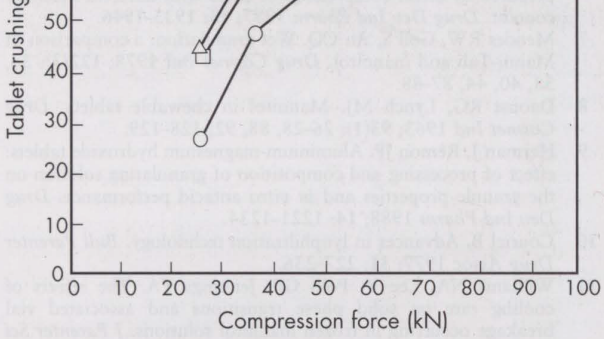

Figure 1: Compression characteristics of granular mannitol (*Pearlitol*, Roquette Frères).
○: *Pearlitol 300DC*
□: *Pearlitol 400DC*
△: *Pearlitol 500DC*
Tablet diameter: 20 mm
Lubricant: magnesium stearate 0.7% w/w for *Pearlitol 400DC* and *Pearlitol 500DC*; magnesium stearate 1% w/w for *Pearlitol 300DC*.

11 Stability and Storage Conditions

Mannitol is stable in the dry state and in aqueous solutions. Solutions may be sterilized by filtration or by autoclaving and if necessary may be autoclaved repeatedly with no adverse physical or chemical effects.[22] In solution, mannitol is not attacked by cold, dilute acids or alkalis, nor by atmospheric oxygen in the absence of catalysts. Mannitol does not undergo Maillard reactions.

The bulk material should be stored in a well-closed container in a cool, dry place.

12 Incompatibilities

Mannitol solutions, 20% w/v or stronger, may be salted out by potassium chloride or sodium chloride.[23] Precipitation has been reported to occur when a 25% w/v mannitol solution was allowed to contact plastic.[24] Sodium cephapirin at 2 mg/mL and 30 mg/mL is incompatible with 20% w/v aqueou
tol solution. Mannitol is incompatible with xylitol
and may form complexes with some metals such as aluminum,

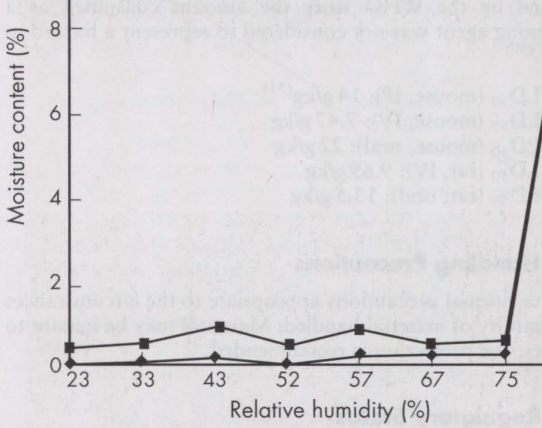

Figure 2: Sorption–desorption isotherm for mannitol.
◆: Sorption equilibrium moisture
■: Desorption equilibrium moisture

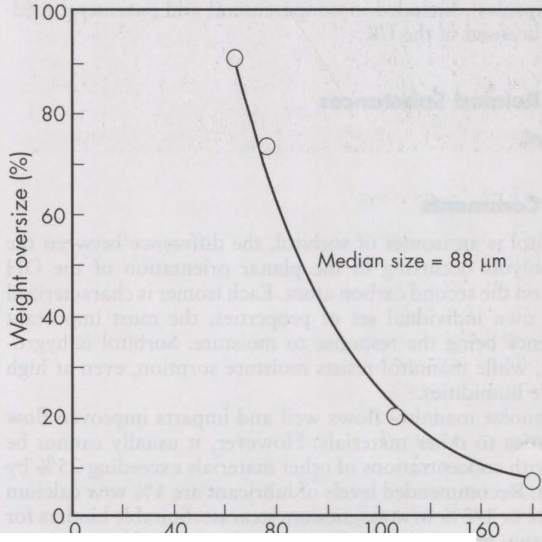

Figure 3: Particle size distribution of mannitol powder.

specified by the WHO since the amount consumed as a sweetening agent was not considered to represent a hazard to health.[30]

LD_{50} (mouse, IP): 14 g/kg[31]
LD_{50} (mouse, IV): 7.47 g/kg
LD_{50} (mouse, oral): 22 g/kg
LD_{50} (rat, IV): 9.69 g/kg
LD_{50} (rat, oral): 13.5 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Mannitol may be irritant to the eyes; eye protection is recommended.

16 Regulatory Status

GRAS listed. Accepted for use as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (IP, IM, IV, and SC injections; infusions; buccal, oral and sublingual tablets and capsules). Included in nonparenteral and parenteral medicines licensed in the UK.

17 Related Substances

Sorbitol.

18 Comments

Mannitol is an isomer of sorbitol, the difference between the two polyols occurring in the planar orientation of the OH group on the second carbon atom. Each isomer is characterized by its own individual set of properties, the most important difference being the response to moisture. Sorbitol is hygroscopic, while mannitol resists moisture sorption, even at high relative humidities.

Granular mannitol flows well and imparts improved flow properties to other materials. However, it usually cannot be used with concentrations of other materials exceeding 25% by weight. Recommended levels of lubricant are 1% w/w calcium stearate or 1–2% w/w magnesium stearate. Suitable binders for preparing granulations of powdered mannitol are methylcellulose 400, starch paste, povidone, and s
Usually, 3–6 times as much magnesium stearate or 1.5–3

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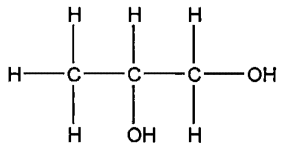
827.

(+)-1,2-Propanediol [4254-15-3]

4 Empirical Formula Molecular Weight

$C_3H_8O_2$ 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.

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/cm^3 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

MY

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 wh
most frequently in patients with renal impairment.
effects are more likely to occur following consumption of large

LD_{50} (rat, SC): 22.5 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circum
and quantity of material handled. Propylene glycol sh
handled in a well-ventilated environment; eye protec
recommended. In the UK, the long-term (8-hour
occupational exposure limit for propylene glycol vap
particulates is 474 mg/m^3 (150 ppm) and 10 mg/m^3 fo
culates.[13]

16 Regulatory Status

GRAS listed. Accepted for use as a food additive in E
Included in the FDA Inactive Ingredients Guide (den
parations, IM and IV injections, inhalations, ophthalmi
otic, percutaneous, rectal, topical, and vaginal prepar
Included in nonparenteral and parenteral medicines lice
the UK.

17 Related Substances

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18 Comments

In addition to its uses as an excipient, propylene glycol
in veterinary medicine as an oral glucogenic in rumina
The EINECS number for propylene glycol is 200-338-

19 Specific References

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