

Sorbic Acid

1 Nonproprietary Names

BP: Sorbic acid
PhEur: Acidum sorbicum
USPNF: Sorbic acid

2 Synonyms

E200; (2-butenylidene) acetic acid; crotylidene acetic acid; hexadienic acid; hexadienoic acid; 2,4-hexadienoic acid; 1,3-pentadiene-1-carboxylic acid; 2-propenylacrylic acid; (*E,E*)-sorbic acid; *Sorbistat K*.

3 Chemical Name and CAS Registry Number

(*E,E*)-Hexa-2,4-dienoic acid [22500-92-1]

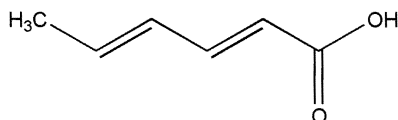
4 Empirical Formula

C₆H₈O₂

Molecular Weight

112.13

5 Structural Formula



6 Functional Category

Antimicrobial preservative.

7 Applications in Pharmaceutical Formulation or Technology

Sorbic acid is an antimicrobial preservative⁽¹⁾ with antibacterial and antifungal properties used in pharmaceuticals, foods, enteral preparations, and cosmetics. Generally, it is used at concentrations of 0.05–0.2% in oral and topical pharmaceutical formulations, especially those containing nonionic surfactants. Sorbic acid is also used with proteins, enzymes, gelatin, and vegetable gums.⁽²⁾ It has been shown to be an effective preservative for promethazine hydrochloride solutions in a concentration of 1 g/L.⁽³⁾

Sorbic acid has limited stability and activity against bacteria and is thus frequently used in combination with other antimicrobial preservatives or glycols, when synergistic effects appear to occur; see Section 10.

8 Description

Sorbic acid is a tasteless, white to yellow-white crystalline powder with a faint characteristic odor.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for sorbic acid.

Test	PhEur 2002	USPNF 20
Identification	+	+
Appearance of solution	+	—
Melting range	132–136°C	132–135°C
Water	≤ 1.0%	≤ 0.5%
Residue on ignition	—	≤ 0.2%
Sulfated ash	≤ 0.2%	—
Heavy metals	≤ 10 ppm	≤ 0.001%
Aldehyde (as C ₂ H ₄ O)	≤ 0.15%	—
Organic volatile impurities	—	+
Assay (anhydrous basis)	99.0–101.0%	99.0–101.0%

10 Typical Properties

Antimicrobial activity: sorbic acid is primarily used as an antifungal agent, although it also possesses antibacterial properties. The optimum antibacterial activity is obtained at pH 4.5; and practically no activity is observed above pH 6.^(4,5) The efficacy of sorbic acid is enhanced when it is used in combination with other antimicrobial preservatives or glycols since synergistic effects occur.⁽⁶⁾ Reported minimum inhibitory concentrations (MICs) at pH 6 are shown in Table II.⁽⁷⁾

Table II: Minimum inhibitory concentrations (MICs) of sorbic acid at pH 6.

Microorganism	MIC (μg/mL)
<i>Aspergillus niger</i>	200–500
<i>Candida albicans</i>	25–50
<i>Clostridium sporogenes</i>	100–500
<i>Escherichia coli</i>	50–100
<i>Klebsiella pneumoniae</i>	50–100
<i>Penicillium notatum</i>	200–300
<i>Pseudomonas aeruginosa</i>	100–300
<i>Pseudomonas cepacia</i>	50–100
<i>Pseudomonas fluorescens</i>	100–300
<i>Saccharomyces cerevisiae</i>	200–500
<i>Staphylococcus aureus</i>	50–100

Boiling point: 228°C with decomposition.

Density: 1.20 g/cm³

Dissociation constant: pK_a = 4.76

Flash point: 127°C

Melting point: 134.5°C

Solubility: see Table III. In syrup, the solubility of sorbitol decreases with increasing sugar content.

Table III: Solubility of sorbic acid.

Solvent	Solubility at 20°C unless otherwise stated
Acetone	1 in 11
Chloroform	1 in 15
Ethanol	1 in 8
Ethanol (95%)	1 in 10
Ether	1 in 30
Glycerin	1 in 320
Methanol	1 in 8
Propylene glycol	1 in 19
Water	1 in 400 at 30°C 1 in 26 at 100°C

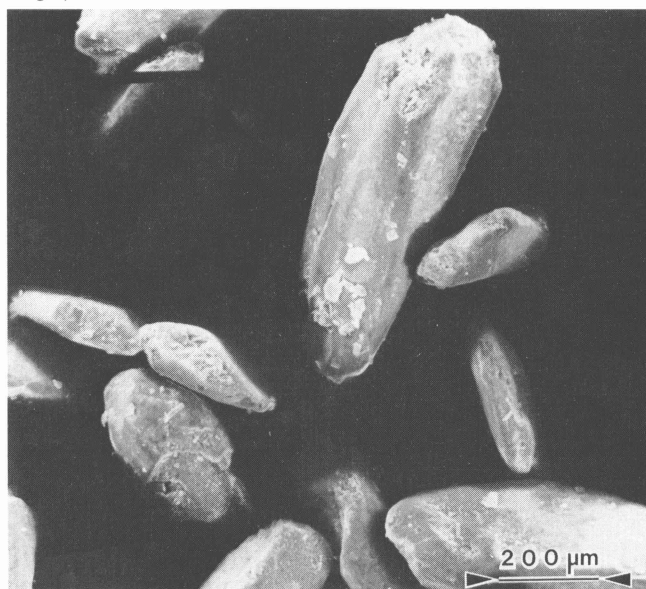
Vapor pressure: <1.3 Pa (<0.01 mmHg) at 20°C

SEM: 1

Excipient: Sorbic acid

Manufacturer: Pfizer Ltd.

Magnification: 60 ×



11 Stability and Storage Conditions

Sorbic acid is sensitive to oxidation, particularly in the presence of light; oxidation occurs more readily in aqueous solution than in the solid form. Sorbic acid may be stabilized by phenolic antioxidants such as 0.02% propyl gallate.⁽⁶⁾

Sorbic acid is combustible when exposed to heat or flame. When heated to decomposition, it emits acrid smoke and irritating fumes. The bulk material should be stored in a well-closed container, protected from light, at a temperature not exceeding 40°C.

12 Incompatibilities

Sorbic acid is incompatible with bases, oxidizing agents, and reducing agents. Some loss of antimicrobial activity occurs in the presence of nonionic surfactants and plastics. Oxidation is

catalyzed by heavy-metal salts. Sorbic acid will also react with sulfur-containing amino acids, although this can be prevented by the addition of ascorbic acid, propyl gallate, or butylhydroxytoluene.

When stored in glass containers, the solution becomes very pH sensitive; therefore, preparations using sorbic acid as a preservative should be tested for their microbial purity after prolonged periods of storage.

Aqueous solutions of sorbic acid without the addition of antioxidants are rapidly decomposed when stored in polypropylene, polyvinylchloride, and polyethylene containers.

13 Method of Manufacture

Naturally occurring sorbic acid may be extracted as the lactone (parasorbic acid) from the berries of the mountain ash *Sorbus aucuparia* L. (Fam. Rosaceae). Synthetically, sorbic acid may be prepared by the condensation of crotonaldehyde and ketene in the presence of boron trifluoride; by the condensation of crotonaldehyde and malonic acid in pyridine solution; or from 1,1,3,5-tetraalkoxyhexane. Fermentation of sorbaldehyde or sorbitol with bacteria in a culture medium has also been used.

14 Safety

Sorbic acid is used as an antimicrobial preservative in oral and topical pharmaceutical formulations and is generally regarded as a nontoxic material. However, adverse reactions to sorbic acid and potassium sorbate, including irritant skin reactions⁽⁸⁻¹¹⁾ and allergic hypersensitivity skin reactions (which are less frequent), have been reported.⁽¹²⁻¹⁴⁾

Other adverse reactions that have been reported include exfoliative dermatitis due to ointments that contain sorbic acid,⁽¹⁵⁾ and allergic conjunctivitis caused by contact lens solutions preserved with sorbic acid.⁽¹⁶⁾

No adverse reactions have been described after systemic administration of sorbic acid, and it has been reported that it can be ingested safely by patients who are allergic to sorbic acid.⁽¹⁷⁾ However, peroral contact urticaria has been reported.⁽¹¹⁾

The WHO has set an estimated total acceptable daily intake for sorbic acid, calcium sorbate, potassium sorbate, and sodium sorbate, expressed as sorbic acid, at up to 25 mg/kg body-weight.^(18,19)

Animal toxicological studies have shown no mammalian carcinogenicity or teratogenicity for sorbic acid consumed at up to 10% of the diet.⁽²⁰⁾

LD₅₀ (mouse, IP): 2.82 g/kg⁽²¹⁾

LD₅₀ (mouse, oral): 3.20 g/kg

LD₅₀ (mouse, SC): 2.82 g/kg

LD₅₀ (rat, oral): 7.36 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Sorbic acid can be irritant to the skin, eyes, and respiratory system. Eye protection, gloves, and a dust mask or respirator are recommended.

16 Regulatory Status

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

17 Related Substances

Calcium sorbate; potassium sorbate; sodium sorbate.

Calcium sorbate

Empirical formula: $C_{12}H_{14}O_4Ca$

Synonyms: E203

Molecular weight: 262.33

CAS number: [7492-55-9]

Appearance: white, odorless, tasteless, crystalline powder.

Solubility: soluble 1 in 83 parts of water; practically insoluble in fats.

Comments: the EINECS number for calcium sorbate is 231-321-6.

Sodium sorbate

Empirical formula: $C_6H_7O_2Na$

Synonyms: E201; sodium (*E,E*)-hexa-2,4-dienoate.

Molecular weight: 134.12

CAS number: [42788-83-0]

Appearance: light, white, crystalline powder.

Solubility: soluble 1 in 3 parts of water.

Comments: the EINECS number for sodium sorbate is 231-819-3.

18 Comments

The *trans,trans*-isomer of sorbic acid is the commercial product.

The EINECS number for sorbic acid is 203-768-7.

19 Specific References

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20 General References

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21 Author

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22 Date of Revision

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