

Benzalkonium Chloride

B

1 Nonproprietary Names

BP: Benzalkonium Chloride

JP: Benzalkonium Chloride

PhEur: Benzalkonium Chloride

USP–NF: Benzalkonium Chloride

2 Synonyms

Alkylbenzyltrimethylammonium chloride; alkyl dimethyl benzyl ammonium chloride; benzalkonii chloridum; BKC; *Hyamine 3500*; *Pentonium*; *Zephiran*.

3 Chemical Name and CAS Registry Number

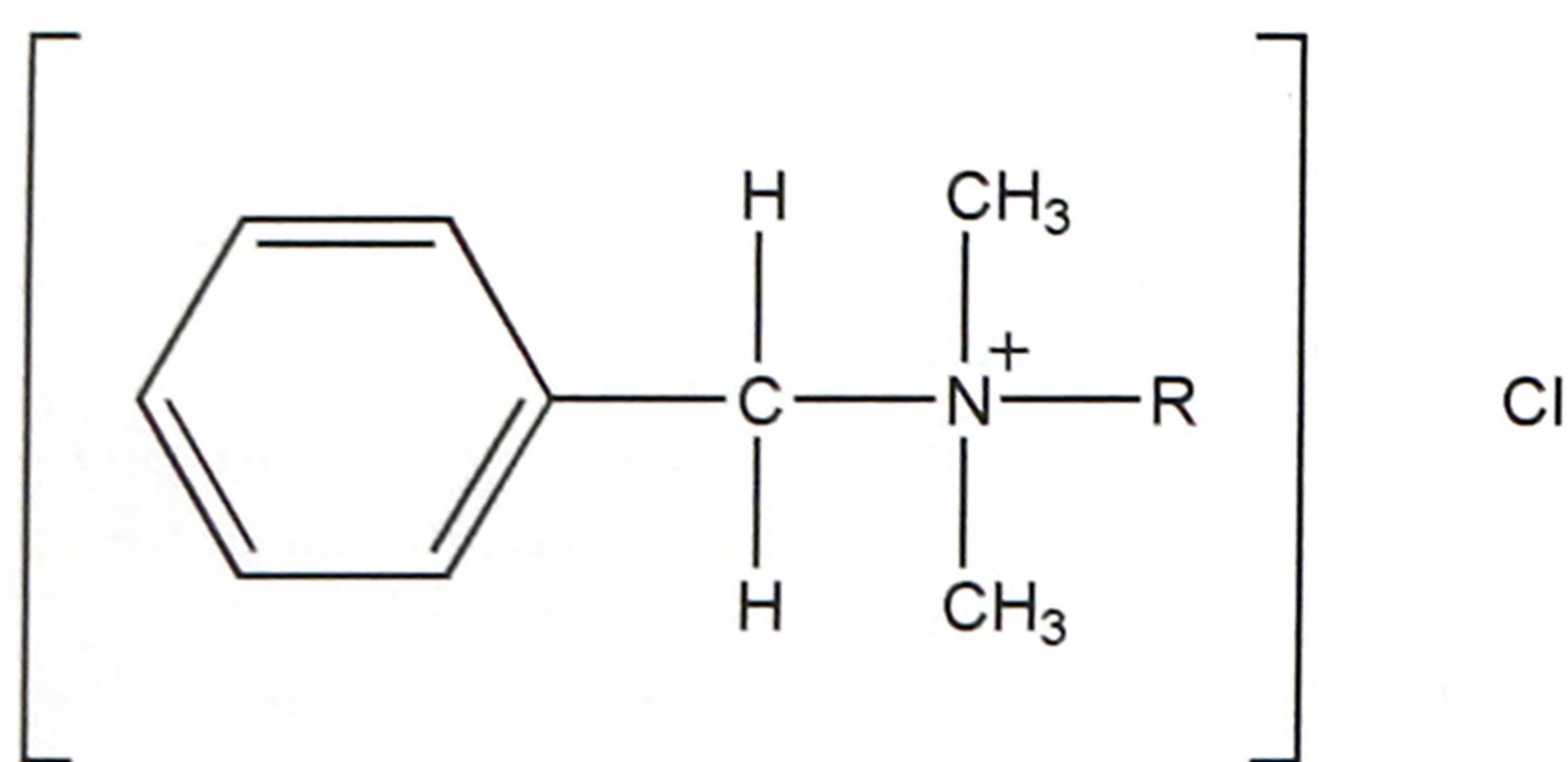
Alkyldimethyl(phenylmethyl)ammonium chloride [8001-54-5]

4 Empirical Formula and Molecular Weight

The USP 40–NF 35 S1 describes benzalkonium chloride as a mixture of alkylbenzyltrimethylammonium chlorides of the general formula $[C_6H_5CH_2N(CH_3)_2R]Cl$, where R represents a mixture of alkyls, including all or some of the group beginning with $n-C_8H_{17}$ and extending through higher homologs, with $n-C_{12}H_{25}$, $n-C_{14}H_{29}$, and $n-C_{16}H_{33}$ comprising the major portion.

The average molecular weight of benzalkonium chloride is 360.

5 Structural Formula



R = mixture of alkyls: $n-C_8H_{17}$ to $n-C_{18}H_{37}$; mainly $n-C_{12}H_{25}$ (dodecyl), $n-C_{14}H_{29}$ (tetradecyl), and $n-C_{16}H_{33}$ (hexadecyl).

6 Functional Category

Antimicrobial preservative; cationic surfactant; penetration enhancer; solubilizing agent.

7 Applications in Pharmaceutical Formulation or Technology

Benzalkonium chloride is a quaternary ammonium compound used in pharmaceutical formulations as an antimicrobial preservative in applications similar to other cationic surfactants, such as cetrimide.

In ophthalmic preparations, benzalkonium chloride is one of the most widely used preservatives,⁽¹⁾ at a concentration of 0.01–0.02% w/v. Often it is used in combination with other preservatives or excipients, particularly 0.1% w/v edetate disodium, to enhance its antimicrobial activity against strains of *Pseudomonas*.

In nasal⁽²⁾ and otic formulations a concentration of 0.002–0.02% w/v is used, sometimes in combination with 0.002–0.005% w/v thimerosal. Benzalkonium chloride 0.01% w/v is also employed as a preservative in small-volume parenteral products.

Benzalkonium chloride is also used in topical preparations, and has been shown to enhance the topical penetration of lorazepam⁽³⁾ and olanzapine.⁽⁴⁾

Benzalkonium chloride is additionally used as a preservative in cosmetics.

8 Description

Benzalkonium chloride occurs as a white or yellowish-white amorphous powder, a thick gel, or gelatinous flakes. It is hygroscopic, soapy to the touch, and has a mild aromatic odor and very bitter taste.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for benzalkonium chloride.

Test	JP XVII	PhEur 9.2	USP 40–NF 35 S1
Identification	+	+	+
Characters	+	+	–
Acidity or alkalinity	–	+	+
Appearance of solution	+	+	–
Water	≤15.0%	≤10.0%	≤15.0%
Residue on ignition	≤0.2%	–	≤2.0%
Sulfated ash	–	≤0.1%	–
Water-insoluble matter	–	–	+
Amines and amine salts	–	+	0.1 mmol/g
Ratio of alkyl components	–	+	+
Petroleum ether-soluble substances	≤1.0%	–	–
Benzyl alcohol	–	≤0.5%	≤0.5%
Benzaldehyde	–	≤0.15%	≤0.15%
Chloromethylbenzene	–	≤0.05%	≤0.05%
Assay (dried basis)			
of $n-C_{12}H_{25}$	–	≥40.0%	≥40.0%
of $n-C_{14}H_{29}$	–	≥20.0%	≥20.0%
of $n-C_{12}H_{25}$ and $n-C_{14}H_{29}$	–	≥70.0%	≥70.0%
for total alkyl content	95.0–105.0%	95.0–104.0%	97.0–103.0%

10 Typical Properties

Acidity/alkalinity pH = 5–8 for a 10% w/v aqueous solution.

Antimicrobial activity Benzalkonium chloride solutions are active against a wide range of bacteria, yeasts, and fungi. Activity is more marked against Gram-positive than Gram-negative bacteria and minimal against bacterial endospores and acid-fast bacteria, see Table II. The antimicrobial activity of benzalkonium chloride is significantly dependent upon the alkyl composition of the homolog mixture.⁽⁵⁾ Benzalkonium chloride is ineffective against some *Pseudomonas aeruginosa* strains, *Mycobacterium tuberculosis*, *Trichophyton interdigitale*, and *T. rubrum*. However, combined with edetate disodium (0.01–0.1% w/v), benzyl alcohol, phenylethanol, or phenylpropanol, the activity against *Pseudomonas aeruginosa* is