

Butylparaben

1 Nonproprietary Names

BP: Butyl hydroxybenzoate
JP: Butyl parahydroxybenzoate
PhEur: Butylis parahydroxybenzoas
USPNF: Butylparaben

2 Synonyms

4-Hydroxybenzoic acid butyl ester; *Lexgard B*; *Nipabutyl*; *Tegosept B*; *TriseptB*; *Uniphen P-23*; *Unisept B*.

3 Chemical Name and CAS Registry Number

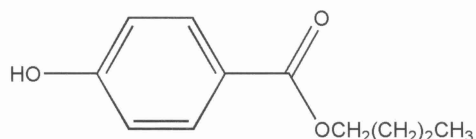
Butyl-4-hydroxybenzoate [94-26-8]

4 Empirical Formula Molecular Weight

C₁₁H₁₄O₃

194.23

5 Structural Formula



6 Functional Category

Antimicrobial preservative.

7 Applications in Pharmaceutical Formulation or Technology

Butylparaben is widely used as an antimicrobial preservative in cosmetics and pharmaceutical formulations; *see* Table I.

It may be used either alone or in combination with other paraben esters or with other antimicrobial agents. In cosmetics, it is the fourth most frequently used preservative.⁽¹⁾

As a group, the parabens are effective over a wide pH range and have a broad spectrum of antimicrobial activity, although they are most effective against yeasts and molds; *see* Section 10.

Owing to the poor solubility of the parabens, paraben salts, particularly the sodium salt, are frequently used in formulations. However, this may raise the pH of poorly buffered formulations.

See Methylparaben for further information.

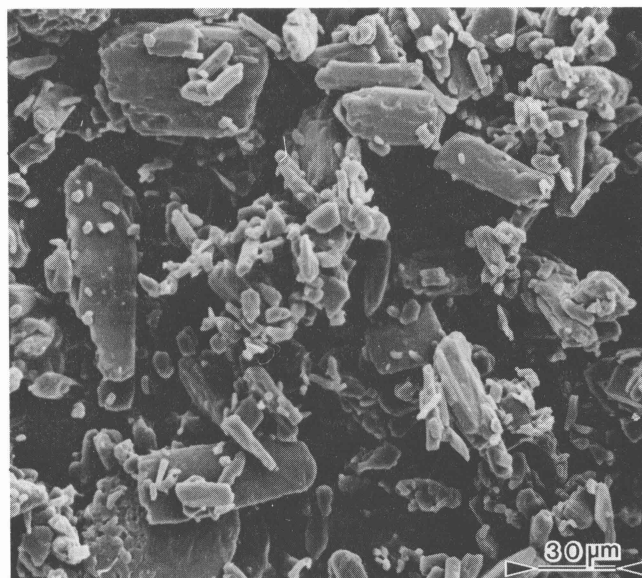
Table I: Uses of butylparaben.

Use	Concentration (%)
Oral suspensions	0.006–0.05
Topical preparations	0.02–0.4

SEM: 1

Excipient: Butylparaben

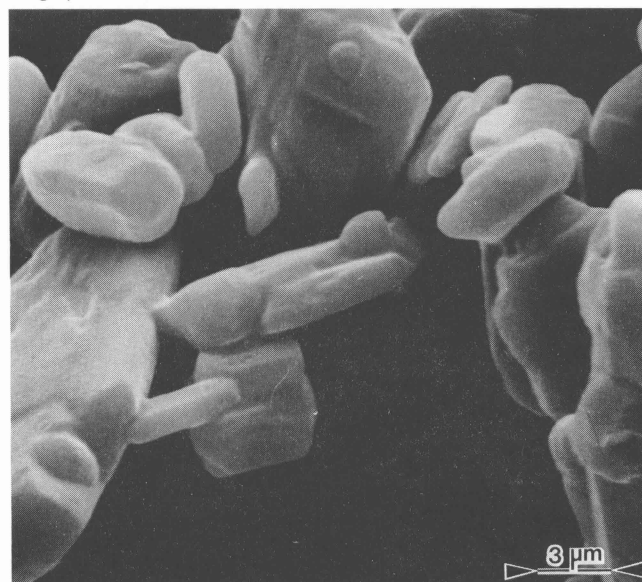
Magnification: 240 ×



SEM: 2

Excipient: Butylparaben

Magnification: 2400 ×



8 Description

Butylparaben occurs as colorless crystals or a white, crystalline, odorless or almost odorless, tasteless powder.

9 Pharmacopeial Specifications

See Table II.

Table II: Pharmacopeial specifications for butylparaben.

Test	JP 2001	PhEur 2002 (Suppl 4.2)	USPNF 20
Identification	+	+	+
Characters	—	+	—
Appearance of solution	—	+	—
Melting range	69–72°C	68–71°C	68–72°C
Acidity	—	+	+
Loss on drying	≤0.5%	—	≤0.5%
Residue on ignition	≤0.1%	—	≤0.05%
Sulfated ash	—	≤0.1%	—
Related substances	—	+	—
Chloride	≤0.035%	—	—
Sulfate	≤0.024%	—	—
Heavy metals	≤20 ppm	—	—
Readily carbonizable substances	+	—	—
Parahydroxybenzoic acid and salicylic acid	+	—	—
Organic volatile impurities	—	—	+
Assay (dried basis)	≥99.0%	98.0–102.0%	99.0–100.5%

10 Typical Properties

Antimicrobial activity: butylparaben exhibits antimicrobial activity between pH 4–8. Preservative efficacy decreases with increasing pH owing to the formation of the phenolate anion. Parabens are more active against yeasts and molds than against bacteria. They are also more active against Gram-positive than against Gram-negative bacteria; *see* Table III.

The activity of the parabens increases with increasing chain length of the alkyl moiety, but solubility decreases. Butylparaben is thus more active than methylparaben. Activity may be improved by using combinations of parabens since synergistic effects occur. Activity has also been reported to be improved by the addition of other excipients; *see* Methylparaben for further information.

Table III: Minimum inhibitory concentrations (MICs) for butylparaben in aqueous solution.⁽²⁾

Microorganism	MIC (μg/mL)
<i>Aerobacter aerogenes</i> ATCC 8308	400
<i>Aspergillus niger</i> ATCC 9642	125
<i>Aspergillus niger</i> ATCC 10254	200
<i>Bacillus cereus</i> var. <i>mycoides</i> ATCC 6462	63
<i>Bacillus subtilis</i> ATCC 6633	250
<i>Candida albicans</i> ATCC 10231	125
<i>Enterobacter cloacae</i> ATCC 23355	250
<i>Escherichia coli</i> ATCC 8739	5000
<i>Escherichia coli</i> ATCC 9637	5000
<i>Klebsiella pneumoniae</i> ATCC 8308	250
<i>Penicillium chrysogenum</i> ATCC 9480	70
<i>Penicillium digitatum</i> ATCC 10030	32
<i>Proteus vulgaris</i> ATCC 13315	125
<i>Pseudomonas aeruginosa</i> ATCC 9027	>1000
<i>Pseudomonas aeruginosa</i> ATCC 15442	>1000
<i>Pseudomonas stutzeri</i>	500
<i>Rhizopus nigricans</i> ATCC 6227A	63
<i>Saccharomyces cerevisiae</i> ATCC 9763	35
<i>Salmonella typhosa</i> ATCC 6539	500
<i>Serratia marcescens</i> ATCC 8100	500
<i>Staphylococcus aureus</i> ATCC 6538P	125
<i>Staphylococcus epidermidis</i> ATCC 12228	250
<i>Trichophyton mentagrophytes</i>	35

Density (bulk): 0.731 g/cm³

Density (tapped): 0.819 g/cm³

Melting point: 68–72°C

Partition coefficients: values for different vegetable oils vary considerably and are affected by the purity of the oil; *see* Table IV.

Solubility: *see* Table V.

Table IV: Partition coefficients for butylparaben between oils and water⁽³⁾

Solvent	Partition coefficient oil : water
Mineral oil	3.0
Peanut oil	280
Soybean oil	280

Table V: Solubility of butylparaben.

Solvent	Solubility at 20°C unless otherwise stated
Acetone	Freely soluble
Ethanol	1 in 0.5
Ethanol (95%)	1 in 1
Ether	Freely soluble
Glycerin	1 in 330
Methanol	1 in 0.5
Mineral oil	1 in 1000
Peanut oil	1 in 20
Propylene glycol	1 in 1
Water	1 in >5000
	1 in 670 at 80°C

11 Stability and Storage Conditions

Aqueous butylparaben solutions at pH 3–6 can be sterilized by autoclaving, without decomposition.⁽⁴⁾ At pH 3–6, aqueous solutions are stable (less than 10% decomposition) for up to about 4 years at room temperature, while solutions at pH 8 or above are subject to rapid hydrolysis (10% or more after about 60 days at room temperature).⁽⁵⁾

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

12 Incompatibilities

The antimicrobial activity of butylparaben is considerably reduced in the presence of nonionic surfactants as a result of micellization.⁽⁶⁾ Absorption of butylparaben by plastics has not been reported but appears probable given the behavior of other parabens. Some pigments, e.g., ultramarine blue and yellow iron oxide, absorb butylparaben and thus reduce its preservative properties.⁽⁷⁾

Butylparaben is discolored in the presence of iron and is subject to hydrolysis by weak alkalis and strong acids.

See also Methylparaben.

13 Method of Manufacture

Butylparaben is prepared by esterification of *p*-hydroxybenzoic acid with *n*-butanol.

14 Safety

Butylparaben and other parabens are widely used as antimicrobial preservatives in cosmetics and oral and topical pharmaceutical formulations.

Systemically, no adverse reactions to parabens have been reported, although they have been associated with hypersensitivity reactions. *See* Methylparaben for further information.

LD₅₀ (mouse, IP): 0.23 g/kg⁽⁸⁾

LD₅₀ (mouse, oral): 13.2 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Butylparaben may be irritant to the skin, eyes, and mucous membranes and should be handled in a well-ventilated environment. Eye protection, gloves, and a dust mask or respirator are recommended.

16 Regulatory Status

Included in the FDA Inactive Ingredients Guide (injections, oral capsules, solutions, suspensions, syrups and tablets, rectal, and topical preparations). Included in nonparenteral medicines licensed in the UK.

17 Related Substances

Butylparaben sodium; ethylparaben; methylparaben; propylparaben.

Butylparaben sodium

Empirical formula: C₁₁H₁₃NaO₃

Molecular weight: 216.23

CAS number: [36457-20-2]

Synonyms: butyl-4-hydroxybenzoate sodium salt; sodium butyl hydroxybenzoate.

Appearance: white, odorless or almost odorless, hygroscopic powder.

Acidity/alkalinity: pH = 9.5–10.5 (0.1% w/v aqueous solution)

Solubility: 1 in 10 of ethanol (95%); 1 in 1 of water.

Comments: butylparaben sodium may be used instead of butylparaben because of its greater aqueous solubility. In unbuffered formulations, pH adjustment may be required.

18 Comments

See Methylparaben for further information and references.

The EINECS number for butylparaben is 202-318-7.

19 Specific References

- 1 Decker RL, Wenninger JA. Frequency of preservative use in cosmetic formulas as disclosed to FDA—1987. *Cosmet Toilet* 1987; **102**(12): 21–24.
- 2 Haag TE, Loncrini DF. Esters of para-*hydroxybenzoic acid*. In: Kabara JJ, ed. *Cosmetic and Drug Preservation*. New York: Marcel Dekker, 1984: 63–77.
- 3 Wan LSC, Kurup TRR, Chan LW. Partition of preservatives in oil/water systems. *Pharm Acta Helv* 1986; **61**: 308–313.
- 4 Aalto TR, Firman MC, Rigler NE. *p*-Hydroxybenzoic acid esters as preservatives I: uses, antibacterial and antifungal studies, properties and determination. *J Am Pharm Assoc (Sci)* 1953; **42**: 449–457.
- 5 Kamada A, Yata N, Kubo K, Arakawa M. Stability of *p*-hydroxybenzoic acid esters in acidic medium. *Chem Pharm Bull* 1973; **21**: 2073–2076.
- 6 Aoki M, Kameta A, Yoshioka I, Matsuzaki T. Application of surface active agents to pharmaceutical preparations I: effect of Tween 20 upon the antifungal activities of *p*-hydroxybenzoic acid esters in solubilized preparations [in Japanese]. *J Pharm Soc Jpn* 1956; **76**: 939–943.
- 7 Sakamoto T, Yanagi M, Fukushima S, Mitsui T. Effects of some cosmetic pigments on the bactericidal activities of preservatives. *J Soc Cosmet Chem* 1987; **38**: 83–98.
- 8 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000: 648.

See also Methylparaben.

20 General References

Golightly LK, Smolinske SS, Bennett ML, *et al.* Pharmaceutical excipients associated with inactive ingredients in drug products (part I). *Med Toxicol* 1988; **3**: 128–165.

See also Methylparaben.

21 Author

MM Rieger.

22 Date of Revision

4 October 2002.