Saccharin Sodium

1 Nonproprietary Names

BP: Saccharin sodium
JP: Saccharin sodium
PhEur: Saccharinum natricum
USP: Saccharin sodium

2 Synonyms

1,2-Benzisothiazolin-3-one 1,1-dioxide, sodium salt; *Crystallose*; E954; sodium *o*-benzosulfimide; soluble gluside; soluble saccharin; *Sucaryl Sodium*.

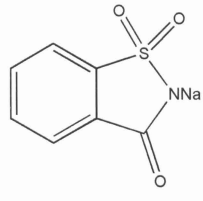
3 Chemical Name and CAS Registry Number

1,2-Benzisothiazol-3(2*H*)-one 1,1-dioxide, sodium salt
[6155-57-3] for the dihydrate
[128-44-9] for the anhydrous material
See also Section 8.

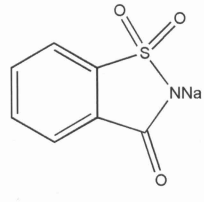
4 Empirical Formula and Molecular Weight

Empirical Formula	Molecular Weight
$C_7H_4NNaO_3S$	205.16
$C_7H_4NNaO_3S \cdot {}^2/_3H_2O$ (84%)	217.24
$C_7H_4NNaO_3S \cdot 2H_2O$ (76%)	241.19

5 Structural Formula



$\cdot 2H_2O$ 76% saccharin sodium (dihydrate)



$\cdot {}^2/_3 H_2O$ 84% saccharin sodium

6 Functional Category

Sweetening agent.

7 Applications in Pharmaceutical Formulation or Technology

Saccharin sodium is an intense sweetening agent used in beverages, food products, table-top sweeteners,[1] and pharmaceutical formulations such as tablets, powders, medicated confectionery, gels, suspensions, liquids, and mouthwashes;[2] *see* Table I. It is also used in vitamin preparations.

Saccharin sodium is considerably more soluble in water than saccharin, and is more frequently used in pharmaceutical formulations. Its sweetening power is approximately 300 times that of sucrose. Saccharin sodium enhances flavor systems and may be used to mask some unpleasant taste characteristics.

Injection of saccharin sodium has been used to measure the arm-to-tongue circulation time.

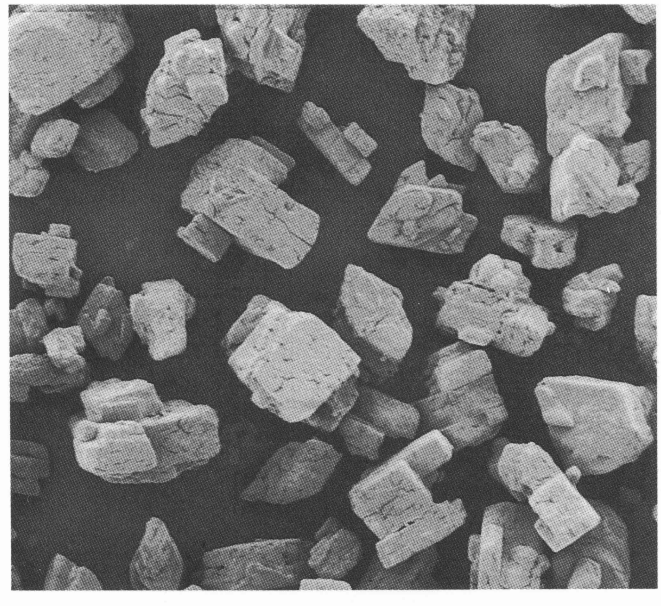
Table I: Uses of saccharin sodium.

Use	Concentration (%)
Dental paste/gel	0.12–0.3
IM/IV injections	0.9
Oral solution	0.075–0.6
Oral syrup	0.04–0.25

8 Description

Saccharin sodium occurs as a white, odorless or faintly aromatic, efflorescent, crystalline powder. It has an intensely sweet taste, with a metallic aftertaste that at normal levels of use can be detected by approximately 25% of the population. Saccharin sodium can contain variable amounts of water.

SEM: 1
Excipient: Saccharin sodium
Magnification: 35 ×
Voltage: 5 kV



9 Pharmacopeial Specifications

See Table II.

Table II: Pharmacopeial specifications for saccharin sodium.

Test	JP 2001	PhEur 2002	USP 25
Identification	+	+	+
Characters	+	+	—
Clarity and color of solution	+	+	—
Alkalinity	—	—	+
Water	+	≤15.0%	≤15.0%
Benzoate and salicylate	+	—	+
Arsenic	≤2 ppm	—	—
Selenium	—	—	+
Acidity or alkalinity	+	+	+
Toluenesulfonamides	+	+	+
Heavy metals	≤20 ppm	≤20 ppm	≤0.001%
Readily carbonizable substances	+	—	+
Organic volatile impurities	—	—	+
Assay (anhydrous basis)	≥98.0%	99.0–101.0%	98.0–101.0%

10 Typical Properties

Unless stated, data refer to either 76% or 84% saccharin sodium.

Acidity/alkalinity: pH = 6.6 (10% w/v aqueous solution)

Density (bulk):
0.8–1.1 g/cm^3 (76% saccharin sodium)
0.86 g/cm^3 (84% saccharin sodium)

Density (particle): 1.70 g/cm^3 (84% saccharin sodium)

Density (tapped):
0.9–1.2 g/cm^3 (76% saccharin sodium)
0.96 g/cm^3 (84% saccharin sodium)

Melting point: decomposes upon heating.

Moisture content: saccharin sodium 76% contains 14.5% w/w water; saccharin sodium 84% contains 5.5% w/w water. During drying, water evolution occurs in two distinct phases. The 76% material dries under ambient conditions to approximately 5.5% moisture (84% saccharin sodium); the remaining moisture is then removed only by heating.

Solubility: *see* Table III.

Table III: Solubility of saccharin sodium.

Solvent	Solubility at 20°C unless otherwise stated
Buffer solutions:	
pH 2.2 (phthalate)	1 in 1.15 1 in 0.66 at 60°C
pH 4.0 (citrate–phosphate)	1 in 1.21 1 in 0.69 at 60°C
pH 7.0 (citrate–phosphate)	1 in 1.21 1 in 0.66 at 60°C
pH 9.0 (borate)	1 in 1.21 1 in 0.69 at 60°C
Ethanol	1 in 102
Ethanol (95%)	1 in 50
Propylene glycol	1 in 3.5
Propan-2-ol	Practically insoluble
Water	1 in 1.2

Specific surface area: 0.25 m^2/g

11 Stability and Storage Conditions

Saccharin sodium is stable under the normal range of conditions employed in formulations. Only when it is exposed to a high temperature (125°C) at a low pH (pH 2) for over 1 hour does significant decomposition occur. The 84% grade is the most stable form of saccharin sodium since the 76% form will dry further under ambient conditions.

Saccharin sodium should be stored in a well-closed container in a cool, dry place.

12 Incompatibilities

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13 Method of Manufacture

Saccharin is produced by the oxidation of *o*-toluene sulfonamide by potassium permanganate in a solution of sodium hydroxide. Acidification of the solution precipitates saccharin, which is then dissolved in water at 50°C and neutralized by addition of sodium hydroxide. Rapid cooling of the solution initiates crystallization of saccharin sodium from the liquors.

14 Safety

There has been considerable controversy concerning the safety of saccharin and saccharin sodium in recent years; however, it is now generally regarded as a safe, intense sweetener. *See* Saccharin for further information.

The WHO has set a temporary acceptable daily intake of up to 2.5 mg/kg body-weight for saccharin, including its salts.[3] In the UK, the Committee on Toxicity of Chemicals in Food, Consumer Products, and the Environment (COT) has set an acceptable daily intake for saccharin and its salts (expressed as saccharin sodium) at up to 5 mg/kg body-weight.[4]

LD_{50} (mouse, oral): 17.5 g/kg[5]
LD_{50} (rat, IP): 7.1 g/kg
LD_{50} (rat, oral): 14.2 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection and a dust mask are recommended.

16 Regulatory Status

Accepted for use as a food additive in Europe 'E954' is applied to both saccharin and saccharin salts. Included in the FDA Inactive Ingredients Guide (buccal and dental preparations; IM and IV injections; oral and topical preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Saccharin.

18 Comments

The perceived intensity of sweeteners relative to sucrose depends upon their concentration, temperature of tasting, and pH, and on the flavor and texture of the product concerned.

Intense sweetening agents will not replace bulk, textural, or preservative characteristics of sugar if sugar is removed from a formulation.

Synergistic effects for combinations of sweeteners have been reported. Saccharin sodium is often used in combination with

cyclamates and aspartame since the saccharin sodium content may be reduced to minimize any aftertaste.

19 Specific References

1 Kloesel L. Sugar substitutes. *Int J Pharm Compound* 2000; **4**(2): 86–87.
2 Ungphaiboon S, Maitani Y. *In vitro* permeation studies of triamcinolone acetonide mouthwashes. *Int J Pharm* 2001; **220**(1–2): 111–117.
3 FAO/WHO. Evaluation of certain food additives and contaminants. Twenty-eighth report of the FAO/WHO expert committee on food additives. *World Health Organ Tech Rep Ser* 1984; No. 710.
4 Food Advisory Committee. FAC further advice on saccharin. FdAC/REP/9. London: MAFF, 1990.
5 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 3276–3277.

See Saccharin for further references.

20 General References

Anonymous. Saccharin is safe. *Chem Br* 2001; **37**(4): 18.
Lindley MG. Sweetener markets, marketing and product developments. In: Marie S, Piggott JR, eds. *Handbook of Sweeteners*. Glasgow: Blackie, 1991: 186.

21 Authors

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22 Date of Revision

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