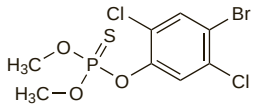
Bromophos

Bromofós; Bromofos; OMS-658. *O*-4-Bromo-2,5-dichlorophenyl *O,O*-dimethyl phosphorothioate.

$C_8H_8BrCl_2O_3PS$ = 366.0.

CAS — 2104-96-3.

ATC Vet — QP53AF11.



Profile

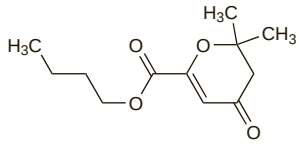
Bromophos is an organophosphorus insecticide (p.2047) used in veterinary practice for the control of ectoparasites in the environment. It has also been used as an agricultural insecticide.

Butopyronoxyl

Butopiroxinilo; Indalone. Butyl 3,4-dihydro-2,2-dimethyl-4-oxo-2*H*-pyran-6-carboxylate.

$C_{12}H_{18}O_4$ = 226.3.

CAS — 532-34-3.



Profile

Butopyronoxyl has been used as an insect repellent.

Carbamate Insecticides

Insecticidas del grupo de los carbamatos.

Description. The carbamate insecticides are *N*-substituted esters of carbamic acid.

◊ References.

1. WHO. Carbamate pesticides: a general introduction. *Environmental Health Criteria 64*. Geneva: WHO, 1986. Available at: http://www.inchem.org/documents/ehc/ehc/ehc64.htm (accessed 24/07/08)

Adverse Effects

As for Organophosphorus Insecticides, p.2047.

The carbamates are cholinesterase inhibitors, differing from the organophosphorus insecticides in that the inhibition they produce is generally less intense and more rapidly reversible. In addition, they do not appear to enter the CNS as readily and severe central effects are therefore uncommon.

Treatment of Adverse Effects

If substantial amounts of carbamate insecticides have been ingested the use of gastric lavage should be considered if the patient presents within 1 hour. Contaminated clothing should be removed and the skin washed with soap and water. Treatment is largely symptomatic and supportive and includes atropine, but this may not always be necessary due to the rapidly reversible nature of the cholinesterase inhibition produced. Pralidoxime is thought to be generally unnecessary; some *animal* studies have suggested that it may increase the toxicity of carbamates.

◊ References.

1. WHO. Safe use of pesticides: fourteenth report of the WHO expert committee on vector biology and control. *WHO Tech Rep Ser 813* 1991. Available at: http://libdoc.who.int/trs/WHO_TRS_813.pdf (accessed 21/07/08)
2. Proudfoot A, ed. *Pesticide poisoning: notes for the guidance of medical practitioners*. 2nd ed. London: DoH, The Stationery Office, 1996.

Carbaryl *(BAN)*

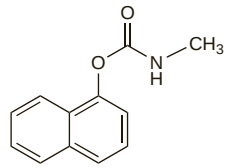
Carbaril *(pINN)*; Carbarilo; Carbarilum; Karbaril; OMS-29. 1-Naphthyl methylcarbamate.

Карбарил

$C_{12}H_{11}NO_2$ = 201.2.

CAS — 63-25-2.

ATC Vet — QP53AE01.



Pharmacopoeias. In *Br.*

BP 2008 (Carbaryl). A white to off-white or light grey powder which darkens on exposure to light. Very slightly soluble in water; soluble in alcohol and in acetone. Store at a temperature not exceeding 25°. Protect from light.

Adverse Effects and Treatment

As for Carbamate Insecticides, above. Carbaryl may be absorbed after ingestion, inhalation, or skin contamination.

Carbaryl has been reported to produce neoplasms in *mice* and *rats* and in late 1995 the UK DoH advised that it would be prudent to consider carbaryl as a potential human carcinogen; its medicinal use was limited to prescription only. However, the DoH emphasised that the risk was a theoretical one and that any risk from the intermittent use of head lice preparations was likely to be very small.

Uses and Administration

Carbaryl is a carbamate insecticide (above). It is used as a 0.5 or 1.0% lotion or shampoo in the treatment of head and pubic pediculosis (p.2034). Lotions are generally preferred to shampoos as the contact time is longer. Aqueous lotions are preferred to treat pubic lice because alcoholic lotions are irritant to excoriated skin and the genitalia; aqueous lotions may also be preferable in asthmatic subjects or children to avoid alcoholic fumes. Skin or hair treated with an alcohol-based preparation should be allowed to dry naturally.

Carbaryl is also used as a topical ectoparasiticide in veterinary practice and as an agricultural, horticultural, and household insecticide.

◊ References.

1. WHO. Carbaryl health and safety guide. *IPCS Health and Safety Guide 78*. Geneva: WHO, 1993. Available at: http://www.inchem.org/documents/hsg/hsg/hsg78_e.htm (accessed 23/04/04)
2. WHO. Carbaryl. *Environmental Health Criteria 153*. Geneva: WHO, 1994. Available at: http://www.inchem.org/documents/ehc/ehc/ehc153.htm (accessed 23/04/04)

Preparations

BP 2008: Carbaryl Lotion.

Proprietary Preparations (details are given in Part 3)

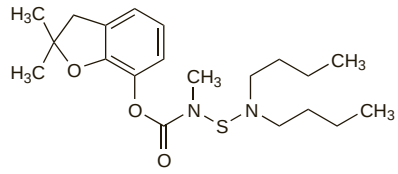
Israel: Hafif; ***UK:*** Carylderm.

Carbosulfan

Carbosulfán. 2,3-Dihydro-2,2-dimethylbenzofuran-7-yl (dibutylaminothio)methylcarbamate.

$C_{20}H_{32}N_2O_3S$ = 380.5.

CAS — 55285-14-8.



Profile

Carbosulfan is a carbamate insecticide (p.2037) used in agriculture and for the larvicidal treatment of rivers in the control of onchocerciasis (p.137).

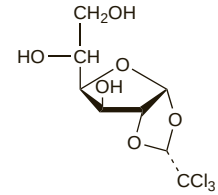
Chloralose *(rINN)*

Alphachloralose; Chloralosane; α-Chloralose; Chloralosum; Cloralosa; Glucochloral. (*R*)-1,2-*O*-(2,2,2-Trichloroethylidene)-α-D-glucofuranose.

Хлоралоза

$C_8H_{11}Cl_3O_6$ = 309.5.

CAS — 15879-93-3.



Profile

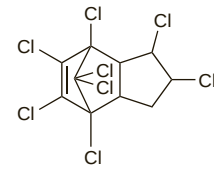
Chloralose has general properties similar to those of cloral hydrate (p.979), of which it is a derivative. It is used as a rodenticide. It was formerly used for its hypnotic properties.

Chlordane

Chlordan; Clordano. 1,2,4,5,6,7,8,8-Octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene.

$C_{10}H_6Cl_8$ = 409.8.

CAS — 57-74-9.



Profile

Chlordane is a chlorinated insecticide (p.2037). Its use is limited, or even prohibited, in some countries because of toxicity due to its persistent nature.

◊ References.

1. Kutz FW, *et al.* A fatal chlordane poisoning. *J Toxicol Clin Toxicol* 1983; **20:** 167–74.
2. Olanoff LS, *et al.* Acute chlordane intoxication. *J Toxicol Clin Toxicol* 1983; **20:** 291–306.
3. WHO. Chlordane. *Environmental Health Criteria 34*. Geneva: WHO, 1984. Available at: http://www.inchem.org/documents/ehc/ehc/ehc34.htm (accessed 23/04/04)
4. WHO. Chlordane health and safety guide. *IPCS Health and Safety Guide 13*. Geneva: WHO, 1988. Available at: http://www.inchem.org/documents/hsg/hsg/hsg013.htm (accessed 23/04/04)

Chlorinated Insecticides

Insecticidas clorados.

Adverse Effects

Chlorinated or organochlorine insecticides form a very wide group and the toxicity of individual members varies considerably. In general these insecticides produce symptoms consistent with CNS stimulation. They may be absorbed through the respiratory and gastrointestinal tracts and through the skin.

Symptoms of acute poisoning include nausea and vomiting, paraesthesia, giddiness, tremors, convulsions, coma, and respiratory failure. Liver, kidney, and myocardial toxicity have been reported. Effects on the blood include agranulocytosis and aplastic anaemia. Symptoms may be complicated by the effects of the solvent.

Chlorinated insecticides have been reported to enhance microsomal hepatic enzyme activity. Skin reactions can occur after contact.

Polychlorinated biphenyl (PCB) and terphenyl compounds were formerly used as insecticides in many countries. They accumulate in body fat and are not readily excreted, although they are distributed into breast milk and possibly cross the placenta; because of this and because of accidental contamination they remain a cause for concern. The related polybrominated biphenyl compounds (PBB), which have no insecticidal uses, have also been absorbed by humans after accidental contamination of the food chain.

Some chlorinated insecticides have weak oestrogenic effects; it has been proposed that exposure may increase the risk of breast cancer.

Treatment of Adverse Effects

If chlorinated insecticides have been ingested gastric lavage or activated charcoal may be considered if the patient presents within 1 hour. Contaminated clothing should be removed and the skin washed with soap and water. Treatment is largely symptomatic

and supportive with treatment of CNS stimulation such as hyperactivity and convulsions.

◊ References.

1. WHO. Safe use of pesticides: fourteenth report of the WHO expert committee on vector biology and control. *WHO Tech Rep Ser 813* 1991. Available at: http://libdoc.who.int/trs/WHO_TRS_813.pdf (accessed 24/07/08)
2. Proudfoot A, ed. Pesticide poisoning: notes for the guidance of medical practitioners. 2nd ed. London: DoH, The Stationery Office, 1996.

Uses
The chlorinated or organochlorine insecticides were widely used but, because of persistence in man, many have been banned or restricted.

◊ References.

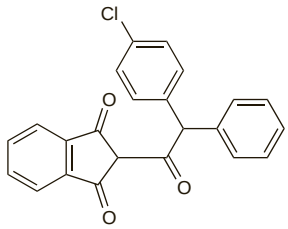
1. WHO. Polychlorinated biphenyls and terphenyls. *Environmental Health Criteria 140*. Geneva: WHO, 1992. Available at: http://www.inchem.org/documents/ehc/ehc/ehc140.htm (accessed 28/05/04)
2. WHO. Polychlorinated biphenyls and polychlorinated terphenyls (PCBs and PCTs) health and safety guide. *IPCS Health and Safety Guide 68*. Geneva: WHO, 1992. Available at: http://www.inchem.org/documents/hsg/hsg/hsg68.htm (accessed 28/05/04)

Chlorophacinone

Clorofacinona; LM-91. 2-[2-(4-Chlorophenyl)-2-phenylacetyl]indane-1,3-dione.

$C_{23}H_{15}ClO_3$ = 374.8.

CAS — 3691-35-8.



Profile
Chlorophacinone is an indanedione derivative used as an anticoagulant rodenticide. It is also reported to uncouple oxidative phosphorylation with consequent stimulation of cellular metabolism which may contribute to its toxicity.

◊ References.

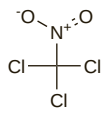
1. Burucoa C, *et al.* Chlorophacinone intoxication: biological and toxicological study. *J Toxicol Clin Toxicol* 1989; **27:** 79–89.
2. WHO. Anticoagulant rodenticides. *Environmental Health Criteria 175*. Geneva: WHO, 1995. Available at: http://www.inchem.org/documents/ehc/ehc/ehc175.htm (accessed 28/05/04)
3. Lagrange F, *et al.* Toxicological management of chlorophacinone poisoning. *Acta Clin Belg Suppl* 1999; **1:** 13–16.
4. Papin F, *et al.* Lethal paradoxical cerebral vein thrombosis due to suspicious anticoagulant rodenticide intoxication with chlorophacinone. *Forensic Sci Int* 2007; **166:** 85–90.

Chloropicrin

Cloropicrina; Nitrochloroform. Trichloronitromethane.

CCl_3NO_2 = 164.4.

CAS — 76-06-2.



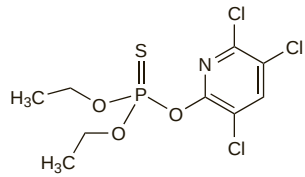
Profile
Chloropicrin is a lachrymatory agent with an intense odour. It is intensely irritating to the skin and mucous membranes. It is an insecticide and is used for fumigating stored grain and soil. Chloropicrin is also added to other fumigants as a warning gas.

Chlorpyrifos *(BAN)*

Clorpirifós. *O,O*-Diethyl *O*-3,5,6-trichloro-2-pyridyl phosphorothioate.

$C_9H_{11}Cl_3NO_3PS$ = 350.6.

CAS — 2921-88-2.



Profile
Chlorpyrifos is an organophosphorus insecticide (p.2047) used in agriculture.

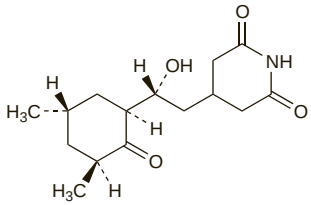
Cycloheximide *(rINN)*

Cicloheximida; Cicloheximidum; Cycloheximide *(USAN)*; U-4527. 3-{(2*R*)-2-[(1*S*,3*S*,5*S*)-3,5-Dimethyl-2-oxocyclohexyl]-2-hydroxyethyl}glutarimide.

Циклогексимид

$C_{15}H_{23}NO_4$ = 281.3.

CAS — 66-81-9.



Profile
Cycloheximide is an antimicrobial substance produced by strains of *Streptomyces griseus*. It has antifungal properties and has been used for the treatment and control of certain mycotic plant diseases.

Clofenotane *(rINN)*

Clorofenotano; Chlorophenothane; Chlorphenothanum; Cloféнotane; Clofenotano; Clofenotanum; DDT; Dichlorodiphenyltrichloroethane; Dichophanum; Dicophane; Klofenotaani; Klofenotan. 1,1,1-Trichloro-2,2-bis(4-chlorophenyl)ethane.

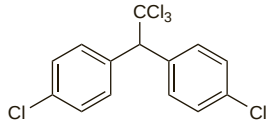
Клофенотан

$C_{14}H_9Cl_5$ = 354.5.

CAS — 50-29-3.

ATC — P03AB01.

ATC Vet — QP53AB01.



Pharmacopoeias. In *It.*

Adverse Effects and Treatment
As for Chlorinated Insecticides, p.2037.

◊ References.

1. WHO. DDT and its derivatives. *Environmental Health Criteria 9*. Geneva: WHO, 1979. Available at: http://www.inchem.org/documents/ehc/ehc/ehc009.htm (accessed 28/05/04)
2. WHO. DDT and its derivatives—environmental aspects. *Environmental Health Criteria 83*. Geneva: WHO, 1989. Available at: http://www.inchem.org/documents/ehc/ehc/ehc83.htm (accessed 28/05/04)

Carcinogenicity. Some small epidemiological studies have suggested that certain organochlorines, namely 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (DDE), a metabolite of clofenotane, and polychlorinated biphenyls (PCBs), might increase the risk of breast cancer in women. However, re-analysis[1,2] of the available data indicated that an association with breast cancer was unlikely for clofenotane; there was no evidence for an association with the PCBs. Any link between exposure to clofenotane and the development of testicular cancer in men was also refuted[3] after long-term monitoring of populations in Scandinavia.

1. Key T, Reeves G. Organochlorines in the environment and breast cancer. *BMJ* 1994; **308:** 1520–1.
2. van't Veer P, *et al.* DDT (dicophane) and postmenopausal breast cancer in Europe: case-control study. *BMJ* 1997; **315:** 81–5.
3. Ekbom A, *et al.* DDT and testicular cancer. *Lancet* 1996; **347:** 553–4.

Effects on fertility. A metabolite of clofenotane, 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (DDE), was reported[1] to have anti-androgenic properties in *rats* and exposure to clofenotane might account for a previously reported decline in male fertility and an increase in male reproductive abnormalities.

1. Keke WR, *et al.* Persistent DDT metabolite p,p′-DDE is a potent androgen receptor antagonist. *Nature* 1995; **375:** 581–5.

Effects on the nervous system. A retrospective study[1] found that retired malaria workers exposed long-term to clofenotane did less well in neurobehavioural tests than a control group, and had an increase in neuropsychological and psychiatric symptoms.

1. van Wendel de Joode B, *et al.* Chronic nervous-system effects of long-term occupational exposure to DDT. *Lancet* 2001; **357:** 1014–16.

Pregnancy. In a large prospective study[1] of children born between 1959 and 1966, an association was found between preterm births and small-for-gestational-age babies, and maternal concentrations of a metabolite of clofenotane, 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (DDE) measured in serum samples which had been stored during pregnancy.

1. Longnecker MP, *et al.* Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth. *Lancet* 2001; **358:** 110–14.

Pharmacokinetics
Clofenotane may be absorbed after ingestion or inhalation or through the skin. Clofenotane is stored in the body, particularly in body fat, and is very slowly eliminated. It crosses the placenta and appears in breast milk. It is metabolised in the body to the ethylene derivative, 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (DDE); the acetic acid derivative (DDA) also appears in the urine.

Uses
Clofenotane is a chlorinated insecticide (p.2037). It is a stomach and contact poison and retains its activity for long periods under a variety of conditions. It is effective against disease vectors such as fleas, lice, and mosquitoes and has been applied topically for pediculosis (p.2034) and scabies (p.2035), although more suitable alternatives exist.

Because of the extreme persistence of clofenotane, concern over its effect in the environment, and the problem of resistance, the widespread use of clofenotane is now generally discouraged. It is no longer used in some countries while in others its use is limited.

◊ Despite reservations regarding the use of clofenotane for vector control, many countries have relied on it for the control of both malaria and visceral leishmaniasis. WHO has concluded[1,2] that clofenotane might be used provided:

- that it was used only for indoor spraying
- that it was known to be effective
- that it was manufactured to WHO's specifications
- that the necessary safety precautions were taken in its use and disposal

However, they recommended further investigation of the effects of clofenotane in breast milk and of suspected carcinogenicity, as well as clarification of the significance of the reduced density of muscarinic receptors caused by clofenotane.

1. WHO. WHO expert committee on malaria: twentieth report. *WHO Tech Rep Ser 892* 2000. Available at: http://libdoc.who.int/trs/WHO_TRS_892.pdf (accessed 21/07/08)
2. WHO Global Malaria Programme. Indoor residual spraying: use of indoor residual spraying for scaling up global malaria control and elimination 2006. Available at: http://malaria.who.int/docs/IRS-position.pdf (accessed 21/04/08)

Preparations
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: *Ital.:* Antiscabbia Candioli al DDT Terapeutico.

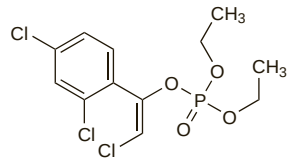
Clofenvinfos *(BAN, rINN)*

Chlorfenvinphos; Chlorofenwinfos; Clofenvinfós; Clofenvinfosum. 2-Chloro-1-(2,4-dichlorophenyl)vinyl diethyl phosphate.

Клофенвинфос

$C_{12}H_{14}Cl_3O_4P$ = 359.6.

CAS — 470-90-6.



Profile
Clofenvinfos is an organophosphorus insecticide (p.2047) used in agriculture.