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21 Author

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22 Date of Revision

4 May 2017.

Chlorobutanol

1 Nonproprietary Names

BP: Chlorobutanol
JP: Chlorobutanol
PhEur: Chlorobutanol, Anhydrous
USP–NF: Chlorobutanol

2 Synonyms

Acetone chloroform; anhydrous chlorbutol; chlorbutanol; chlorobutanolum anhydricum; chlorbutol; chloretone; *Coliquifilm*; methaform; sedaform; trichloro-*tert*-butanol; β,β,β-trichloro-*tert*-butyl alcohol; trichloro-*t*-butyl alcohol.

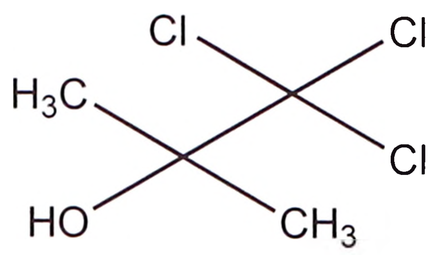
3 Chemical Name and CAS Registry Number

1,1,1-Trichloro-2-methyl-2-propanol [57-15-8]
1,1,1-Trichloro-2-methyl-2-propanol hemihydrate [6001-64-5]

4 Empirical Formula and Molecular Weight

$C_4H_7Cl_3O$ 177.46 (for anhydrous)
$C_4H_7Cl_3O \cdot \frac{1}{2}H_2O$ 186.46 (for hemihydrate)

5 Structural Formula



6 Functional Category

Antimicrobial preservative; plasticizing agent.

7 Applications in Pharmaceutical Formulation or Technology

Chlorobutanol is primarily used in ophthalmic or parenteral dosage forms as an antimicrobial preservative at concentrations up to 0.5% w/v; *see* Section 10. It is commonly used as an antibacterial agent for epinephrine solutions, posterior pituitary extract solutions, and ophthalmic preparations intended for the treatment of miosis. It is especially useful as an antibacterial agent in nonaqueous formulations. Chlorobutanol is also used as a preservative in cosmetics (*see* Section 16); as a plasticizer for cellulose esters and ethers.

8 Description

Volatile, colorless or white crystals with a musty, camphoraceous odor.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for chlorobutanol.

Test	JP XVII	PhEur 9.2	USP 40–NF 35 S1
Identification	+	+	+
Characters	+	+	–
Appearance of solution	–	+	–
Melting point	≥76°C	+	–
Anhydrous	–	≈95°C	–
Hemihydrate	–	≈78°C	–
Acidity	+	+	+
Water (anhydrous form)	≤6.0%	≤1.0%	≤1.0%
Hemihydrate	–	4.5–5.5%	≤6.0%
Chloride	≤0.071%	+	≤0.07%
Anhydrous	–	≤300 ppm	–
Hemihydrate	–	≤100 ppm	–
Residue on ignition	≤0.10%	–	–
Sulfated ash	–	≤0.1%	–
Assay (anhydrous basis)	≥98.0%	98.0–101.0%	98.0–100.5%

Note: the JP XVII and USP 40–NF 35 S1 allow either the anhydrous form or the hemihydrate; the PhEur includes them as separate monographs.

10 Typical Properties

Antimicrobial activity Chlorobutanol has both antibacterial and antifungal properties. It is effective against Gram-positive and Gram-negative bacteria and some fungi, e.g. *Candida albicans*, *Pseudomonas aeruginosa*, and *Staphylococcus albus*. Antimicrobial activity is bacteriostatic, rather than bactericidal, and is considerably reduced above pH 5.5. In addition, activity may also be reduced by increasing heat and by incompatibilities between chlorobutanol and other excipients or packaging materials; *see* Sections 11 and 12. However, activity may be increased by combination with other antimicrobial preservatives; *see* Section 18. Typical minimum inhibitory concentrations (MICs) are: Gram-positive bacteria 650 µg/mL; Gram-negative bacteria 1000 µg/mL; yeasts 2500 µg/mL; fungi 5000 µg/mL.
Boiling point 167°C
Melting point
76–78°C for the hemihydrate;
95–97°C for the anhydrous form.
Partition coefficient Octanol : water log k_{ow} = 2.03
Refractive index n_D^{25} = 1.4339
Solubility *see* Table II.