water and in alcohol; slightly soluble in glycerol and in liquid paraffin. A 1% solution in water has a pH of 5.0 to 7.0. Protect from light.

Incompatibility. The activity of bronopol can be reduced by sodium metabisulfite, sodium thiosulfate, cysteine hydrochloride, and compounds with a thiol group. Incompatibility with unprotected aluminium affects packaging.

Stability. The stability of bronopol is affected by increases in temperature and by increases in pH above 8.

Creams and shampoos containing bronopol 0.01% as a preservative were found to contain free nitrite and, as a result of amines present in the preparations, nitrosamines.[1] It was recommended that nitrosamine formation could be reduced in preparations containing amines and bronopol by limiting the bronopol concentration to 0.01% and inclusion of alpha tocopherol 0.2% or butylated hydroxytoluene 0.05%.

1. Dunnett PC, Telling GM. Study of the fate of bronopol and the effects of antioxidants on N-nitrosamine formation in shampoos and skin creams. *Int J Cosmet Sci* 1984; **6:** 241–7.

Adverse Effects
Bronopol may be irritant when applied topically and cases of contact dermatitis have been reported.

Pharmacokinetics
Bronopol is absorbed following topical use.

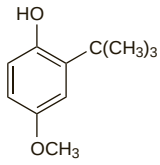
Uses
Bronopol is active against a wide range of bacteria, including *Pseudomonas aeruginosa*, but is less active against moulds and yeasts. Bronopol is used as a preservative in shampoos, cosmetics, and both topical and oral pharmaceutical preparations; concentrations in pharmaceutical preparations range from 0.01 to 0.1%, with the usual concentration being 0.02%. It is also used for its antimicrobial properties in various industrial applications, including in air conditioning systems.

Butylated Hydroxyanisole *(BAN)*

BHA; Butilhidroksianizolas; Butilhidroxianisol; Butil-hidroxianizol; Butilidrossianisolo; Butylhydroxianisol; Butylhydroxyanisol; Butylhydroxyanisole; Butylhydroxyanisolum; Butylohydroksyanizol; Butyylihydroksianisoli; E320. 2-*tert*-Butyl-4-methoxyphenol; 2-(1,1-dimethylethyl)-4-methoxyphenol.

$C_{11}H_{16}O_2$ = 180.2.

CAS — 25013-16-5.



Pharmacopoeias. In *Eur.* (see p.vii) and *Int.* Also in *USNF.*
Ph. Eur. 6.2 (Butylhydroxyanisole; Butylated Hydroxyanisole BP 2008). A white, yellowish, or slightly pinkish, crystalline powder. It contains not more than 10% of 3-(1,1-dimethylethyl)-4-methoxyphenol. Practically insoluble in water; freely soluble in alcohol and in fatty oils; very soluble in dichloromethane; it dissolves in dilute solutions of alkali hydroxides. Protect from light.
USNF 26 (Butylated Hydroxyanisole). A white, or slightly yellow, waxy solid with a faint characteristic odour. Insoluble in water; soluble 1 in 4 of alcohol, 1 in 2 of chloroform, and 1 in 1.2 of ether; freely soluble in propylene glycol.

Incompatibility. Butylated hydroxyanisole is incompatible with oxidising agents and ferric salts. Traces of metals can cause loss of activity.

Adverse Effects
Butylated hydroxyanisole can be irritant to the eyes, skin, and mucous membranes and can cause depigmentation. There are also reports of contact urticaria.

Carcinogenicity. There has been concern as to whether butylated hydroxyanisole may be a carcinogen.[1,2] These concerns stem from a study in which *rodents* given food containing 1 to 2% butylated hydroxyanisole developed squamous cell carcinoma of the forestomach. No similar malignancies were found in studies with *animals* that do not have a forestomach. The International Agency for Research on Cancer has concluded[2] that there is sufficient evidence for the carcinogenicity of butylated hydroxyanisole in *animals* but that there is no data on its carcinogenicity in humans.

1. FAO/WHO. Evaluation of certain food additives and contaminants: thirty-third report of the joint FAO/WHO expert committee on food additives. *WHO Tech Rep Ser 776* 1989. Available at: http://libdoc.who.int/trs/WHO_TRS_776.pdf (accessed 27/08/08)
2. IARC/WHO. Some naturally occurring and synthetic food components, furocoumarins and ultraviolet radiation. *IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans volume 40* 1986. Available at: http://monographs.iarc.fr/ENG/Monographs/vol40/volume40.pdf (accessed 23/05/06)

Effects on the blood. For a report of methaemoglobinaemia associated with the antoxidants (butylated hydroxyanisole, butylated hydroxytoluene, and propyl gallate) used to preserve the oil in a soybean infant feed, see under Adverse Effects in Alkyl Gallates (p.1628).

Pharmacokinetics
Butylated hydroxyanisole is absorbed from the gastrointestinal tract, then metabolised and conjugated, and excreted in the urine; less than 1% is excreted in the urine as unchanged drug within 24 hours of ingestion.

Uses
Butylated hydroxyanisole is an antoxidant with some antimicrobial activity. It is used as a preservative in cosmetics and foods as well as pharmaceutical preparations, particularly to delay or prevent oxidative rancidity of fats and oils in concentrations of up to 0.02%; higher concentrations have been used for essential oils. It is also used to prevent the loss of activity of oil-soluble vitamins. To improve efficacy, butylated hydroxyanisole is frequently used with other antoxidants such as butylated hydroxytoluene or an alkyl gallate and with sequestrants or synergists such as citric acid.

Commercial supplies of butylated hydroxyanisole used in food technology consist of mixtures of the 2-*tert* and 3-*tert* isomers.

Use in food. In the UK the Food Advisory Committee has recommended that the use of butylated hydroxyanisole and butylated hydroxytoluene should no longer be permitted as additives for infant formulas as they are no longer required for the economic manufacture of vitamin A and vitamin A esters.[1]

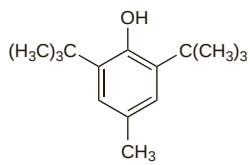
1. MAFF. Food Advisory Committee: report on the review of the use of additives in foods specially prepared for infants and young children. *FdAC/REP/12.* London: HMSO, 1992.

Butylated Hydroxytoluene *(BAN)*

BHT; Butilhidroksitoluenas; Butilhidroxitolueno; Butil-hidroxitoluol; Butylhydroxitoluen; Butylhydroxitoluenum; Butylhydroxytoluen; Butylhydroxytoluène; Butylhydroxytoluene; Butylhydroxytoluenum; Butylohydroksytoluen; Butyylihydroksitolueeni; E321. 2,6-Di-*tert*-butyl-*p*-cresol.

$C_{15}H_{24}O$ = 220.4.

CAS — 128-37-0.



Pharmacopoeias. In *Eur.* (see p.vii) and *Int.* Also in *USNF.*
Ph. Eur. 6.2 (Butylhydroxytoluene; Butylated Hydroxytoluene BP 2008). A white or yellowish-white, crystalline powder. F.p. 69° to 70°. Practically insoluble in water; freely soluble in alcohol and in vegetable oils; very soluble in acetone.
USNF 26 (Butylated Hydroxytoluene). A white crystalline solid with a faint characteristic odour. Insoluble in water and in propylene glycol; soluble 1 in 4 of alcohol and 1 in 1.1 of chloroform and of ether.

Incompatibility. Butylated hydroxytoluene is incompatible with oxidising agents and ferric salts. Traces of metals can cause loss of activity.

Adverse Effects
As for Butylated Hydroxyanisole, p.1633.

Effects on the blood. For a report of methaemoglobinaemia associated with the antoxidants (butylated hydroxyanisole, butylated hydroxytoluene, and propyl gallate) used to preserve the oil in a soybean infant feed formula, see under Adverse Effects in Alkyl Gallates, p.1628.

Poisoning. A 22-year-old woman experienced severe epigastric cramping, nausea and vomiting, and generalised weakness, followed by dizziness, confusion, and a brief loss of consciousness after ingesting 4 g of butylated hydroxytoluene. She recovered after conservative treatment, which was given 2 days later. The antoxidant had been taken as an unauthorised remedy for genital herpes simplex.[1]

1. Shlian DM, Goldstone J. Toxicity of butylated hydroxytoluene. *N Engl J Med* 1986; **314:** 648–9.

Pharmacokinetics
Butylated hydroxytoluene is readily absorbed from the gastrointestinal tract. It is excreted in the urine mainly as glucuronide conjugates of oxidation products.

Uses
Butylated hydroxytoluene is an antoxidant with uses similar to those of Butylated Hydroxyanisole, p.1633.

Preparations
Proprietary Preparations (details are given in Part 3)
Belg.: Proseptine-Plus.
Multi-ingredient: ***Fr.:*** Cinq sur Cinq.

Cadexomer-Iodine *(BAN)*

Cadexomer Iodine *(USAN)*; Cadexomerjod; Cadexómero yodado; Cadexomerum Iodum; Kadeksomeerijodi. 2-Hydroxymethylene cross-linked (1→4)-α-D-glucan carboxymethyl ether containing iodine.

CAS — 94820-09-4.
ATC — D03AX01.
ATC Vet — QD03AX01.

Adverse Effects and Precautions
As for Povidone-Iodine, p.1659. Some patients have experienced stinging and erythema on application of cadexomer-iodine to their ulcers. Free iodine is released during exposure of cadexomer-iodine preparations to wound exudate and absorption of iodine may occur. Prolonged treatment with cadexomer-iodine should be given with caution in patients with thyroid disorders.

Uses and Administration
Cadexomer-iodine, like povidone-iodine (p.1659), is an iodophore that releases iodine. It is used for its absorbent and antiseptic properties in the management of venous leg ulcers and pressure sores. It is applied as a powder, ointment, or paste containing iodine 0.9%; sufficient powder or ointment should be applied to form a layer about 3 mm thick. Treatment should not usually be continued for more than 3 months.

Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: Iodosorb†; ***Austria:*** Iodosorb; ***Canad.:*** Iodosorb; ***Denm.:*** Iodosorb; ***Fin.:*** Iodosorb; ***Fr.:*** Iodosorb†; ***Ger.:*** Iodosorb†; ***Gr.:*** Iodosorb; ***Irl.:*** Iodoflex; ***Ital.:*** Iodosorb; ***Neth.:*** Iodosorb; ***Singapore:*** Iodoflex; Iodosorb; ***Spain:*** Iodosorb†; ***Swed.:*** Iodosorb; ***Switz.:*** Iodosorb; ***UK:*** Iodoflex; Iodosorb.

Calcium Peroxide

Calcium Dioxide; E930.

Пероксид Кальция

CaO_2 = 72.08.

CAS — 1305-79-9;.

Profile
The action of calcium peroxide is similar to that of hydrogen peroxide (p.1647). Calcium peroxide is used in dental products for tooth whitening. It is also used as a flour bleaching and improving agent.

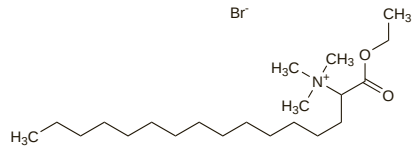
Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Arg.:*** Hexiben.

Carbaethopendecinium Bromide

Carbethopendecinii Bromidum; Carbethoxypentadecyltrimethylammonium Bromide; Karbethopendecinium bromid. 1-Ethoxy-*N,N,N*-trimethyl-1-oxo-2-hexadecanaminium bromide.

$C_{21}H_{44}NO_2Br$ = 422.5.

CAS — 10567-02-9.



Profile
Carbaethopendecinium bromide is a quaternary ammonium antiseptic with actions and uses similar to those of other cationic surfactants (see Cetrimide, p.1634). It is used in topical preparations for disinfection of skin and mucous membranes.

Preparations
Proprietary Preparations (details are given in Part 3)
Cz.: Mukoseptonex; Ophthalmo-Septonex; Septonex.
Multi-ingredient: ***Cz.:*** Mesocain; Mukoseptonex E; N-Septonex†; Ophthalmo-Septonex; Paradentol†; Septonex; Septonex Plus; Triamcinolon-Ivax.