molecule of hypochlorous acid (on which activity is based), while hypochlorites and chloramines yield one molecule of hypochlorous acid for each atom of chlorine as shown in the following equations:

$$Cl_2 + H_2O \leftrightarrow HOCl + H^+ + Cl^-$$

$$NaOCl + H_2O \leftrightarrow HOCl + NaOH$$

Thus the assayed chlorine in such compounds has to be multiplied by 2 to produce 'available chlorine'. The term 'active chlorine' has been used confusingly for either 'available chlorine' (Cl_2) or 'combined chlorine' (Cl).

Because they have relatively low residual toxicity, chlorine compounds are useful for the disinfection of relatively clean impervious surfaces, such as babies' feeding bottles, baths, and food and dairy equipment. A concentration of 100 to 300 ppm of 'available chlorine' is used; a detergent may be added to ensure wetting of the surface. Solutions containing 1000 ppm 'available chlorine' are recommended for minor surface contamination and as part of general good hygiene practice. Solutions containing 10 000 ppm 'available chlorine' are used to disinfect surfaces contaminated with spilled blood or body fluids; this strength is effective against viruses including human immunodeficiency virus (HIV) and hepatitis B virus (p.1623). A concentration providing 20 000 ppm 'available chlorine' is used for material from patients with Creutzfeldt-Jakob disease (p.1622).

On a large scale, chlorine gas is used to disinfect public water supplies. On a smaller scale, the use of chlorine compounds is more convenient and sodium hypochlorite, tosylchloramide sodium, chlorinated lime, chlorine dioxide, or halazone are used. After satisfying the chlorine demand (the amount of chlorine needed to react with organic matter and other substances), a free-residual content of 0.2 to 0.4 ppm 'available chlorine' should be maintained, though more is required for alkaline waters with a pH of 9 or more. For the disinfection of potentially contaminated water a concentration of 1 ppm is recommended. Excessive residual chlorine may be removed by adding a little citric acid or sodium thiosulfate.

For use in small swimming pools, sodium or calcium hypochlorite may be added daily to maintain a free-residual 'available chlorine' concentration of 1 to 3 ppm. Tosylchloramide sodium, chlorinated lime, and the isocyanurates (see Troclosene, p.1665) may also be used. To minimise irritation of the eyes, maintain disinfectant activity, prevent precipitation of salts, and prevent metal corrosion, a pH of 7.2 to 7.8 should be maintained.

Solutions of chlorine-releasing compounds are also used in wound desloughing and disinfection (but see Disinfection: Wounds, under Sodium Hypochlorite, p.1662).

Chlorine Dioxide

926; Cloro, dióxido de.

ClO_2 = 67.45.

CAS — 10049-04-4.

Profile

Chlorine dioxide is a strong oxidising agent with the general properties of chlorine (p.1638). It is rapidly active against vegetative bacteria, including mycobacteria, and viruses and is also sporicidal. It is used for disinfection of medical equipment either in gaseous form or in a solution that requires activation before use and yields 700 to 1100 ppm 'available chlorine' (see p.1638) . Chlorine dioxide is irritant to the skin, eyes, and respiratory tract and should be stored in sealed containers. It is potentially corrosive to many materials and solutions may contain corrosion inhibitors.

Chlorine dioxide is also used for treatment and disinfection of water supplies.

◊ General references.

1. WHO. Chlorine dioxide (gas). *Concise International Chemical Assessment Document 37* Geneva: WHO, 2002. Available at: http://www.who.int/ipcs/publications/cicad/en/cicad37.pdf (accessed 14/03/06)

Disinfection of endoscopes. Chlorine dioxide solutions are used as an alternative to glutaral for the disinfection of endoscopes (p.1623).

Halitosis. Chlorine dioxide has been used in mouthwashes for the control of halitosis.[1]

1. Frascella J, *et al.* Odor reduction potential of a chlorine dioxide mouthrinse. *J Clin Dent* 1998; **9:** 39–42.

Preparations

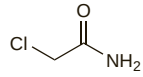
Proprietary Preparations (details are given in Part 3)
Belg.: Retardex; ***Philipp.:*** Oracare; ***UK:*** Retardex.

Chloroacetamide

Chloracetamide; Cloroacetamida. 2-Chloroacetamide.

C_2H_4ClNO = 93.51.

CAS — 79-07-2.



Profile

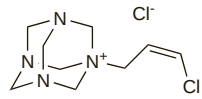
Chloroacetamide is a preservative that has been used in topical pharmaceutical preparations and cosmetics.

N-(3-Chloroallyl)hexaminium Chloride

N-(3-Cloroalil)hexaminio, cloruro de; Quaternium-15. 1-(3-Chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride.

$C_9H_{16}Cl_2N_4$ = 251.2.

CAS — 4080-31-3.



Profile

N-(3-Chloroallyl)hexaminium chloride is an antimicrobial preservative used in pharmaceutical preparations and cosmetics. Skin reactions have been reported.

Chlorobutanol *(BAN, rINN)*

Acetone-Chloroforme; Alcohol Trichlorisobutylicus; Chlorbutanol; Chlorbutanolum; Chlorbutol; Chloretone; Chlorobutanolis; Chlorobutanolum; Clorobutanol; Klooributanoli; Klorbutanol; Klorobutanol; Trichlorbutanolum. 1,1,1-Trichloro-2-methylpropan-2-ol.

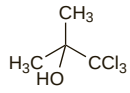
Хлоробутанол

$C_4H_7Cl_3O$ = 177.5.

CAS — 57-15-8 (anhydrous chlorobutanol); 6001-64-5 (chlorobutanol hemihydrate).

ATC — A04AD04.

ATC Vet — QA04AD04.



Pharmacopoeias. *Eur.* (see p.vii), *Int.*, and *USNF* allow either the anhydrous form or the hemihydrate; *Eur.* includes them as separate monographs. *Chin.* specifies the hemihydrate. *Jpn* permits up to 6% of water.

Ph. Eur. 6.2 (Chlorobutanol Hemihydrate; Chlorobutanol BP 2008). A white or almost white, crystalline powder or colourless crystals. It sublimes readily. M.p. about 78°. Slightly soluble in water; very soluble in alcohol; soluble in glycerol (85%). Store in airtight containers.

Ph. Eur. 6.2 (Chlorobutanol, Anhydrous). A white or almost white, crystalline powder or colourless crystals. It sublimes readily. M.p. about 95°. Slightly soluble in water; very soluble in alcohol; soluble in glycerol (85%). Store in airtight containers.

USNF 26 (Chlorobutanol). It is anhydrous or contains not more than one-half molecule of water of hydration. Colourless or white crystals with a characteristic, somewhat camphoraceous odour. M.p. about 76° for the hemihydrate and about 95° for the anhydrous form. Soluble 1 in 125 of water, 1 in 1 of alcohol, and 1 in 10 of glycerol; freely soluble in chloroform, in ether, and in volatile oils. Store in airtight containers.

Incompatibility and stability. The activity of chlorobutanol can be adversely affected by the presence of other compounds as well as by the packaging material. There may be sorption onto substances like magnesium trisilicate, bentonite, carmellose,[1] polyethylene,[2,3] or polyhydroxy-ethylmethacrylate that has been used in soft contact lenses.[4] Increasing heat[2,3] or pH[5,6] can reduce stability and activity.

1. Yousef RT, *et al.* Effect of some pharmaceutical materials on the bactericidal activities of preservatives. *Can J Pharm Sci* 1973; **8:** 54–6.
2. Friesen WT, Plein EM. The antibacterial stability of chlorobutanol stored in polyethylene bottles. *Am J Hosp Pharm* 1971; **28:** 507–12.
3. Holdsworth DG, *et al.* Fate of chlorbutol during storage in polyethylene dropper containers and simulated patient use. *J Clin Hosp Pharm* 1984; **9:** 29–39.
4. Richardson NE, *et al.* The interaction of preservatives with polyhydroxy-ethylmethacrylate (polyHEMA). *J Pharm Pharmacol* 1978; **30:** 469–75.
5. Nair AD, Lach JL. The kinetics of degradation of chlorobutanol. *J Am Pharm Assoc (Sci)* 1959; **48:** 390–5.
6. Patwa NV, Huyck CL. Stability of chlorobutanol. *J Am Pharm Assoc* 1966; **NS6:** 372–3.

Adverse Effects

Acute poisoning with chlorobutanol may produce CNS depression with weakness, loss of consciousness, and depressed respiration. Delayed (type IV) hypersensitivity reactions have been reported rarely.

◊ References.

1. Nordt SP. Chlorobutanol toxicity. *Ann Pharmacother* 1996; **30:** 1179–80.

Effects on the cardiovascular system. Rapid falls in arterial blood pressure were observed after injections of heparin containing chlorobutanol in patients undergoing coronary bypass.[1] No fall in blood pressure was seen in patients who received preservative-free heparin injection.

1. Bowler GMR, *et al.* Sharp fall in blood pressure after injection of heparin containing chlorbutol. *Lancet* 1986; **i:** 848–9.

Effects on mental function. The sedative effects of chlorobutanol have been reported to be a problem in a patient dependent on large doses (0.9 to 1.5 g daily with salicylamide 1.8 to 3.0 g daily)[1] and in another patient given high doses of morphine in an infusion preserved with chlorobutanol.[2]

1. Borody T, *et al.* Chlorbutol toxicity and dependence. *Med J Aust* 1979; **i:** 288.
2. DeChristoforo R, *et al.* High-dose morphine infusion complicated by chlorobutanol-induced somnolence. *Ann Intern Med* 1983; **98:** 335–6.

Hypersensitivity. A delayed, cellular type of hypersensitivity reaction to chlorobutanol used to preserve heparin injection after subcutaneous injection has been reported.[1] Pruritus from intranasal desmopressin has been attributed to the chlorobutanol preservative.[2]

1. Dux S, *et al.* Hypersensitivity reaction to chlorbutanol-preserved heparin. *Lancet* 1981; **i:** 149.
2. Itabashi A, *et al.* Hypersensitivity to chlorobutanol in DDAVP solution. *Lancet* 1982; **i:** 108.

Uses and Administration

Chlorobutanol has antibacterial and antifungal properties and it is used at a concentration of 0.5% as a preservative in injections and in eye drops as well as cosmetics.

Chlorobutanol has been used as a mild sedative and local analgesic but other compounds are preferred. It has been used in preparations for inflammatory and painful conditions of the ear and oropharynx.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Optrex; ***Port.:*** Vizoptal†.

Multi-ingredient: ***Arg.:*** Eludril; Otocalmia; ***Austral.:*** Cerumol; ***Austria:*** Aleot; ***Belg.:*** Eludril; Givalex; Prurisedine; ***Braz.:*** Auritricin; Lavolho†; ***Canad.:*** Cerumol; ***Fr.:*** Alodont; Balsamorhinol; Eludril; Givalex; ***Ger.:*** Givalex†; ***Hong Kong:*** Fungifax†; ***India:*** Andre; Clearwax; Waxolve; ***Irl.:*** Cerumol; Karvol; ***Israel:*** Cepadont; Cerumol; Dentin; Karvol; Pitrisan; ***Ital.:*** Fialetta Odontalgica Dr Knapp; Odontalgiche (Dentali)†; ***Malaysia:*** Cerumol; ***NZ:*** Frador; ***Port.:*** Eludril; Otoceril; ***Rus.:*** Eludril (Элюдрил); ***S.Afr.:*** Aurone Forte; Cerumol; Chamberlains Traditional Colic Remedy; Karvol; ***Singapore:*** Cerumol; Eludril; Karvol; ***Spain:*** Eludril; Otocerum; ***Switz.:*** Alodont†; Cerumenol; Eludril; ***Thai.:*** Opplin†; Optal; Optic; ***Turk.:*** Disinol; ***UK:*** Cerumol; Cetanorm; DDD; Dermidex; Eludril; Frador; Karvol; Monphytol†; ***USA:*** Outgro.

Chlorocarvacrol

5-Chlorocarvacrol; Clorcarvacrol; Clorcarvacrolum; Kloorikarvakroli; Klorkarvakrol; Monochloroisothymol. 4-Chloro-5-isopropyl-2-methylphenol.

$C_{10}H_{13}ClO$ = 184.7.

CAS — 5665-94-1.

Profile

Chlorocarvacrol is a phenolic antiseptic that is used as an ingredient of preparations for anorectal disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Delta-Hadensa; Hadensa; Haemanal; ***Chile:*** Vatanal; ***Fin.:*** Hadensa; ***Ger.:*** Alcos-Anal†; ***Neth.:*** Epianal; ***Norw.:*** Alcos-Anal; ***Spain:*** Hadensa; ***Turk.:*** Hedensa.