Sodium Benzoate

1 Nonproprietary Names

BP: Sodium benzoate
JP: Sodium benzoate
PhEur: Natrii benzoas
USPNF : Sodium benzoate

2 Synonyms

Antimol; benzoic acid sodium salt; benzoate of soda; E211; natrium benzoicum; sobenate; sodii benzoas; sodium benzoic acid.

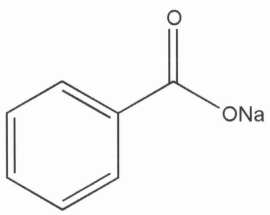
3 Chemical Name and CAS Registry Number

Sodium benzoate [532-32-1]

4 Empirical Formula and Molecular Weight

$C_7H_5NaO_2$ 144.11

5 Structural Formula



6 Functional Category

Antimicrobial preservative; tablet and capsule lubricant.

7 Applications in Pharmaceutical Formulation or Technology

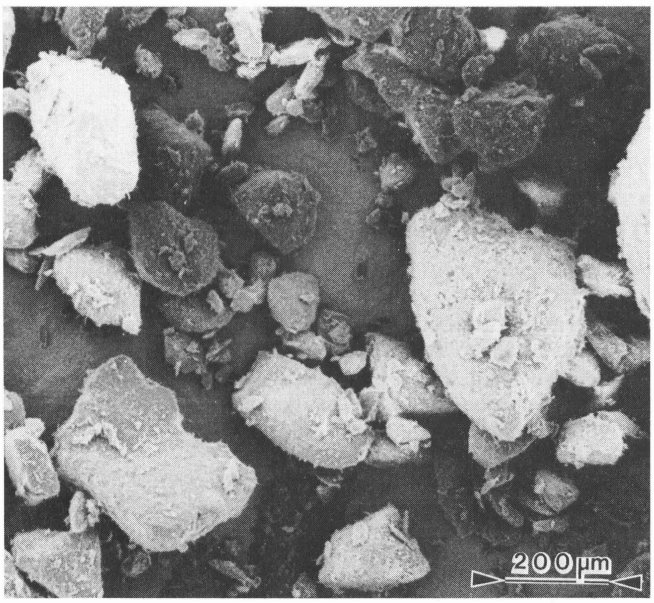
Sodium benzoate is used primarily as an antimicrobial preservative in cosmetics, foods, and pharmaceuticals. It is used in concentrations of 0.02–0.5% in oral medicines, 0.5% in parenteral products, and 0.1–0.5% in cosmetics. The usefulness of sodium benzoate as a preservative is limited by its effectiveness over a narrow pH range; *see* Section 10.

Sodium benzoate is used in preference to benzoic acid in some circumstances, owing to its greater solubility. However, in some applications it may impart an unpleasant flavor to a product. Sodium benzoate has also been used as a tablet lubricant[1] at 2–5% w/w concentrations. Solutions of sodium benzoate have also been administered, orally or intravenously, in order to determine liver function.

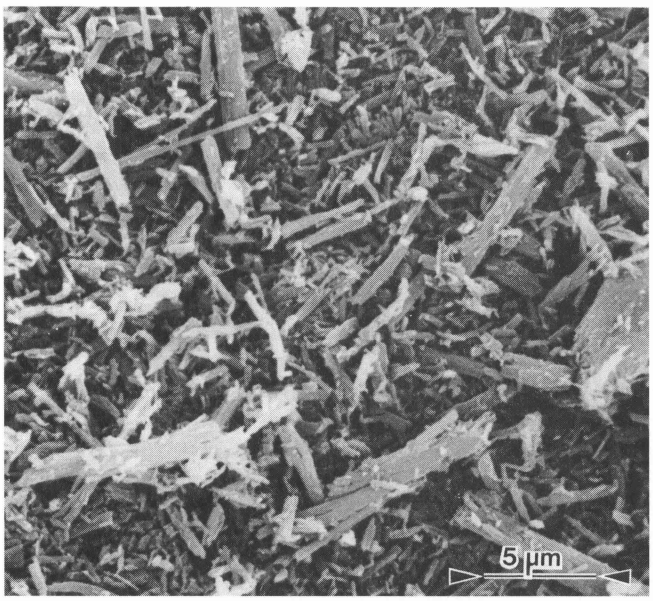
8 Description

Sodium benzoate occurs as a white granular or crystalline, slightly hygroscopic powder. It is odorless, or with faint odor of benzoin and has an unpleasant sweet and saline taste.

SEM: 1
Excipient: Sodium benzoate
Manufacturer: Bush Boake Allen Corp.
Magnification: 60 ×



SEM: 2
Excipient: Sodium benzoate
Manufacturer: Bush Boake Allen Corp.
Magnification: 2400 ×



9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for sodium benzoate.

Test	JP 2001	PhEur 2002	USPNF 20
Identification	+	+	+
Acidity or alkalinity	+	+	+
Appearance of solution	+	+	—
Arsenic	≤2 ppm	—	—
Chloride	+	≤200 ppm	—
Heavy metals	≤20 ppm	≤10 ppm	≤0.001%
Organic volatile impurities	—	—	+
Loss on drying	≤1.5%	≤2.0%	≤1.5%
Phthalic acid	+	—	—
Sulfate	+	—	—
Total chlorine	—	≤300 ppm	—
Assay (dried basis)	≥99.0%	99.0–100.5%	99.0–100.5%

10 Typical Properties

Acidity/alkalinity: pH = 8.0 (saturated aqueous solution at 25 °C). It is relatively inactive above approximately pH 5.

Antimicrobial activity: sodium benzoate has both bacteriostatic and antifungal properties attributed to undissociated benzoic acid, hence preservative efficacy is best seen in acidic solutions (pH 2–5). In alkaline conditions it is almost without effect.

Density: 1.497–1.527 g/cm^3 at 24 °C

Freezing point depression: 0.24 °C (1.0% w/v)

Osmolarity: a 2.25% w/v aqueous solution is iso-osmotic with serum.

Partition coefficients: Vegetable oil : water = 3–6

Solubility: *see* Table II.

Table II: Solubility for sodium benzoate.

Solvent	Solubility at 20 °C unless otherwise stated
Ethanol (95%)	1 in 75
Ethanol (90%)	1 in 50
Water	1 in 1.8
	1 in 1.4 at 100 °C

11 Stability and Storage Conditions

Aqueous solutions may be sterilized by autoclaving or filtration.

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

12 Incompatibilities

Incompatible with quaternary compounds, gelatin, ferric salts, calcium salts, and salts of heavy metals, including silver, lead, and mercury. Preservative activity may be reduced by interactions with kaolin[2] or nonionic surfactants.

13 Method of Manufacture

Prepared by the treatment of benzoic acid with either sodium carbonate or sodium bicarbonate.

14 Safety

Ingested sodium benzoate is conjugated with glycine in the liver to yield hippuric acid, which is excreted in the urine. Symptoms of systemic benzoate toxicity resemble those of salicylates.[3] Whereas oral administration of the free-acid form may cause severe gastric irritation, benzoate salts are well tolerated in large quantities: e.g., 6 g of sodium benzoate in 200 mL of water is administered orally as a liver function test.

Clinical data have indicated that sodium benzoate can produce nonimmunological contact uricartia and nonimmunological immediate contact reactions.[4] However, it is also recognized that these reactions are strictly cutaneous, and can therefore be used safely at concentrations up to 5%. However, this nonimmunological phenomenon should be considered when designing formulations for infants and children.

Other adverse effects include anaphylaxis[5,6,7] and urticarial reactions, although a controlled study has shown that the incidence of urticaria in patients given benzoic acid is no greater than that with a lactose placebo.[8]

It has been recommended that caffeine and sodium benzoate injection should not be used in neonates;[9] however, sodium benzoate has been used by others in the treatment of some neonatal metabolic disorders.[10]

The WHO acceptable daily intake of total benzoates, calculated as benzoic acid, has been estimated at up to 5 mg/kg of body-weight.[11,12]

LD_{50} (mouse, IM): 2.3 g/kg[12,13]
LD_{50} (mouse, IV): 1.4 g/kg
LD_{50} (mouse, oral): 1.6 g/kg
LD_{50} (rabbit, oral): 2.0 g/kg
LD_{50} (rat, IV): 1.7 mg/kg
LD_{50} (rat, oral): 4.1 g/kg

See also Benzoic Acid.

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Sodium benzoate may be irritant to the eyes and skin. Eye protection and rubber or plastic gloves are recommended.

16 Regulatory Status

GRAS listed. Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (dental preparations, IM and IV injections, oral capsules, solutions and tablets, rectal and topical preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Benzoic acid; potassium benzoate.

18 Comments

The EINECS number for sodium benzoate is 208-534-8.

19 Specific References

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2 Clarke CD, Armstrong NA. Influence of pH on the adsorption of benzoic acid by kaolin. *Pharm J* 1972; **209**: 44–45.

3 Michils A, Vandermoten G, Duchateau J, Yernault J-C. Anaphylaxis with sodium benzoate [letter]. *Lancet* 1991; **337**: 1424–1425.
4 Nair B. Final report on the safety assessment of benzyl alcohol, benzoic acid, and sodium benzoate. *Int J Toxicol* 2001; **20**(Suppl.3): 23–50.
5 Rosenhall L. Evaluation of intolerance to analgesics, preservatives and food colorants with challenge tests. *Eur J Respir Dis* 1982; **63**: 410–419.
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7 Warin RP, Smith RJ. Challenge test battery in chronic urticaria. *Br J Dermatol* 1976; **94**: 401–406.
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20 General References

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21 Author

SC Owen.

22 Date of Revision

16 April 2002.