

Uses and Administration

Benzoates have antibacterial and antifungal properties. Their antimicrobial activity is due to the undissociated benzoic acid and is therefore pH-dependent. They are relatively inactive above a pH of about 5.

Benzoates are used as preservatives in pharmaceutical formulations including oral preparations; benzoic acid and sodium benzoate are typically used in concentrations of up to 0.2% and 0.5%, respectively. They are used as preservatives in foods, (and are also present naturally in some foods), and at similar concentrations in cosmetics.

Benzoic acid 6% with salicylic acid 3%, as Compound Benzoic Acid Ointment (BP 2008) (Whitfield's Ointment) has a long history of use as an antifungal (see Skin Infections, p.521). Benzoic acid has also been used in desloughing preparations and has been given as a urinary antiseptic.

An injection of caffeine and sodium benzoate has been used as a CNS stimulant, but see Neonates, under Adverse Effects and Precautions, above for a caution against its use in neonates.

Sodium benzoate is used as part of the treatment of hyperammonaemia that occurs in inborn errors of the urea cycle. It has also been reported to be effective in reducing plasma-glycine concentrations in nonketotic hyperglycaemia (p.2393), although it may not be effective in preventing mental retardation.

Sodium benzoate is a common ingredient of cough preparations.

Hyperammonaemia. Sodium benzoate is used for treatment of hyperammonaemia (p.1929).¹⁻³ It is given with sodium phenylacetate (see p.2390 for doses) and a combined preparation is available in some countries.

1. Maestri NE, et al. Long-term survival of patients with argininosuccinate synthetase deficiency. *J Pediatr* 1995; **127**: 929-35.
2. Maestri NE, et al. Long-term treatment of girls with ornithine transcarbamylase deficiency. *N Engl J Med* 1996; **335**: 855-9.
3. Zammarchi E, et al. Neonatal onset of hyperornithinemia-hyperammonemia-homocitrullinuria syndrome with favorable outcome. *J Pediatr* 1997; **131**: 440-3.

Preparations

BP 2008: Benzoic Acid Solution; Compound Benzoic Acid Ointment; Toluflavour Solution;
USP 31: Benzoic and Salicylic Acids Ointment; Caffeine and Sodium Benzoate Injection.

Proprietary Preparations (details are given in Part 3)

Indon.: Topix; Yodsaben; **Mex.:** Colufasej.

Multi-ingredient: **Arg.:** Expectosan Hierbas y Miel; Fungicida; Ixana; No-Tos Adultos; No-Tos Infantil; Pectobron; Refenax Jarabe; Solvex Liquido Fungicida; Torfan H; **Austral.:** Whitfields (Benzoic Acid Compound) Ointment; **Austria:** Acerbine; Mycopol; **Belg.:** Colimax; Kamfeine; Pholco-Mereprine; Toplexil; Tux; **Braz.:** ABC Solucao; Antimicon; Benzomel; Bronquidex; Bronquigom; Cessatosse; Dermicon; Dermycose; Eaca Balsamico; Egotussano; Expec; Expectobron; Frenotosse; Fungolab; Gotas Nican; Iodesin; Iodeto de Potasio; Iodopulmin; Ioli; Ipecol; KI-Expectorante; Limao Bravo; Micoctiazol; Micoctox; Micoz; Peitoral Angico Pelotense; Penetro; Po Antisseptico; Pulmoforte; Pulmoverina; Rhum Creosotado; Tiratosse; Toplexil; Tossanil; Tussodina; Tussol; Tussucalmant; Xarope de Caraguata; Xarope Peitoral de Ameixa Composto; Xarope Sao Joao; Xpe SPC; **Canad.:** Bronco Asmol; MRX; Plax; **Chile:** Broncodeina; Canstop; Gotas Nican; Gruben; Listerine; Pectoral Pasteur; Pectoserum; Pulmagol; Summer's Eve Hierbas; Summer's Eve Vinagre y Agua; **Denm.:** Pectyl; **Fr.:** Broncalene; Broncalene Nourisson; Codotussyl Maux de Gorge; Dermacide; Dimetane Expectant Infantil; Dinacode avec codeine; Dinacode; Ephydion; Fluocail blancheur; Germose; Listerine; Neo-Codion; Ozothine; Paregonique; Passedy; Pulmofluide Simple; Quintopan; Rhinamide; Silomat; **Ger.:** Sagrosept; **Hong Kong:** Fungifax; Gly Thymol; Listerine; Listerine Tartar Control; Listerine Teeth and Gum Defence; **Hung.:** Glycosept; **India:** Keralin; Mycoderm; Pragmatar; Zoderin; **Indon.:** Kalpanax; Kopame; Listerine Coolmint; Mikorex; Saponia; **Israel:** Oxacatin; Pertussol; Phytoderm Compositum; Pitrasin; Shiulon; Spirit Whitfield; Toplexil; Tussophedrine New Formula; **Ital.:** Borocaina; Dentaline; Neo Borocollina; Paracodina; Sedocalcio; Ticoscol; Tionamil; **Malaysia:** Nixodem; **Mex.:** Pulmoval; **NZ:** Egomycol; Listerine; Listerine Tartar Control; **Philipp.:** Dermalin; Listerine Coolmint; Listerine Freshburst; Listerine Original; Listerine Teeth & Gum Defence; United Home Whitfield's Ointment; **Port.:** Broncodiazina; Bronquiasmol; Calmarum; Codo; Drenoflu; Micaeven; **Rus.:** Neo-Codion Babies (Neo-Кодион Для Маленьких); **S.Afr.:** Aserbine; Dry & Clear Medicated Skin Cleanser; **Singapore:** Listerine; Listerine Cool Mint; Listerine Fresh Burst; Listerine Tartar Control; Whitfield; **Spain:** Acerbiol; Broncoformol Muco Dexa; Broncovital; Bronquidiazina CR; Bronquimar; Etemol Antitusivo; Neumopectolina; Pastillas Pectoral Kely; Pazbronqal; Pulmo Menal; Pulmofasa; Tos Mai; **Switz.:** Acerbine; Dinacode N; Foral; Gem; Nasobol; Neo-DP; Nican; Onguent aux herbes Keller; Phol-Tussil; Phol-Tux; Saintbois; Toplexil; **Turk.:** Artu; Gayabeksin; Latusin; Nesganin; **UK:** Aserbine; Ecema Ointment; Hemocane; Potters Gees Linctus; Sanderson's Throat Specific; Toepedo; **USA:** Ammonul; Atrosept; Bensal HP; Cystex; Dolsed; MHP-A; Prosed/DS; Trac Tabs 2X; UAA; Ucephan; Unidom Modified; Urised; Uri-septic; Uritact; **Venez.:** Acetoben; Amodion; Boramint; Corsaben; Dromil Saucos; Fedratal; Isacol; Kantoli; Metalfedrin; Niosilin; Photoderm AKN; Pi-Fedrin; Tabonuco; Yerba Santa; Yodalmina;†

Benzododecinium Bromide

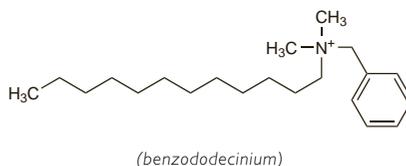
Benzododecinio, bromuro de. Benzylododecyltrimethylammonium bromide.

$C_{21}H_{38}BrN = 384.4$.

CAS — 10328-35-5 (benzododecinium); 7281-04-1 (benzododecinium bromide).

ATC — D09AA05.

ATC Vet — QD09AA05.



Pharmacopoeias. In Fr.

Benzododecinium Chloride (rINN)

Benzododecinii Chloridum; Benzododécinium, Chlorure de; Cloruro de benzododecinio; Lauralkonium Chloride, Benzylododecyltrimethylammonium chloride.

Бензододэциния Хлорид

$C_{21}H_{38}ClN = 340.0$.

CAS — 139-07-1.

ATC — D09AA05.

ATC Vet — QD09AA05.

NOTE. The name Lauralkonium Chloride is also a rINN for another quaternary ammonium compound ($C_{29}H_{44}ClNO_2$; CAS — 19486-61-4).

Profile

Benzododecinium bromide is a quaternary ammonium antiseptic with properties similar to those of other cationic surfactants (see Cetrimide, p.1634). It is used in mouthwashes, eye preparations, and nasal sprays and solutions for the treatment of minor infections. It has also been used as a spermicide. Benzododecinium chloride has also been used.

Preparations

Proprietary Preparations (details are given in Part 3)

Cz.: Ajatin; **Fr.:** Rhimedrine.

Multi-ingredient: **Cz.:** Ophtal; **Fr.:** Prorhinel; Sedacollyre; **Switz.:** Kermerhinoze; Prorhinel.

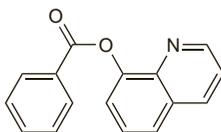
Benzoxiquine (USAN, rINN)

Benzoxiquina; Benzoxiquinum; NSC-3951. 8-Quinololinol benzoate (ester).

Бензоксиквин

$C_{16}H_{11}NO_2 = 249.3$.

CAS — 86-75-9.



Profile

Benzoxiquine is an antiseptic that has been included in cosmetic products and multi-ingredient preparations used typically for the treatment of fungal infections. The salicylate has also been used.

Benzoxonium Chloride (rINN)

Benzoxonii Chloridum; Benzoxonium, Chlorure de; Cloruro de benzoxonio. Benzylododecylbis(2-hydroxyethyl)ammonium chloride.

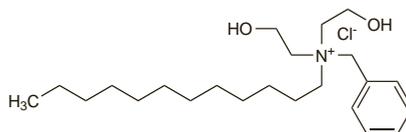
Бензоксония Хлорид

$C_{23}H_{42}ClNO_2 = 400.0$.

CAS — 19379-90-9.

ATC — A01AB14; D08AJ05.

ATC Vet — QA01AB14; QD08AJ05.



Profile

Benzoxonium chloride is a quaternary ammonium antiseptic used for disinfection of the skin and mucous membranes. It is also used for instrument disinfection. Allergic contact dermatitis from benzoxonium chloride has been reported.

Preparations

Proprietary Preparations (details are given in Part 3)

Belg.: Orolar; **Chile:** Bialcol; **Gr.:** Orocol; **Ital.:** Bactofen; Bialcol.

Multi-ingredient: **Belg.:** Orolar Lidocaine; **Chile:** Alcolex; **Cz.:** Orolar; **Ger.:** Loscon; **Gr.:** Orocol Lido; **Hung.:** Mebucain; Vita-Merfen; **Israel:** Merfen; Vita-Merfen NF; **Philipp.:** Orolar-L; **Pol.:** Orolar; **Port.:** Orolar; **Rus.:** Theraflu Lar (Терафлю Лар); **Switz.:** Mebucalets f; Merfen; Orolar; Vita-Merfen.

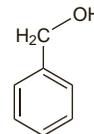
Benzyl Alcohol (rINN)

Alcohol benzílico; Alcohol benzylicus; Alcoholum Benzylicum; Alcool Benzylique; Alkohol benzylowy; Bensylalkohol; Benzylalkohol; Benzenemethanol; Benzil-alkohol; Benzilo alkoholis; Benzylalkohol; Benzylique, alcool; Fenilmetanol; Phenylcarbinol; Phenylmethanol.

Бензиловый спирт

$C_6H_5CH_2OH = 108.1$.

CAS — 100-51-6.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, and *Jpn.* Also in *USNF*.

Ph. Eur. 6.2 (Benzyl Alcohol). A clear colourless, oily liquid. Soluble in water; miscible with alcohol, and with fatty and essential oils. Store under nitrogen in airtight containers at a temperature of 2° to 8°. Protect from light.

USNF 26 (Benzyl Alcohol). A clear, colourless, oily liquid. Sparingly soluble in water; freely soluble in alcohol (50%); miscible with alcohol, with chloroform, and with ether. It is neutral to litmus.

Incompatibility. Benzyl alcohol is incompatible with oxidising agents and strong acids. The antimicrobial activity may be reduced by nonionic surfactants and benzyl alcohol may be lost from solutions stored in polyethylene containers.

Stability. Benzyl alcohol oxidises to produce benzaldehyde and benzoic acid and oxidation may take place slowly on exposure to air. Benzaldehyde may also be produced on autoclaving.

Adverse Effects and Precautions

There have been a few reports of hypersensitivity reactions to benzyl alcohol when used as a preservative.

The pure alcohol is irritant and requires handling with care; ingestion or inhalation can cause nausea, vomiting, diarrhoea, headache, and vertigo. Overexposure results in respiratory failure and CNS depression. However, concentrations of benzyl alcohol normally used for preservation are not associated with such effects.

There have been some instances of neurotoxic effects in patients given intrathecal injections that contained benzyl alcohol.

A fatal toxic syndrome in premature infants was attributed to benzyl alcohol present as a preservative in solutions used to flush intravenous catheters. This has led to restriction on the use of benzyl alcohol in neonates and young children, (see below).

Effects on the lungs. Severe bronchitis and haemoptysis was reported in a patient with obstructive pulmonary disease who, over a period of 2 years, had inhaled salbutamol nebuliser solution diluted with a bacteriostatic sodium chloride solution containing benzyl alcohol.¹

1. Reynolds RD. Nebulizer bronchitis induced by bacteriostatic saline. *JAMA* 1990; **264**: 35.

Effects on the nervous system. Rapid development of flaccid areflexic paraplegia, total anaesthesia below the groin, and radicular abdominal pain occurred in a 64-year-old man after a lumbar intrathecal injection of cytarabine that contained 1.5% benzyl alcohol.¹ The patient recovered fully after 100 mL of CSF was replaced with sodium chloride 0.9% and 40 mg of methylprednisolone. Intrathecal injections of cytarabine dissolved in sterile distilled water before and after the episode of paraplegia caused no neurologic symptoms. On reviewing 20 other cases of paraparesis associated with methotrexate or cytarabine intrathecal injections, benzyl alcohol had been used as a preservative in