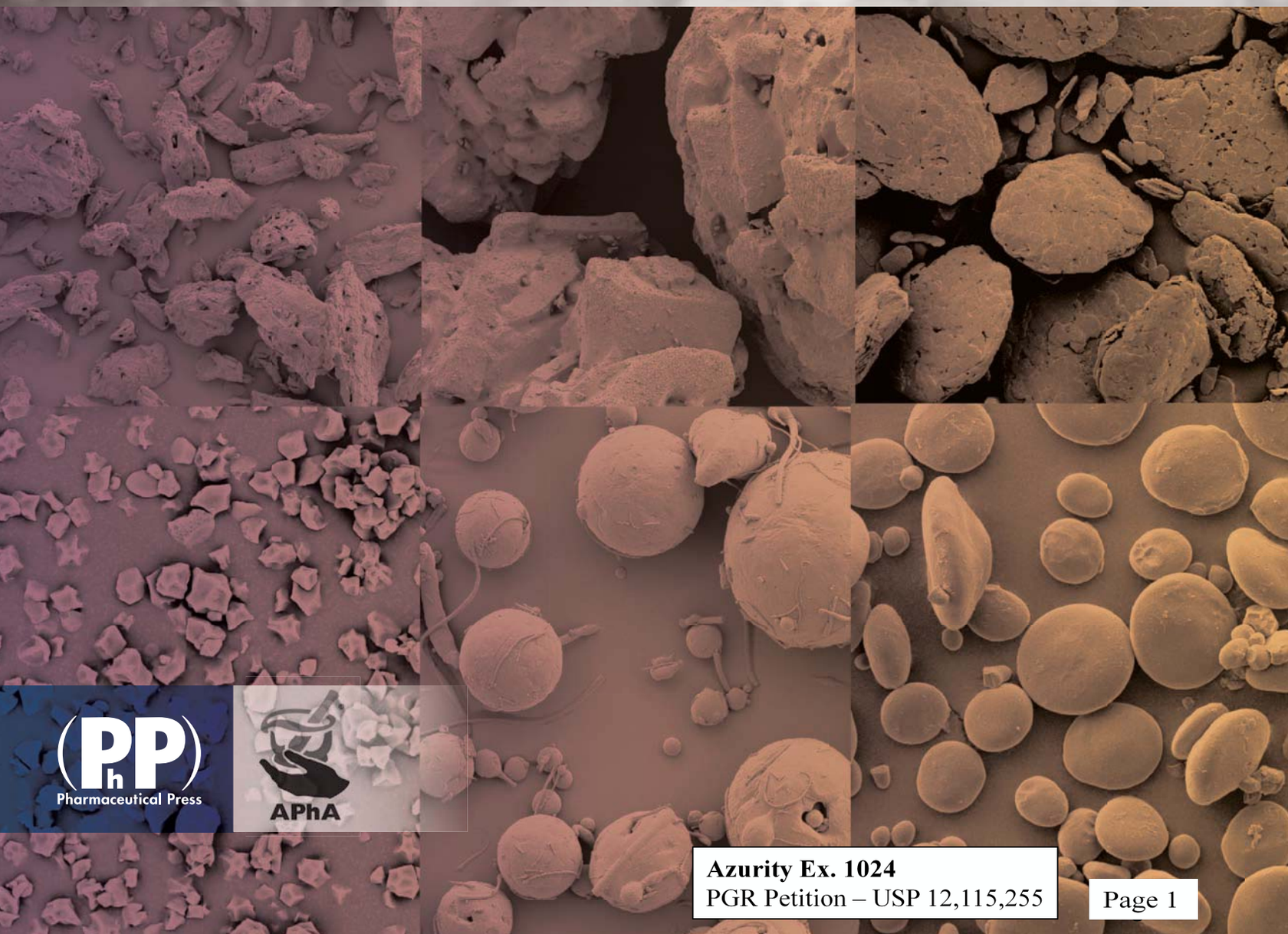
Handbook of Pharmaceutical Excipients

Sixth edition

Edited by
Raymond C Rowe, Paul J Sheskey and Marian E Quinn



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SIXTH EDITION

Edited by

Raymond C Rowe BPharm, PhD, DSC, FRPharmS, FRSC, CPhys, MInstP

Chief Scientist

Intelligensys Ltd, Stokesley, North Yorkshire, UK

Paul J Sheskey BSc, RPh

Application Development Leader

The Dow Chemical Company, Midland, MI, USA

Marian E Quinn BSc, MSc

Development Editor

Royal Pharmaceutical Society of Great Britain, London, UK

APhA

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18 Comments

A specification for glucose syrup is contained in the Food Chemicals Codex (FCC).[2] The PhEur 6.4 also includes a specification for glucose, liquid, spray-dried.

The EINECS number for glucose is 200-075-1.

19 Specific References

1 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 11th edn. New York: Wiley, 2004; 1860–1861.
2 *Food Chemicals Codex*, 6th edn. Bethesda, MD: United States Pharmacopeia, 2008; 403.

20 General References

Dziedzic SZ, Kearsley MW, eds. *Glucose Syrups: Science and Technology*. New York: Elsevier Applied Science, 1984.
Hoynak RX, Bolcenback GN. *This is Liquid Sugar*, 2nd edn. Yonkers, NY: Refined Syrup and Sugars Inc., 1966; 205, 226.
Inglett GE, ed. *Symposium on Sweeteners*. New York: AVI, 1974.

21 Author

A Day.

22 Date of Revision

18 February 2009.

G

Glycerin

1 Nonproprietary Names

BP: Glycerol
JP: Concentrated Glycerin
PhEur: Glycerol
USP: Glycerin

2 Synonyms

Croderol; E422; glicerol; glycerine; glycerolum; *Glycon G-100*; *Kemstrene*; *Optim*; *Pricerine*; 1,2,3-propanetriol; trihydroxypropane glycerol.

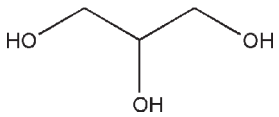
3 Chemical Name and CAS Registry Number

Propane-1,2,3-triol [56-81-5]

4 Empirical Formula and Molecular Weight

$C_3H_8O_3$ 92.09

5 Structural Formula



6 Functional Category

Antimicrobial preservative; cosolvent; emollient; humectant; plasticizer; solvent; sweetening agent; tonicity agent.

7 Applications in Pharmaceutical Formulation or Technology

Glycerin is used in a wide variety of pharmaceutical formulations including oral, otic, ophthalmic, topical, and parenteral preparations; *see* Table I.

In topical pharmaceutical formulations and cosmetics, glycerin is used primarily for its humectant and emollient properties. Glycerin is used as a solvent or cosolvent in creams and emulsions.[1–3] Glycerin is additionally used in aqueous and nonaqueous gels and also as an additive in patch applications.[4–6] In parenteral formulations, glycerin is used mainly as a solvent and cosolvent.[7–10]

In oral solutions, glycerin is used as a solvent,[10] sweetening agent, antimicrobial preservative, and viscosity-increasing agent. It is also used as a plasticizer and in film coatings.[11–14]

Glycerin is used as a plasticizer of gelatin in the production of soft-gelatin capsules and gelatin suppositories.

Glycerin is employed as a therapeutic agent in a variety of clinical applications,[15] and is also used as a food additive.

Table I: Uses of glycerin.

Use	Concentration (%)
Antimicrobial preservative	<20
Emollient	⩽30
Gel vehicle, aqueous	5.0–15.0
Gel vehicle, nonaqueous	50.0–80.0
Humectant	⩽30
Ophthalmic formulations	0.5–3.0
Patch additive	Variable
Plasticizer in tablet film coating	Variable
Solvent for parenteral formulations	⩽50
Sweetening agent in alcoholic elixirs	⩽20

8 Description

Glycerin is a clear, colorless, odorless, viscous, hygroscopic liquid; it has a sweet taste, approximately 0.6 times as sweet as sucrose.

9 Pharmacopeial Specifications

See Table II. *See also* Section 18.

10 Typical Properties

Boiling point 290°C (with decomposition)
Density
1.2656 g/cm^3 at 15°C;
1.2636 g/cm^3 at 20°C;
1.2620 g/cm^3 at 25°C.
Flash point 176°C (open cup)
Freezing point *see* Table III.
Hygroscopicity Hygroscopic.
Melting point 17.8°C

Table II: Pharmacopeial specifications for glycerin.

Test	JP XV	PhEur 6.0	USP 32
Identification	+	+	+
Characters	—	+	—
Appearance of solution	+	+	+
Acidity or alkalinity	+	+	—
Refractive index	⩽1.470	1.470–1.475	—
Aldehydes	—	⩽10 ppm	—
Related substances	—	+	—
Halogenated compounds	—	⩽35 ppm	—
Limit of chlorinated compounds	—	—	+
Sugars	—	+	—
Chloride	⩽0.001%	⩽10 ppm	⩽0.001%
Heavy metals	⩽5 ppm	⩽5 ppm	⩽5 µg/g
Water	—	⩽2.0%	⩽5.0%
Sulfated ash	⩽0.01%	⩽0.01%	⩽0.01%
Specific gravity	⩾1.258	—	⩾1.249
Sulfate	⩽0.002%	—	⩽0.002%
Esters	—	+	—
Ammonium	+	—	—
Calcium	+	—	—
Arsenic	⩽2 ppm	—	—
Acrolein, glucose or other reducing substances	+	—	—
Fatty acids and esters	+	—	+
Diethylene glycol and ethylene glycol impurities	—	—	+
Readily carbonizable substances	+	—	—
Assay	98.0–101.0%	98.0–101.0%	99.0–101.0%

Table III: Freezing points of aqueous glycerin solutions.

Concentration of aqueous glycerin solution (% w/w)	Freezing point (°C)
10.0	–1.6
20.0	–4.8
30.0	–9.5
40.0	–15.4
50.0	–23
60.0	–34.7
66.7	–46.5
80.0	–20.3
90.0	–1.6

NIR spectra *see* Figure 1.
Osmolarity A 2.6% v/v aqueous solution is isoosmotic with serum.
Refractive index
$n_D^{15} = 1.4758$;
$n_D^{20} = 1.4746$;
$n_D^{25} = 1.4730$.
Solubility *see* Table IV.
Specific gravity *see* Table V.
Surface tension 63.4 mN/m (63.4 dynes/cm) at 20°C.
Vapor density (relative) 3.17 (air = 1)
Viscosity (dynamic) *see* Table VI.

11 Stability and Storage Conditions

Glycerin is hygroscopic. Pure glycerin is not prone to oxidation by the atmosphere under ordinary storage conditions, but it decomposes on heating with the evolution of toxic acrolein. Mixtures of glycerin with water, ethanol (95%), and propylene glycol are chemically stable.

Table IV: Solubility of glycerin.

Solvent	Solubility at 20°C
Acetone	Slightly soluble
Benzene	Practically insoluble
Chloroform	Practically insoluble
Ethanol (95%)	Soluble
Ether	1 in 500
Ethyl acetate	1 in 11
Methanol	Soluble
Oils	Practically insoluble
Water	Soluble

Table V: Specific gravity of glycerin.

Concentration of aqueous glycerin solution (% w/w)	Specific gravity at 15°C	Specific gravity at 20°C
5	1.01	—
10	—	1.024
20	1.049	1.049
30	—	1.075
40	—	1.101
50	1.129	1.128
60	1.157	1.156
70	1.185	—
80	1.213	—
90	1.240	1.238
95	1.253	1.251

Table VI: Viscosity (dynamic) of aqueous glycerin solutions.

Concentration of aqueous glycerin solution (% w/w)	Viscosity at 20°C (mPa s)
5	1.143
10	1.311
25	2.095
50	6.05
60	10.96
70	22.94
83	111.0

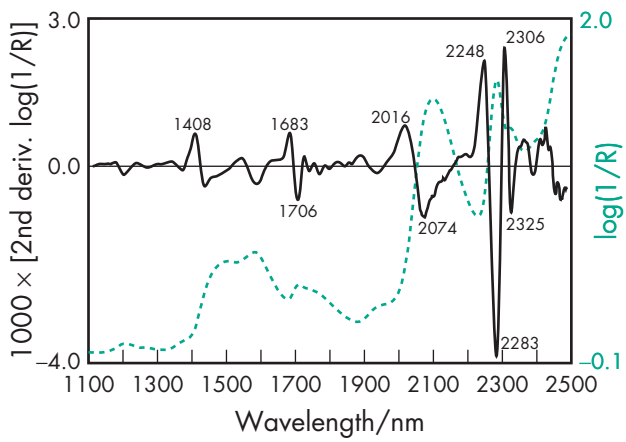


Figure 1: Near-infrared spectrum of glycerin measured by transflectance (1 mm path-length). The small peak at approx. 1950 nm is due to a trace of water (<0.5% m/m).

Glycerin may crystallize if stored at low temperatures; the crystals do not melt until warmed to 20°C.

Glycerin should be stored in an airtight container, in a cool, dry place.

12 Incompatibilities

Glycerin may explode if mixed with strong oxidizing agents such as chromium trioxide, potassium chlorate, or potassium permanganate. In dilute solution, the reaction proceeds at a slower rate with several oxidation products being formed. Black discoloration of glycerin occurs in the presence of light, or on contact with zinc oxide or basic bismuth nitrate.

An iron contaminant in glycerin is responsible for the darkening in color of mixtures containing phenols, salicylates, and tannin.

Glycerin forms a boric acid complex, glyceroboric acid, that is a stronger acid than boric acid.

13 Method of Manufacture

Glycerin is mainly obtained from oils and fats as a by-product in the manufacture of soaps and fatty acids. It may also be obtained from natural sources by fermentation of, for example, sugar beet molasses in the presence of large quantities of sodium sulfite. Synthetically, glycerin may be prepared by the chlorination and saponification of propylene.

14 Safety

Glycerin occurs naturally in animal and vegetable fats and oils that are consumed as part of a normal diet. Glycerin is readily absorbed from the intestine and is either metabolized to carbon dioxide and glycogen or used in the synthesis of body fats.

Glycerin is used in a wide variety of pharmaceutical formulations including oral, ophthalmic, parenteral, and topical preparations. Adverse effects are mainly due to the dehydrating properties of glycerin.[15]

Oral doses are demulcent and mildly laxative in action. Large doses may produce headache, thirst, nausea, and hyperglycemia. The therapeutic parenteral administration of very large glycerin doses, 70–80 g over 30–60 minutes in adults to reduce cranial pressure, may induce hemolysis, hemoglobinuria, and renal failure.[16] Slower administration has no deleterious effects.[17]

Glycerin may also be used orally in doses of 1.0–1.5 g/kg bodyweight to reduce intraocular pressure.

When used as an excipient or food additive, glycerin is not usually associated with any adverse effects and is generally regarded as a nontoxic and nonirritant material.

LD_{50} (guinea pig, oral): 7.75 g/kg[18]
LD_{50} (mouse, IP): 8.70 g/kg
LD_{50} (mouse, IV): 4.25 g/kg
LD_{50} (mouse, oral): 4.1 g/kg
LD_{50} (mouse, SC): 0.09 g/kg
LD_{50} (rabbit, IV): 0.05 g/kg
LD_{50} (rabbit, oral): 27 g/kg[19]
LD_{50} (rat, IP): 4.42 g/kg
LD_{50} (rat, oral): 5.57 g/kg[19]
LD_{50} (rat, oral): 12.6 g/kg
LD_{50} (rat, SC): 0.1 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection and gloves are recommended. In the UK, the recommended long-term (8-hour TWA) workplace exposure limit for glycerin mist is 10 mg/m^3.[20] Glycerin is combustible and may react explosively with strong oxidizing agents; *see* Section 12.

16 Regulatory Status

GRAS listed. Accepted for use as a food additive in Europe. Included in the FDA Inactive Ingredients Database (dental pastes; buccal preparations; inhalations; injections; nasal and ophthalmic preparations; oral capsules, solutions, suspensions and tablets; otic, rectal, topical, transdermal, and vaginal preparations). Included in nonparenteral and parenteral medicines licensed in the UK. Included in the Canadian List of Acceptable Non-medicinal Ingredients.

17 Related Substances

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18 Comments

Glycerin is one of the materials that have been selected for harmonization by the Pharmacopeial Discussion Group. For further information see the General Information Chapter <1196> in the USP32–NF27, the General Chapter 5.8 in PhEur 6.0, along with the 'State of Work' document on the PhEur EDQM website, and also the General Information Chapter 8 in the JP XV.

Some pharmacopeias also contain specifications for diluted glycerin solutions. The JP XV contains a monograph for 'glycerin' that contains 84–87% of propane-1,2,3-triol ($C_3H_8O_3$). The PhEur 6.0 contains a monograph for 'glycerol 85 per cent' that contains 83.5–88.5% of propane-1,2,3-triol ($C_3H_8O_3$).

A specification for glycerin is contained in the Food Chemicals Codex (FCC).[21]

The EINECS number for glycerin is 200-289-5.

19 Specific References

1 Viegas TX *et al.* Evaluation of creams and ointments as suitable formulations for peldesine. *Int J Pharm* 2001; **219**(1–2): 73–80.
2 Sheu MT *et al.* Simultaneous optimization of percutaneous delivery and adhesion for ketoprofen poultice. *Int J Pharm* 2002; **233**: 257–262.
3 Barichello JM *et al.* Combined effect of liposomalization and addition of glycerol on the transdermal delivery of isosorbide 5-nitrate in rat skin. *Int J Pharm* 2008; **357**(1–2): 199–205.
4 A-Sasutjarit R *et al.* Viscoelastic properties of carbopol 940 gels and their relationships to piroxicam diffusion coefficients in gel bases. *Pharm Res* 2005; **22**(12): 2134–2140.
5 Chow TC *et al.* Formulation of hydrophilic non-aqueous gel: drug stability in different solvents and rheological behaviour of gel matrices. *Pharm Res* 2008; **25**(1): 207–217.
6 Abu-Huwaij R *et al.* Potential mucoadhesive dosage form of lidocaine hydrochloride: II in vitro and in vivo evaluation. *Drug Dev Ind Pharm* 2007; **33**(4): 437–448.
7 Spiegel AJ, Noseworthy MM. Use of nonaqueous solvents in parenteral products. *J Pharm Sci* 1963; **52**(10): 917–927.
8 Strickley RG. Solubilizing excipients in oral and injectable formulations. *Pharm Res* 2004; **21**(2): 201–230.
9 Powell MF *et al.* Compendium of excipients for parenteral formulations. *PDA J Pharm Sci Technol* 1998; **52**(5): 238–311.
10 Millard JW *et al.* Solubilization by cosolvents establishing useful constants for the log-linear model. *Int J Pharm* 2002; **245**(1–2): 153–166.
11 Kumar V *et al.* Preparation and characterization of spray-dried oxidized cellulose particles. *Pharm Dev Technol* 2001; **6**(3): 449–458.
12 Palviainen P *et al.* Corn starches as film formers in aqueous-based film coating. *Pharm Dev Technol* 2001; **6**(3): 353–361.
13 Pongjanyakul T, Puttipipatkhachorn S. Alginate-magnesium aluminium silicate films: effect on plasticizer on film properties, drug permeation and drug release from coated tablets. *Int J Pharm* 2007; **333**(1–2): 34–44.
14 Bonacucina G *et al.* Effect of plasticizers on properties of pregelatinised starch acetate (Amprac 01) free films. *Int J Pharm* 2006; **313**(1–2): 72–77.
15 Sweetman SC, ed. *Martindale: The Complete Drug Reference*, 36th edn. London: Pharmaceutical Press, 2009; 2314–2315.
16 Hägnevik K *et al.* Glycerol-induced haemolysis with haemoglobinuria and acute renal failure. Report of three cases. *Lancet* 1974; **303**(7847): 75–77.
17 Welch KMA *et al.* Glycerol-induced haemolysis [letter]. *Lancet* 1974; **303**(7847): 416–417.
18 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 11th edn. New York: Wiley, 2004; 1865.

19 Health Evaluation Report on Lauric Acid Exposure during Flaking and Bagging Operations at Emery Industries, Los Angeles, CA. National Institute for Occupational Safety and Health, HHE 80-160-897, NTIS Doc.. No. PB 82-25694-2, 1981.
20 Anonymous. Final report on the safety assessment of oleic acid, lauric acid, palmitic acid, myristic acid, and stearic acid. *J Am Coll Toxicol* 1987; **6**(3): 321–401.
21 Verschueren K. *Handbook of Environmental Data of Organic Chemicals*, 2nd edn. New York: Van Nostrand Reinhold, 1983; 793.
22 Swern D *et al*. Investigation of fatty acids and derivatives for carcinogenic activity. *Cancer Res* 1970; **30**: 1037.
23 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 11th edn. New York: Wiley, 2004; 2204.
24 Oro R, Wretlind A. Pharmacological effects of fatty acids, triolein, and cottonseed oil. *Acta Pharmacol Toxicol* 1961; **18**: 141.
25 *Food Chemicals Codex*, 6th edn. Bethesda, MD: United States Pharmacopeia, 2008; 247.
26 *Food Chemicals Codex*, 6th edn. Bethesda, MD: United States Pharmacopeia, 2008; 529.

20 General References

Babu R.J *et al*. Fatty alcohols and fatty acids. Smith EW, Maibach HI, eds. *Percutaneous Penetration Enhancers*. Boca Raton, FL: CRC Press, 2006; 137–158.

21 Author

PE Luner.

22 Date of Revision

27 February 2009.

Lecithin

L

1 Nonproprietary Names

USP-NF: Lecithin

See also Section 4.

2 Synonyms

E322; egg lecithin; *LSC 5050*; *LSC 6040*; mixed soybean phosphatides; ovolecithin; *Phosal 53 MCT*; *Phospholipon 100 H*; *ProKote LSC*; soybean lecithin; soybean phospholipids; *Sternpur*; vegetable lecithin.

3 Chemical Name and CAS Registry Number

Lecithin [8002-43-5]

The chemical nomenclature and CAS Registry numbering of lecithin is complex. The commercially available lecithin, used in cosmetics, pharmaceuticals, and food products, is a complex mixture of phospholipids and other materials. However, it may be referred to in some literature sources as 1,2-diacyl-*sn*-glycero-3-phosphocholine (trivial chemical name, phosphatidylcholine). This material is the principal constituent of egg lecithin and has the same CAS Registry Number. The name lecithin and the CAS Registry Number above are thus used to refer to both lecithin and phosphatidylcholine in some literature sources.

Another principal source of lecithin is from an extract of soybeans (CAS [8030-76-0]). Egg yolk lecithin (CAS [93685-90-6]) is also listed in *Chemical Abstracts*.

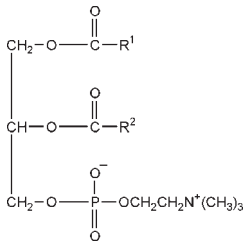
See also Section 4.

4 Empirical Formula and Molecular Weight

The USP32–NF27 describes lecithin as a complex mixture of acetone-insoluble phosphatides that consists chiefly of phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol, combined with various amounts of other substances such as triglycerides, fatty acids, and carbohydrates as separated from a crude vegetable oil source.

The composition of lecithin (and hence also its physical properties) varies enormously depending upon the source of the lecithin and the degree of purification. Egg lecithin, for example, contains 69% phosphatidylcholine and 24% phosphatidylethanolamine, while soybean lecithin contains 21% phosphatidylcholine, 22% phosphatidylethanolamine, and 19% phosphatidylinositol, along with other components.[1]

5 Structural Formula



α-Phosphatidylcholine

R^1 and R^2 are fatty acids, which may be different or identical.

Lecithin is a complex mixture of materials; *see* Section 4. The structure above shows phosphatidylcholine, the principal component of egg lecithin, in its α-form. In the β-form, the phosphorus-containing group and the R^2 group exchange positions.

6 Functional Category

Emollient; emulsifying agent; solubilizing agent.

7 Applications in Pharmaceutical Formulation or Technology

Lecithins are used in a wide variety of pharmaceutical applications; *see* Table I. They are also used in cosmetics[2] and food products.

Lecithins are mainly used in pharmaceutical products as dispersing, emulsifying, and stabilizing agents, and are included in intramuscular and intravenous injections, parenteral nutrition formulations, and topical products such as creams and ointments.

Lecithins are also used in suppository bases,[3] to reduce the brittleness of suppositories, and have been investigated for their absorption-enhancing properties in an intranasal insulin formulation.[4] Lecithins are also commonly used as a component of enteral and parenteral nutrition formulations.

There is evidence that phosphatidylcholine (a major component of lecithin) is important as a nutritional supplement to fetal and

infant development. Furthermore, choline is a required component of FDA-approved infant formulas.[5] Other studies have indicated that lecithin can protect against alcohol cirrhosis of the liver, lower serum cholesterol levels, and improve mental and physical performance.[6]

Liposomes in which lecithin is included as a component of the bilayer have been used to encapsulate drug substances; their potential as novel delivery systems has been investigated.[7] This application generally requires purified lecithins combined in specific proportions.

Therapeutically, lecithin and derivatives have been used as a pulmonary surfactant in the treatment of neonatal respiratory distress syndrome.

Table I: Uses of lecithin.

Use	Concentration (%)
Aerosol inhalation	0.1
Biorelevant dissolution media	0.059–0.295
IM injection	0.3–2.3
Oral suspensions	0.25–10.0

8 Description

Lecithins vary greatly in their physical form, from viscous semiliquids to powders, depending upon the free fatty acid content. They may also vary in color from brown to light yellow, depending upon whether they are bleached or unbleached or on the degree of purity. When they are exposed to air, rapid oxidation occurs, also resulting in a dark yellow or brown color.

Lecithins have practically no odor. Those derived from vegetable sources have a bland or nutlike taste, similar to that of soybean oil.

9 Pharmacopeial Specifications

See Table II. *See also* Section 18.

Table II: Pharmacopeial specifications for lecithin.

Test	USP32–NF27
Identification	+
Water	⩽1.5%
Lead	⩽0.001%
Heavy metals	⩽20 μg/g
Acid value	+
Peroxide value	⩽10
Hexane-insoluble matter	⩽0.3%
Acetone-insoluble matter	+

10 Typical Properties

Density

0.97 g/cm^3 for liquid lecithin;

0.5 g/cm^3 for powdered lecithin.

Iodine number

95–100 for liquid lecithin;

82–88 for powdered lecithin.

Isoelectric point ≈3.5

NIR spectra *see* Figure 1.

Saponification value 196

Solubility Lecithins are soluble in aliphatic and aromatic hydrocarbons, halogenated hydrocarbons, mineral oil, and fatty acids. They are practically insoluble in cold vegetable and animal oils, polar solvents, and water. When mixed with water, however, lecithins hydrate to form emulsions.

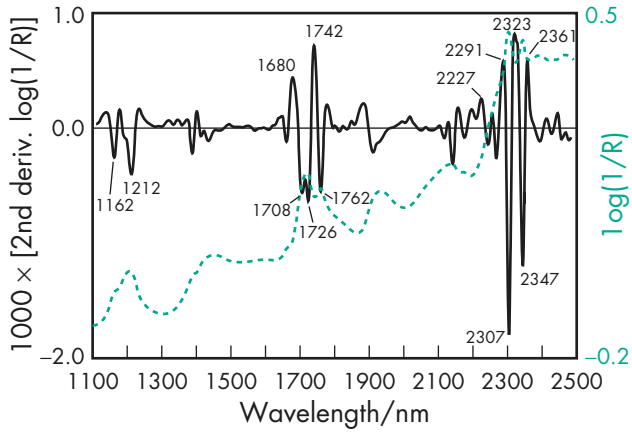


Figure 1: Near-infrared spectrum of lecithin measured by reflectance.

11 Stability and Storage Conditions

Lecithins decompose at extreme pH. They are also hygroscopic and subject to microbial degradation. When heated, lecithins oxidize, darken, and decompose. Temperatures of 160–180°C will cause degradation within 24 hours.

Fluid or waxy lecithin grades should be stored at room temperature or above; temperatures below 10°C may cause separation.

All lecithin grades should be stored in well-closed containers protected from light and oxidation. Purified solid lecithins should be stored in tightly closed containers at subfreezing temperatures.

12 Incompatibilities

Incompatible with esterases owing to hydrolysis.

13 Method of Manufacture

Lecithins are essential components of cell membranes and, in principle, may be obtained from a wide variety of living matter. In practice, however, lecithins are usually obtained from vegetable products such as soybean, peanut, cottonseed, sunflower, rapeseed, corn, or groundnut oils. Soybean lecithin is the most commercially important vegetable lecithin. Lecithin obtained from eggs is also commercially important and was the first lecithin to be discovered.

Vegetable lecithins are obtained as a by-product in the vegetable oil refining process. Polar lipids are extracted with hexane and, after removal of the solvent, a crude vegetable oil is obtained. Lecithin is then removed from the crude oil by water extraction. Following drying, the lecithin may be further purified.[1]

With egg lecithin, a different manufacturing process must be used since the lecithin in egg yolks is more tightly bound to proteins than in vegetable sources. Egg lecithin is thus obtained by solvent extraction from liquid egg yolks using acetone or from freeze-dried egg yolks using ethanol (95%).[1]

Synthetic lecithins may also be produced.

14 Safety

Lecithin is a component of cell membranes and is therefore consumed as a normal part of the diet. Although excessive consumption may be harmful, it is highly biocompatible and oral doses of up to 80 g daily have been used therapeutically in the treatment of tardive dyskinesia.[8] When used in topical formulations, lecithin is generally regarded as a nonirritant and nonsensitizing material.[2] The Cosmetic Ingredients Review Expert Panel (CIR) has reviewed lecithin and issued a tentative report revising the safe concentration of the material from 1.95% to 15.0% in rinse-off and leave-in products. They note, however, that there are insufficient data to rule on products that are likely to be inhaled.[9]

15 Handling Precautions

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

16 Regulatory Status

GRAS listed. Accepted for use as a food additive in Europe. Included in the FDA Inactive Ingredients Database (inhalations; IM and IV injections; otic preparations; oral capsules, suspensions and tablets; rectal, topical, and vaginal preparations). Included in nonparenteral and parenteral medicines licensed in the UK. Included in the Canadian List of Acceptable Non-medicinal Ingredients.

17 Related Substances

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18 Comments

Poloxamer lecithin organogels have been used in topical formulations for the delivery of non-steroidal anti-inflammatory drugs.[10]

Lecithins contain a variety of unspecified materials; care should therefore be exercised in the use of unpurified lecithin in injectable or topical dosage forms, as interactions with the active substance or other excipients may occur. Unpurified lecithins may also have a greater potential for irritancy in formulations.

A specification for soybean lecithin is contained in the *Japanese Pharmaceutical Excipients* (JPE).[11] Suppliers' literature should be consulted for information on the different grades of lecithin available and their applications in formulations.

A specification for lecithin is contained in the Food Chemicals Codex (FCC).[12]

The EINECS number for lecithin is 232-307-2. The PubChem Compound ID (CID) for lecithin is 24798685.

19 Specific References

1 Schneider M. Achieving purer lecithin. *Drug Cosmet Ind* 1992; **150**(2): 54, 56, 62, 64, 66, 101–103.
2 Anonymous. Lecithin: its composition, properties and use in cosmetic formulations. *Cosmet Perfum* 1974; **89**(7): 31–35.
3 Novak E *et al*. Evaluation of cefmetazole rectal suppository formulation. *Drug Dev Ind Pharm* 1991; **17**(3): 373–389.
4 Anonymous. Intranasal insulin formulation reported to be promising. *Pharm J* 1991; **247**: 17.
5 US Congress. Infant Formula Act of 1980. Public Law 96-359, 1980.
6 Canty D *et al*. *Lecithin and Choline Research Update on Health and Nutrition*. Fort Wayne, IN: Central Soya Company, 1996.
7 Grit M *et al*. Hydrolysis of partially saturated egg phosphatidylcholine in aqueous liposome dispersions and the effect of cholesterol incorporation on hydrolysis kinetics. *J Pharm Pharmacol* 1993; **45**: 490–495.
8 Growdon JH *et al*. Lecithin can suppress tardive dyskinesia [letter]. *N Engl J Med* 1978; **298**: 1029–1030.
9 Anonymous. 'The Rose Sheet'. *FDC Reports* 1997; **18**(39): 8.
10 Franckum J *et al*. Pluronic lecithin organogel for local delivery of anti-inflammatory drugs. *Int J Pharm Compound* 2004; **8**(2): 101–105.
11 Japan Pharmaceutical Excipients Council. *Japanese Pharmaceutical Excipients*, 2004. Tokyo: Yakuji Nippo, 2004; 843–844.
12 *Food Chemicals Codex*, 6th edn. Bethesda, MD: United States Pharmacopeia, 2008; 533.

20 General References

Arias C, Rueda C. Comparative study of lipid systems from various sources by rotational viscometry and potentiometry. *Drug Dev Ind Pharm* 1992; **18**: 1773–1786.

Hanin I, Pepeu G, eds. *Phospholipids: Biochemical, Pharmaceutical and Analytical Considerations*. New York: Plenum Press, 1990.

21 Author

JJ Sheng.

22 Date of Revision

18 February 2009.

L

Leucine

1 Nonproprietary Names

BP: Leucine
JP: L-Leucine
PhEur: Leucine
USP: Leucine

2 Synonyms

α-Aminoisocaproic acid; L-α-aminoisocaproic acid; 2-amino-4-methylpentanoic acid; 2-amino-4-methylvaleric acid; α-amino-γ-methylvaleric acid; 1,2-amino-4-methylvaleric acid; D L-leucine; L-leucine; leu; leucinum; 4-methylnorvaline.

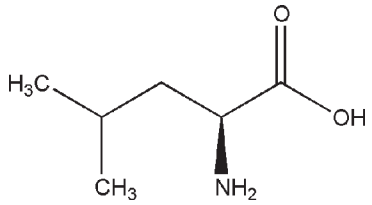
3 Chemical Name and CAS Registry Number

L-Leucine [61-90-5]

4 Empirical Formula and Molecular Weight

$C_6H_{13}NO_2$ 131.17

5 Structural Formula



6 Functional Category

Antiadherent; flavoring agent; lubricant.

7 Applications in Pharmaceutical Formulation or Technology

Leucine is used in pharmaceutical formulations as a flavoring agent.[1] It has been used experimentally as an antiadherent to improve the deagglomeration of disodium cromoglycate micro-

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