

# Benzethonium Chloride

## 1 Nonproprietary Names

BP: Benzethonium chloride  
JP: Benzethonium chloride  
PhEur: Benzethonii chloridum  
USP: Benzethonium chloride

## 2 Synonyms

Benzyl dimethyl-[2-[2-(*p*-1,1,3,3-tetramethylbutylphenoxy)ethoxy]ethyl]ammonium chloride; BZT; diisobutylphenoxyethoxyethyl dimethyl benzyl ammonium chloride; *Hyamine* 1622.

## 3 Chemical Name and CAS Registry Number

*N,N*-Dimethyl-*N*-[2-[2-(4-(1,1,3,3-tetramethylbutyl)phenoxy)ethoxy]ethyl]benzene-methanaminium chloride [121-54-0]

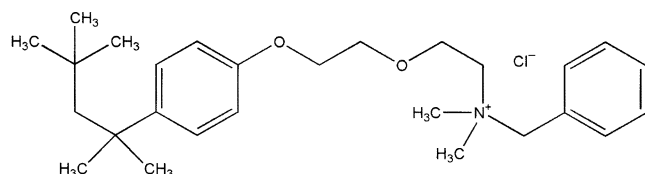
## 4 Empirical Formula

C<sub>27</sub>H<sub>42</sub>ClNO<sub>2</sub>

## Molecular Weight

448.10

## 5 Structural Formula



## 6 Functional Category

Antimicrobial preservative; antiseptic; disinfectant.

## 7 Applications in Pharmaceutical Formulation or Technology

Benzethonium chloride is a quaternary ammonium compound used in pharmaceutical formulations as an antimicrobial preservative. Typically, it is used for this purpose in injections, ophthalmic and otic preparations at concentrations 0.01–0.02% w/v. Benzethonium chloride may also be used as a wetting and solubilizing agent, and as a topical disinfectant.

In cosmetics such as deodorants, benzethonium chloride may be used as an antimicrobial preservative in concentrations up to 0.5% w/v.

The physical properties and applications of benzethonium chloride are similar to those of other cationic surfactants such as cetrimide.

## 8 Description

Benzethonium chloride occurs as a white crystalline material with a mild odor and very bitter taste.

## 9 Pharmacopeial Specifications

See Table I.

**Table I:** Pharmacopeial specifications for benzethonium chloride.

Test	JP 2001	PhEur 2002	USP 25
Identification	+	+	+
Characters	—	+	—
Appearance of solution	—	+	—
Acidity or alkalinity	—	+	—
Melting range	158–164 °C	158–164 °C	158–163 °C
Loss on drying	≤5.0%	≤5.0%	≤5.0%
Residue on ignition	≤0.1%	—	≤0.1%
Sulfated ash	—	≤0.1%	—
Ammonium compounds	+	≤50 ppm	+
Assay (dried basis)	≥97.0%	97.0–103.0%	97.0–103.0%

## 10 Typical Properties

**Acidity/alkalinity:** pH = 4.8–5.5 for a 1% w/v aqueous solution.

**Antimicrobial activity:** optimum antimicrobial activity occurs between pH 4–10. Preservative efficacy is enhanced by ethanol and reduced by soaps and other anionic surfactants. For typical minimum inhibitory concentrations (MICs) see Table II.<sup>(1)</sup>

**Table II:** Minimum inhibitory concentration (MIC) for benzethonium chloride.

Microorganism	MIC (μg/ml)
<i>Aspergillus niger</i>	128
<i>Candida albicans</i>	64
<i>Escherichia coli</i>	32
<i>Penicillium notatum</i>	64
<i>Proteus vulgaris</i>	64
<i>Pseudomonas aeruginosa</i>	250
<i>Pseudomonas cepacia</i>	250
<i>Pseudomonas fluorescens</i>	250
<i>Staphylococcus aureus</i>	0.5
<i>Streptococcus pyogenes</i>	0.5

**Solubility:** soluble 1 in less than 1 of acetone, chloroform, ethanol (95%), and water; soluble 1 in 6000 of ether. Dissolves in water to produce a foamy, soapy solution.

## 11 Stability and Storage Conditions

Benzethonium chloride is stable. Aqueous solutions may be sterilized by autoclaving.

The bulk material should be stored in an airtight container protected from light, in a cool, dry place.

## 12 Incompatibilities

Benzethonium chloride is incompatible with soaps and other anionic surfactants and may be precipitated from solutions greater than 2% w/v concentration by the addition of mineral acids and some salt solutions.

## 13 Method of Manufacture

*p*-Diisobutylphenol is condensed in the presence of a basic catalyst with  $\beta,\beta'$ -dichlorodiethyl ether to yield 2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl chloride. Alkaline dimethylation then produces the corresponding tertiary amine which, after purification by distillation, is dissolved in a suitable organic solvent and treated with benzyl chloride to precipitate benzethonium chloride.<sup>(2)</sup>

## 14 Safety

Benzethonium chloride is readily absorbed and is generally regarded as a toxic substance when administered orally. Ingestion may cause vomiting, collapse, convulsions, and coma. The probable lethal human oral dose is estimated to be 50–500 mg/kg body-weight.

The topical use of solutions containing greater than 5% w/v benzethonium chloride can cause irritation although benzethonium chloride is not regarded as a sensitizer. The use of 0.5% w/v benzethonium chloride in cosmetics is associated with few adverse effects. A maximum concentration of 0.02% w/v benzethonium chloride is recommended for use in cosmetics used in the eye area and this is also the maximum concentration generally used in pharmaceutical formulations such as injections and ophthalmic preparations.<sup>(3)</sup>

See also Benzalkonium Chloride.

- LD<sub>50</sub> (mouse, IP): 15.5 mg/kg<sup>(4)</sup>
- LD<sub>50</sub> (mouse, IV): 30 mg/kg
- LD<sub>50</sub> (mouse, oral): 338 mg/kg
- LD<sub>50</sub> (rat, IP): 16.5 mg/kg
- LD<sub>50</sub> (rat, IV): 19 mg/kg
- LD<sub>50</sub> (rat, oral): 368 mg/kg
- LD<sub>50</sub> (rat, SC): 119 mg/kg

## 15 Handling Precautions

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

## 16 Regulatory Status

Included in the FDA Inactive Ingredients Guide (IM and IV injections, ophthalmic and otic preparations).

## 17 Related Substances

Benzalkonium chloride; cetrimide.

## 18 Comments

Benzethonium chloride has been used therapeutically as a disinfectant and topical anti-infective agent. However, its use in these applications has largely been superseded by other more effective antimicrobials and it is now largely used solely as a preservative in a limited number of pharmaceutical and cosmetic formulations.

The EINECS number for benzethonium chloride is 204-479-9.

## 19 Specific References

- 1 Wallhäusser KH. Benzethonium chloride. In: Kabara JJ, ed. *Cosmetic and Drug Preservation Principles and Practice*. New York: Marcel Dekker, 1984: 734–735.
- 2 Gennaro AR, ed. *Remington: The Science and Practice of Pharmacy*, 20th edn. Baltimore: Lippincott Williams and Wilkins, 2000: 1508.
- 3 The Expert Panel of the American College of Toxicology. Final report on the safety assessment of benzethonium chloride and methylbenzethonium chloride. *J Am Coll Toxicol* 1985; 4: 65–106.
- 4 Lewis RJ, ed. *Sax's Dangerous Properties of Industrial Materials*, 10th edn. New York: Wiley, 2000, 416.

## 20 General References

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## 21 Authors

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## 22 Date of Revision

5 March 2002.