

Docusate Sodium

1 Nonproprietary Names

BP: Docusate sodium
PhEur: Docusatium natricum
USP: Docusate sodium

2 Synonyms

Bis(2-ethylhexyl) sodium sulfosuccinate; dioctyl sodium sulfosuccinate; DSS; sodium dioctyl sulfosuccinate; sulfo-butane-dioic acid 1,4-bis(2-ethylhexyl) ester, sodium salt.

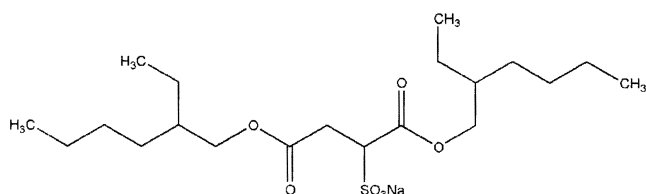
3 Chemical Name and CAS Registry Number

Sodium 1,4-bis(2-ethylhexyl) sulfosuccinate [577-11-7]

4 Empirical Formula Molecular Weight

$C_{20}H_{37}NaO_7S$ 444.56

5 Structural Formula



6 Functional Category

Anionic surfactant; wetting agent.

7 Applications in Pharmaceutical Formulation or Technology

Docusate sodium and docusate salts are widely used as anionic surfactants in pharmaceutical formulations. Docusate sodium is mainly used in capsule and direct-compression tablet formulations to assist in wetting and dissolution.⁽¹⁾ Docusate salts are also used in oral formulations as laxatives and fecal softeners; see Table I.

Table I: Uses of docusate sodium.

Use	Concentration (%)
IM injections	0.015
Surfactant (wetting/dispersing/emulsifying agent)	0.01–1.0
Tablet coating agent	20 ^(a)
Tablet disintegrant	≈ 0.5

^(a) Formulation of a tablet coating solution: 20% docusate sodium; 2–15% sodium benzoate; 0.5% propylene glycol; solution made in ethanol (70%).

8 Description

Docusate sodium is a white or almost white, waxlike, bitter tasting, plastic solid with a characteristic octanol-like odor. It is hygroscopic and usually available in the form of pellets, flakes, or rolls of tissue-thin material.

9 Pharmacopeial Specifications

See Table II.

Table II: Pharmacopeial specifications for docusate sodium.

Test	PhEur 2002 (Suppl 4.1)	USP 25
Identification	+	+
Characters	+	—
Alkalinity	+	—
Bis(2-ethylhexyl) maleate	—	≤ 0.4%
Chlorides	≤ 350 ppm	—
Clarity of solution	—	+
Heavy metals	≤ 10 ppm	≤ 0.001%
Related nonionic substances	+	—
Residue on ignition	—	15.5–16.5%
Sodium sulfate	≤ 2.0%	—
Water	≤ 3.0%	≤ 2.0%
Assay (dried basis)	98.0–100.5%	99.0–100.5%

10 Typical Properties

Acidity/alkalinity: pH = 5.8–6.9 (1% w/v aqueous solution).

Acid value: ≤ 2.5

Critical micelle concentration: 0.11% w/v aqueous solution at 25°C.

Density: 1.16 g/cm³

Hydroxyl value: 6.0–8.0

Interfacial tension: in water versus mineral oil at 25°C, see Table III.

Table III: Interfacial tension of docusate sodium.

Concentration (% w/v)	Interfacial tension (mN/m)
0.01	20.7
0.1	5.9
1.0	1.84

Iodine number: ≤ 0.25

Melting point: 153–157°C

Moisture content: 1.51%

Saponification value: 240–253

Solubility: see Table IV.

Surface tension: see Table V.

Table IV: Solubility of docusate sodium.

Solvent	Solubility at 20°C unless otherwise stated
Acetone	Soluble
Chloroform	1 in 1
Ethanol (95%)	1 in 3
Ether	1 in 1
Glycerin	Freely soluble
Vegetable oils	Soluble
Water	1 in 70 at 25°C ^(a) 1 in 56 at 30°C 1 in 44 at 40°C 1 in 33 at 50°C 1 in 25 at 60°C 1 in 18 at 70°C

^(a) In water, higher concentrations form a thick gel.

Table V: Surface tension of docusate sodium.

Concentration in water at 25°C (% w/v)	Surface tension (mN/m)
0.001	62.8
0.1	28.7
1.0	26.0

11 Stability and Storage Conditions

Docusate sodium is stable in the solid state when stored at room temperature. Dilute aqueous solutions of docusate sodium between pH 1–10 are stable at room temperature. However, at very low pH (<1) and very high pH (>10) docusate sodium solutions are subject to hydrolysis.

The solid material is hygroscopic and should be stored in an airtight container in a cool, dry place.

12 Incompatibilities

Electrolytes, e.g. 3% sodium chloride, added to aqueous solutions of docusate sodium can cause turbidity.^(2,3) However, docusate sodium possesses greater tolerance to calcium, magnesium, and other polyvalent ions than do some other surfactants. Docusate sodium is incompatible with acids at pH <1 and with alkalis at pH >10.

13 Method of Manufacture

Maleic anhydride is treated with 2-ethylhexanol to produce dioctyl maleate, which is then reacted with sodium bisulfite.

14 Safety

Docusate salts are used in oral formulations as therapeutic agents for their fecal softening and laxative properties. As a laxative in adults, up to 500 mg of docusate sodium is administered daily in divided doses; in children over 6 months old, up to 75 mg in divided doses is used. The quantity of docusate sodium used as an excipient in oral formulations should therefore be controlled to avoid unintended laxative effects.⁽⁴⁾ Adverse effects associated with docusate sodium include diarrhea, nausea, vomiting, abdominal cramps, and skin rashes.

Docusate salts are absorbed from the gastrointestinal tract and excreted in bile; they may cause alteration of the gastrointestinal epithelium.^(5,6) The gastrointestinal or hepatic absorption of other drugs may also be affected by docusate salts, enhancing activity and possibly toxicity. Docusate sodium should not be administered with mineral oil as it may increase the absorption of the oil.

LD₅₀ (mouse, IV): 0.06 g/kg⁽⁷⁾

LD₅₀ (mouse, oral): 2.64 g/kg

LD₅₀ (rat, IP): 0.59 g/kg

LD₅₀ (rat, oral): 1.9 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Docusate sodium may be irritant to the eyes and skin, and when inhaled. Eye protection, gloves, and a dust mask or respirator are recommended. When heated to decomposition, docusate sodium emits toxic fumes.

16 Regulatory Status

GRAS listed. Included in the FDA Inactive Ingredients Guide (IM injections, oral capsules, suspensions, and tablets, also topical formulations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Docusate calcium; docusate potassium.

Docusate calcium

Empirical formula: C₄₀H₇₄CaO₁₄S₂

Molecular weight: 883.23

CAS number: [128-49-4]

Synonyms: 1,4-bis(2-ethylhexyl) sulfosuccinate, calcium salt; dioctyl calcium sulfosuccinate.

Appearance: white amorphous solid with a characteristic octanol-like odor.

Solubility: soluble 1 in less than 1 of ethanol (95%), chloroform, and ether, and 1 in 3300 of water; very soluble in corn oil and polyethylene glycol 400.

Docusate potassium

Empirical formula: C₂₀H₃₇KO₇S

Molecular weight: 460.67

CAS number: [7491-09-0]

Synonyms: dioctyl potassium sulfosuccinate; potassium 1,4-bis(2-ethylhexyl) sulfosuccinate.

Appearance: white amorphous solid with a characteristic octanol-like odor.

Solubility: soluble in ethanol (95%) and glycerin; sparingly soluble in water.

18 Comments

A convenient way of making a 1% w/v aqueous solution of docusate sodium is to add 1 g of solid to about 50 mL of water and to apply gentle heat. The docusate sodium dissolves in a short time and the resulting solution can be made up to 100 mL with water. Alternatively, 1 g may be soaked overnight in 50 mL of water and the additional water may then be added with gentle heating and stirring.

Docusate sodium may alter the dissolution characteristics of certain dosage forms and the bioavailability of some drugs.

The EINECS number for docusate sodium is 209-406-4.

19 Specific References

- 1 Brown S, Rowley G, Pearson JT. Surface treatment of the hydrophobic drug danazol to improve drug dissolution. *Int J Pharm* 1998; **165**: 227–237.
- 2 Ahuja S, Cohen J. Dioctyl sodium sulfosuccinate. In: Florey K, ed. *Analytical Profiles of Drug Substances*, volume 2. New York: Academic Press, 1973: 199–219.
- 3 Ahuja S, Cohen J. Dioctyl sodium sulfosuccinate. In: Florey K, ed. *Analytical Profiles of Drug Substances*, volume 12. New York: Academic Press, 1983: 713–720.
- 4 Guidott JL. Laxative components of a generic drug [letter] *Lancet* 1996; **347**: 621.
- 5 Chapman RW, Sillery J, Fontana DD, Matthys C. Effect of oral dioctyl sodium sulfosuccinate on intake–output studies of human small and large intestine. *Gastroenterology* 1985; **89**: 489–493.
- 6 Moriarty KJ, Kelly MJ, Beetham R, Clark ML. Studies on the mechanism of action of dioctyl sodium sulfosuccinate in the human jejunum. *Gut* 1985; **26**: 1008–1013.
- 7 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 1282.

20 General References

- Chambliss WG, Cleary RW, Fischer R, *et al.* Effect of docusate sodium on drug release from a controlled release dosage form. *J Pharm Sci* 1981; **70**: 1248–1251.
- Hogue DR, Zimmardi JA, Shah KA. High-performance liquid chromatographic analysis of docusate sodium in soft gelatin capsules. *J Pharm Sci* 1992; **81**: 359–361.
- Shah DN, Feldkamp JR, White JL, Hem SL. Effect of the pH-zero point of charge relationship on the interaction of ionic compounds and polyols with aluminum hydroxide gel. *J Pharm Sci* 1982; **71**: 266–268.

21 Author

AW Malick.

22 Date of Revision

16 August 2002.