474 mg/m³ (150 ppm) and 10 mg/m³ for particulates.⁽¹³⁾

16 Regulatory Status

GRAS listed. Accepted for use as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (dental preparations, IM and IV injections, inhalations, ophthalmic, oral, otic, percutaneous, rectal, topical, and vaginal preparations). Included in nonparenteral and parenteral medicines licensed in the UK.

17 Related Substances

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18 Comments

In addition to its uses as an excipient, propylene glycol is used in veterinary medicine as an oral glucogenic in ruminants.⁽¹⁴⁾ The EINECS number for propylene glycol is 200-338-0.

19 Specific References

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21 Author

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22 Date of Revision

3 May 2002.