Product: Glycerol

General information

CAS number:	56-81-5
Countries (Providers):	Belgium, Germany, Spain, Malaysia, Japan, United States, United Kingdom, France

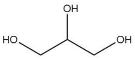

Fig. 1: Structural formula of G.

Other names

Language	Name
English:	Glycerol

Definition

Empirical formula

$C_3H_8O_3$

Structural formula

See Fig. 1.

Molecular mass

92.10

Compendial definitions

- Ph. Eur.

  "Glycerol" is propane-1,2,3-triol. "Glycerol (85 per cent)" is an aqueous solution of propane-1,2,3-triol.
- USP/NF.

  "Glycerin" is 1,2,3-propanetriol.
- JP.

  "Glycerin" contains 84.0 to 87.0 % of glycerin. "Concentrated Glycerin" contains not less than 98.0 % and not more than 101.0 % of glycerin.

Compendial specifications (selection)

Specification	Ph. Eur. 9.6		USP 42/NF 37	JP XVII	
	Glycerol	Glycerol (85 per cent)	Glycerin	Glycerin	Concentrated Glycerin
Acidity or alkalinity	+	+	--	+	+
Acrolein, glucose, and other reducing substances	--	--	--	+	+
Aldehydes	≤10 ppm	≤10 ppm	--	--	--
Ammonium	--	--	--	+	+
Appearance of solution/ Color of solution	+	+	+	+	+
Arsenic	--	--	--	≤2 ppm	≤2 ppm
Assay	98.0 to 101.0 %	83.5 to 88.5 %	99.0 to 101.0 %	84.0 to 87.0 %	98.0 to 101.0 %
Calcium	--	--	--	+	+
Chlorides	≤10 ppm	≤10 ppm	≤10 ppm	≤0.001 %	≤0.001 %
Chlorinated compounds	--	--	+	--	--
Diethylene glycol and ethylene glycol	≤0.10 % (each)	≤0.10 % (each)	≤0.10 % (each)	≤0.10 % (each)	≤0.10 % (each)
Esters	+	+	--	--	--
Fatty acids and esters	--	--	--	+	+
Gravity, specific	1.258 to 1.268	1.221 to 1.232	≥1.249	1.221 to 1.230	≥1.258
Halogenated compounds	≤35 ppm	≤30 ppm	--	--	--
Heavy metals	--	--	--	≤5 ppm	≤5 ppm
Readily carbonizable substances	--	--	--	+	+
Refractive index	1.470 to 1.475	1.449 to 1.455	--	1.449 to 1.454	≥1.470
Related substances	+	+	+	+	+
Residue on ignition	--	--	≤0.01 %	≤0.01 %	≤0.01 %
Sugars	+	+	--	--	--
Sulfated ash	≤0.01 %	≤0.01 %	--	--	--
Sulfates	--	--	≤20 ppm	≤0.002 %	≤0.002 %
Water	≤2.0 %	12.0 to 16.0 %	≤5.0 %	13 to 17 %	≤2.0 %

Synonyms

INN

Ph. Eur.: Glycerol; Glycerol 85 per cent.USP/NF: Glycerin.
JP: Glycerin; Concentrated Glycerin.

INCI

Glycerin.

Synonyms

Glycerin; glycerolum; propanetriol; 1,2,3-propanetriol (trihydroxypropane); trihydroxypropane.

Trade names (selection)

C*PharmGlydex; Croderol GV9000; Ecocerol; Edenor G (Edenor grades); Emery 912, 916, 917; Optim; Palmera grades; Pricerine grades; RTD Glycerine 99.5 %; Superol grades.

CAS

56-81-5

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Properties

Appearance and organoleptic properties

Colorless, clear, highly viscous, odorless, hygroscopic liquid with a sweet taste.

Solubility and miscibility

- Ether: insoluble
- Fats: insoluble
- Naphtha: insoluble
- Water: miscible in all proportions

Physicochemical properties

- Boiling point (1.01 bar): 290 °C
- Boiling point (0.013 bar): 166.1 °C
- Meting point: 17.9 °C
- Density d^{15}: 1.26557
- Flash point: 177 °C
- Heat conductivity: 0.00068 $cal \cdot s^{-1} \cdot cm^{-1} \cdot K^{-1}$
- Heat of solution (25 °C): –5.870 $kJ \cdot mol^{-1}$ [Balk 1985].
- Ignition point: 204 °C
- Refractive index n_D^{20}: 1.4746
- Specific heat capacity (26 °C): 0.5795 $cal \cdot g^{-1}$ (99.94 %)
- Surface tension (20 °C) : 63.4 $mN \cdot m^{-1}$
- Viscosity (20 °C): 939 mPa·s (98 %); 1'410 mPa·s (100 %)
- Vapor pressure (50 °C): 0.0025 mm

Spectral data

IR absorption spectrum: see Fig. 2.

Application characteristics

Reasons for using G. in drug formulations

- Stability
- Hygroscopicity
- Non-volatility
- High viscosity and solvent power
- Good tolerance
- Lack of toxicity
- Sweet taste
- Lack of tendency to crystallization
- Ability to reduce freezing point.

Applications

Use in the pharmaceutical industry

- Solvent in pharmaceutical preparations [Jones 1982].
- Preparation of oil in glycerol/water emulsions using ethoxylated wetting agents [Magdassi 1990].
- Component of auxiliary substances, the glycerides.

  All three OH-groups of G. may be esterified with fatty acids to form triglycerides (fats). If only one or two groups are esterified, mono- or diglycerides are obtained. An overview of the use of G. as an auxiliary substance in pharmaceutical preparations was published by [Jones 1983].

Use in the cosmetic industry

- Report on the use of G. for the manufacture of cosmetic agents [Mast 1991].
- Glycerol may act as a skin moisturizer in dry atmospheres by transforming the lipid phase from the liquid state to the solid crystalline state [Froebe 1990].
- G., although dependent on the composition of the preparation, develops skin care properties for dry skin in higher concentrations [Procter & Gamble 1983].
- Advantages of the use of G. for the manufacture of cosmetic agents were described by [Schweisheimer 1971].

Use in the food industry

The enhancement of intestinal water absorption and sodium transport by G. in rats was investigated. G. could be a useful ingredient in energy-rich beverages and might enhance fluid absorption in humans [Wagner 1996].

Further applications

- G. is widely used to stabilize cytochrome P450 and to prevent its transformation to cytochrome P420 [Yang 1997].
- Important basic chemical in fat chemistry [Steinberner 1987].

Toxicology

Biopharmaceutical profile

- Report on the pharmacokinetics of G. administered to healthy test subjects [Sommer 1993].
- Overview on the pharmacology and pharmacokinetics of G. [Frank 1981].

Toxicological profile

- The toxicity of G. varies according to the route of administration.
- Mutagenicity.

  Negative reaction for G. both in the Ames test and in the chromosome test [Ishidate jr. 1984].
- Genotoxicity.

  No genotoxic effects found in a study by [Doolittle 1989]. This also applies to the metabolites of G.
- Cellular proliferation
  in vitro

  of various cell lines, e.g., human glioma cells is markedly inhibited by the addition of 2–4 % G. to the culture medium [Wiebe 1991].

LD_{50} values

See Table 1.

Table 1: LD_{50} values of G.

Test organism; Route of application	LD_{50} value [per kg b.w.]
Guinea pig; oral	7'750 mg
Rabbit; intraperitoneal	7 mL
Rabbit; subcutaneous	14 mL

Adverse reactions

No side reactions following chronic administration, if the concentration did not exceed 30 %. G. (20 % solution, i.p.) proved to be only slightly less toxic for neonate rats than for adult animals [Guchok 1986].

Allergenic and sensitizing potential

- Allergic contact dermatitis due to 1,3-butylene glycol and G. [Tamagawa-Mineoka 2007].
- Allergic contact dermatitis from glycerin in a moisturizing cream [Preston 2003].

Skin-irritating potential

- Tolerated locally up to 30 % G. Skin irritation only occurs at higher concentrations because of skin dehydration. If the domestic pig is kept at a relative humidity of 10 % dry skin develops after a short while, which can be treated remarkably well with a 20 % aqueous G. solution (2 times per d) [Bissett 1984].
- G. and hydroxyethylated G. (molecular mass: 1'412) have a markedly more adverse influence on the skin in rats and mice in the early postnatal stage than on adult animals, and therefore both substances should be used with caution for the skin care of babies [Guchok 1981].

Stability

Microbiological stability

Various commercial G. samples were studied and found to be practically sterile. Even though *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus* and *Salmonella typhimurium* had been added, the solutions were sterile at specified G. concentrations and after specified storage periods [Mariani jr. 1973].

Analytics

Methods for substance quantification

Analyte(s)	Matrix	Method	Reference
G., sorbitol	Toothpaste	Capillary zone electrophoresis, Amperometry	Fang 1997
G.		Various	Underwood 1991
G., glycols	Cosmetic agents	Gas chromatography	Pant 1989, Ito 1983
G.	Pharmaceutical preparations	Reversed phase HPLC, refractive index detector	Breslin 1985
G., triglycerides		Amperometry (oxygen electrode)	Kelly 1984
G.	Biological tests	HP Liquid chromatography	Matarese 1983
G.	Soaps	HP Liquid chromatography	George 1982
G.	Human fatty cells	Micromethod using Luciferase	Kather 1982
G.		Various	N.N. 1980
G., fructose, glucose, saccharose	Drinks	Quantitative thin layer chromatography	Klaus 1979
G.		Spectrophotometry	Sturgeon 1979
G.		Enzymatic assay, spectrophotometry	Moller 1975, 1974
G., mannitol, sorbitol		Thin layer chromatography separation	Flüdy-Tenger 1972
G.		Malaprade method (according to IUPAC)	Barbour 1972, 1971
G.			Kelley 1969
G.	Water-soluble and/or strongly emulsifying water-soluble monoglycerides		Berner 1969
G.	Cosmetic preparations	Gas (liquid) chromatography	Gross 1967a, 1967b
G.		Colorimetry after periodate oxidation	Pays 1967
G.			Baehler 1965
G.	Medical solution together with sorbitol		Bonini 1965
G.		Volumetric determination as copper complex	McAloren 1965
G.	In the presence of sucrose		Loicono 1964
G.	Solutions, suspensions, suppositories		Berka 1963

Methods for substance characterization

- TLC method for the identification of glycols in G., limit of detection 0.5 % glycol [Thakkar 1988].
- Arsenic in G. [Ullmann 1983].
- The content of reducing substances in G. can be reliably analyzed by transmission measurement [Bölsche 1981].
- Rapid method for the determination of the water content [Campos 1969].

Further information

- During volumetric determination of G. by the periodate method, formic acid evaporates. By addition of sodium formate the reproducibility of the results can be improved [Mormont 1969].
- Analysis of technical G. [Mormont 1972].
- Separation of mannitol, G. and sorbitol succeeds on/over silica gel using the mobile solvent iso-propanol-ethyl acetate-water-0.1 N boric acid solution (28 ml + 10 ml + 44 ml + gtts. XXV) [Flüdy-Tenger 1972].

Remarks

Potential therapeutic uses

- From studies with 6 different rat strains it was concluded that G. does not influence the development of liver tumors [Witschi 1989].
- It has been demonstrated that oral administration of G. (3 times per d, 80 mg per kg b.w. over 8 weeks) does not cause any weight reduction in patients with obesity [Greenway 1981].
- The tolerance of G. solutions used in the rabbit for the treatment of cerebral edema or intraocular hypertension is markedly improved by the addition of sodium ascorbate or glucose (increase in osmotic activity) [Marone 1981].
- Pure G. is suitable for the treatment of seborrheal dermatitis [Benaim-Pinto 1972].

Further remarks

- Effects of G. and PEG 400 in donor and receptor solutions upon skin permeation of drugs [Cho 1996].
- The recommened additive tragacanth may be replaced by flax seed gum in the officinal G. ointment [Suska 1985].
- Using prescribed sterilization procedures, the phenol in G. sometimes causes considerable discoloration. This can be prevented, if heating is performed in the presence of carbon dioxide (170 °C - 60 min.) [N.N. 1984].
- Fats and protein substances can be detected as contaminants in G. [Risko 1970].

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Providers

- Cargill Personal Care
- Sigma-Aldrich
- Panreac
- Pacific Oleochemicals
- OLEON
- NOF
- Merck
- Mallinckrodt Baker
- Kao
- Impag
- Emery Oleochemicals
- Ecogreen
- Dow Chemical
- Croda
- Cognis
- Wagner
- Global Fields
- HallStar
- Hansa Group
- IOI Oleochemicals
- KLK Oleo
- Lion
- Mosselman
- PG Chemicals
- Pharmco
- Prod Hyg
- RITA
- Sakamoto Yakuhin