# Cetrimide

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## 1 Nonproprietary Names

BP: Cetrimide

PhEur: Cetrimide

## 2 Synonyms

*Bromat*; *Cetab*; *Cetavlon*; *Cetraol*; cetrimidum; *Lissolamine V*; *Micol*; *Morpan CHSA*; *Morphans*; *Quammonium*; *Sucticide*.

## 3 Chemical Name and CAS Registry Number

Cetrimide [8044-71-1]

Note that the above name, CAS Registry Number, and synonyms refer to the PhEur 6.0 material which, although it consists predominantly of trimethyltetradecylammonium bromide, may also contain smaller amounts of other bromides; *see* Section 4.

There is some confusion in the literature regarding the synonyms, CAS Registry Number, and molecular weight applied to cetrimide. Chemical Abstracts has assigned [8044-71-1] to cetrimide and describes that material as a mixture of alkyltrimethylammonium bromides of different alkyl chain lengths. Different CAS Registry Numbers have been assigned to the individual pure components. While these numbers should not be interchanged, it is common to find the molecular weight and CAS Registry Number of trimethyltetradecylammonium bromide [1119-97-7] used for cetrimide, as this is the principal component, defined in both the BP 2009 and PhEur 6.0. It should be noted however, that the original BP 1953 described the principal component of cetrimide as hexadecyltrimethylammonium bromide.

The CAS Registry Number for hexadecyltrimethylammonium hydroxide [505-86-2] has also been widely applied to cetrimide. Therefore, careful inspection of experimental details and suppliers' specifications in the literature is encouraged to determine the specific nature of the 'cetrimide' material used in individual studies.

*See* Section 17 for further information.

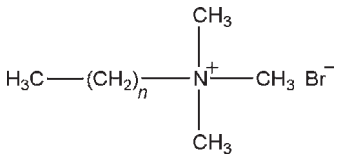
## 4 Empirical Formula and Molecular Weight

Cetrimide consists mainly of trimethyltetradecylammonium bromide ($C_{17}H_{38}BrN$), and may contain smaller amounts of dodecyltrimethylammonium bromide ($C_{15}H_{34}BrN$) and hexadecyltrimethylammonium bromide ($C_{19}H_{42}BrN$).

$C_{17}H_{38}BrN$ 336.40

*See also* Section 17.

## 5 Structural Formula




where

*n* = 11 for dodecyltrimethylammonium bromide
*n* = 13 for trimethyltetradecylammonium bromide
*n* = 15 for hexadecyltrimethylammonium bromide

## 6 Functional Category

Antimicrobial preservative; antiseptic; cationic surfactant; disin-

## 7 Applications in Pharmaceutical Formulation or Technology

Cetrimide is a quaternary ammonium compound that is used in cosmetics and pharmaceutical formulations as an antimicrobial preservative; *see* Section 10. It may also be used as a cationic surfactant. In eye-drops, it is used as a preservative at a concentration of 0.005% w/v.

Therapeutically, cetrimide is used in relatively high concentrations, generally as 0.1–1.0% w/v aqueous solutions, cream or spray as a topical antiseptic for skin, burns, and wounds.[1] Solutions containing up to 10% w/v cetrimide are used as shampoos to remove the scales in seborrheic dermatitis.

Cetrimide is also used as a cleanser and disinfectant for hard contact lenses, although it should not be used on soft lenses; as an ingredient of cetrimide emulsifying wax, and in o/w creams (e.g. cetrimide cream).

## 8 Description

Cetrimide is a white to creamy white, free-flowing powder, with a faint but characteristic odor and a bitter, soapy taste.

## 9 Pharmacopeial Specifications

*See* Table I.

**Table I:** Pharmacopeial specifications for cetrimide.

| Test | PhEur 6.0 |
|---|---|
| Identification | + |
| Characters | + |
| Acidity or alkalinity | + |
| Appearance of solution | + |
| Amines and amine salts | + |
| Loss on drying | ⩽2.0% |
| Sulfated ash | ⩽0.5% |
| Assay (as $C_{17}H_{38}BrN$, dried basis) | 96.0–101.0% |

## 10 Typical Properties

***Acidity/alkalinity*** pH = 5.0–7.5 (1% w/v aqueous solution)

***Antimicrobial activity*** Cetrimide has good bactericidal activity against Gram-positive species but is less active against Gram-negative species. *Pseudomonas* species, particularly *Pseudomonas aeruginosa*, may exhibit resistance. Cetrimide is most effective at neutral or slightly alkaline pH values, with activity appreciably reduced in acidic media and in the presence of organic matter. The activity of cetrimide is enhanced in the presence of alcohols. The activity of cetrimide against resistant strains of *Pseudomonas aeruginosa*, *Aspergillus niger*, and *Candida albicans* is significantly increased by the addition of edetic acid.[2] Cetrimide has variable antifungal activity,[3,4] is effective against some viruses, and is inactive against bacterial spores. Typical minimum inhibitory concentrations (MICs) are shown in Table II.

***Critical micelle concentration*** 3.08 mmol/kg[10] (in water)

***Melting point*** 232–247°C

***Moisture content*** At 40–50% relative humidity and 20°C, cetrimide absorbs sufficient moisture to cause caking and retard flow properties.

***NIR spectra*** *see* Figure 1.

***Partition coefficients***

Liquid paraffin : water = <1:

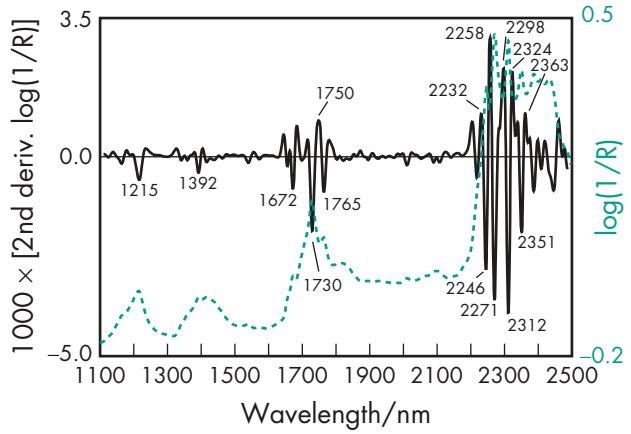



**Figure 1:** Near-infrared spectrum of cetrimide measured by reflectance.

**Table II:** Minimum inhibitory concentrations (MIC) of cetrimide.

| Microorganism | MIC (μg/mL) |
|---|---|
| *Escherichia coli* | 30 |
| *Pseudomonas aeruginosa* | 300 |
| *Staphylococcus aureus* | 10 |
| *Camphylobacter jejuni* | 8[5] |
| *Staphylococcus aureus (NCTC-8325-4)* | 0.25[6] |
| *Staphylococcus aureus (SH1000)* | 0.63[7] |
| *Pseudomonas aeruginosa (PAO1 (ATCC 15692))* | 36[8] |
| *Streptococcus pneumoniae R919* | 1.0[9] |

***Solubility*** Freely soluble in chloroform, ethanol (95%), and water; practically insoluble in ether. A 2% w/v aqueous solution foams strongly on shaking.

## 11 Stability and Storage Conditions

Cetrimide is chemically stable in the dry state, and also in aqueous solution at ambient temperatures. Aqueous solutions may be sterilized by autoclaving. Water containing metal ions and organic matter may reduce the antimicrobial activity of cetrimide.

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

## 12 Incompatibilities

Incompatible with soaps, anionic surfactants, high concentrations of nonionic surfactants, bentonite, iodine, phenylmercuric nitrate, alkali hydroxides, and acid dyes. Aqueous solutions react with metals.

## 13 Method of Manufacture

Cetrimide is prepared by the condensation of suitable alkyl bromides and trimethylamine.

## 14 Safety

Most adverse effects reported relate to the therapeutic use of cetrimide. If ingested orally, cetrimide and other quaternary ammonium compounds can cause nausea, vomiting, muscle paralysis, CNS depression, and hypotension; concentrated solutions may cause esophageal damage and necrosis. The fatal oral human dose is estimated to be 1.0–3.0 g.[11]

At the concentrations used topically, solutions do not generally cause irritation, although concentrated solutions have occasionally been reported to cause burns. Cases of hypersensitivity have been

Adverse effects that have been reported following irrigation of hydatid cysts with cetrimide solution include chemical peritonitis,[14] methemoglobinemia with cyanosis,[15] and metabolic disorders.[16]

## 15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Cetrimide powder and concentrated cetrimide solutions are irritant; avoid inhalation, ingestion, and skin and eye contact. Eye protection, gloves, and a respirator are recommended.[17]

## 16 Regulatory Status

Included in nonparenteral medicines licensed in the UK. Included in the Canadian List of Acceptable Non-medicinal Ingredients.

Cetrimide is on the list of 'Existing Active Substances' on the market in the Europe, and is registered according to REACH regulation. Cetrimide is not present in any approved product in the USA.

## 17 Related Substances

Benzalkonium chloride; benzethonium chloride; dodecyltrimethylammonium bromide; hexadecyltrimethylammonium bromide; trimethyltetradecylammonium bromide.

### Dodecyltrimethylammonium bromide

***Empirical formula*** $C_{15}H_{34}BrN$
***Molecular weight*** 308.35
***CAS number*** [1119-94-4]
***Synonyms*** DTAB; *N*-lauryl-*N*,*N*,*N*-trimethylammonium bromide; *N*,*N*,*N*-trimethyldodecylammonium bromide.
***Safety***

$LD_{50}$ (mouse, IV): 5.2 mg/kg[18]

$LD_{50}$ (rat, IV): 6.8 mg/kg

### Hexadecyltrimethylammonium bromide

***Empirical formula*** $C_{19}H_{42}BrN$
***Molecular weight*** 364.48
***CAS number*** [57-09-0]
***Synonyms*** Cetrimide BP 1953; cetrimonium bromide; cetyltrimethylammonium bromide; CTAB; *N*,*N*,*N*-trimethylhexadecylammonium bromide.
***Appearance*** A white to creamy-white, voluminous, free-flowing powder, with a characteristic faint odor and bitter, soapy taste.
***Melting point*** 237–243°C
***Safety***

$LD_{50}$ (guinea pig, SC): 100 mg/kg[19]

$LD_{50}$ (mouse, IP): 106 mg/kg

$LD_{50}$ (mouse, IV): 32 mg/kg

$LD_{50}$ (rabbit, IP): 125 mg/kg

$LD_{50}$ (rabbit, SC): 125 mg/kg

$LD_{50}$ (rat, IV): 44 mg/kg

$LD_{50}$ (rat, oral): 410 mg/kg

***Solubility*** Freely soluble in ethanol (95%); soluble 1 in 10 parts of water.
***Comments*** The original cetrimide BP 1953 consisted largely of hexadecyltrimethylammonium bromide, with smaller amounts of analogous alkyltrimethylammonium bromides. It contained a considerable proportion of inorganic salts, chiefly sodium bromide, and was less soluble than the present product.

### Trimethyltetradecylammonium bromide

***Empirical formula*** $C_{17}H_{38}BrN$
***Molecular weight*** 336.40

*Synonyms* Myristyltrimethylammonium bromide; tetradecyltrimethylammonium bromide; *N*,*N*,*N*-trimethyl-1-tetradecanaminium bromide.

*Safety*

$LD_{50}$ (mouse, IV): 12 mg/kg[20]

$LD_{50}$ (rat, IV): 15 mg/kg

## 18 Comments

As a precaution against contamination with *Pseudomonas* species resistant to cetrimide, stock solutions may be further protected by adding at least 7% v/v ethanol or 4% v/v propan-2-ol.

The EINECS number for cetrimide is 214-291-9. The PubChem Compound ID (CID) for cetrimide includes 68166 (trimethylhexadecylammonium hydroxide) and 14250 (trimethyltetradecylammonium bromide).

## 19 Specific References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## 21 Author

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## 22 Date of Revision

16 January 2009.