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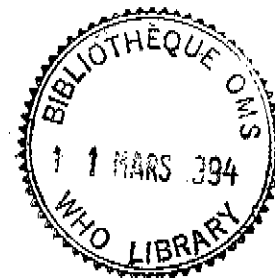
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WHO/FAO DATA SHEET ON PESTICIDES

No. 76

BROMOPHOS

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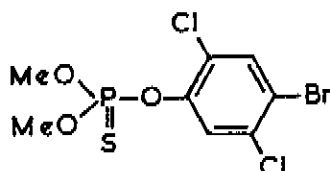
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CLASSIFICATION:

Primary use: Insecticide
 Secondary use: Acaricide
 Chemical group: Organophosphorus compound

1.0 GENERAL INFORMATION**1.1 COMMON NAME:** bromophos (ISO)**1.1.1 Identity**

IUPAC chemical name: O-4-bromo-2,5-dichlorophenyl O,O-dimethyl phosphorothioate.
CAS chemical name: O-(4-bromo-2,5-dichlorophenyl) O,O-dimethyl phosphorothioate.
CAS registry number: 2104-96-3
RTECS number: TE7175000
Molecular formula: C₈H₈BrCl₂O₃PS
Relative molecular mass: 366.0
Structural formula:



Synonyms and tradenames : Bromofos; Brofene^R; Brophene^R; CELA-1942; ENT-27162; Nexion^R; Omexan; OMS-658; S-1942; SHG-1942.

1.2 SYNOPSIS: Bromophos is a broad spectrum, non-cumulative non-systemic organophosphorus insecticide. It is a cholinesterase inhibitor with contact and stomach action, having slight toxicity to mammals, fish and bees. Bromophos is listed in the WHO Recommended Classification of Pesticides by Hazard under class III, "Slightly hazardous".

1.3 SELECTED PROPERTIES

- 1.3.1 Physical characteristics:** Bromophos consists of yellowish crystals with a melting point of 53 °C. It has a boiling point of 140-142 °C. The technical product is 95% pure.
- 1.3.2 Solubility:** In water, solubility is 40 mg/L at 27 °C and it is soluble in most organic solvents.
- 1.3.3 Stability:** Bromophos is stable in aqueous suspension up to pH 9 but it hydrolyses in a stronger alkaline medium.
- 1.3.4 Vapour pressure:** 17 mPa (20 °C).

1.4 AGRICULTURE, HORTICULTURE AND FORESTRY

- 1.4.1 **Common formulations:** These include emulsifiable concentrates of 250 and 400 g a.i./L; wettable powder, 250 g/kg; dusts, 20-50 g/kg; granules, 50-100 g/kg; atomising concentrate, 400 g/L; dip 200 g/L; and coarse powder, 30 g/kg.
- 1.4.2 **Susceptible pests:** Active against *Hemiptera*, *Diptera*, certain *Lepidoptera*, *Coleoptera* and other insects.
- 1.4.3 **Use pattern:** Used at a concentration of 250-1500 g a.i./ha on field, vegetable and fruit crops as well as ornamentals and grain storage. Also used as a sheep dip.
- 1.4.4 **Unintended effects:** Bromophos is not recommended for use on cotton or grapes. Injury has been reported on varieties of cabbage, pears and ornamentals.

1.5 PUBLIC HEALTH USE:

- 1.5.1 **Common formulation:** See section 1.4.1.
- 1.5.2 **Pests controlled:** See section 1.4.2.
- 1.5.3 **Use pattern:** Used in the control of flies and mosquitos at 0.5 g/m².
- 1.5.4 **Unintended effects:** None reported.

1.6 **HOUSEHOLD USE:** No recommended usage reported.

2.0 TOXICOLOGY AND RISKS

2.1 TOXICOLOGY - MAMMALS

- 2.1.1 **Absorption:** Bromophos may be absorbed through intact skin as well as by the respiratory and gastrointestinal tracts.
- 2.1.2 **Mode of action:** Bromophos is an indirect inhibitor of cholinesterase through phosphorylation of the esteratic site of the enzyme. Accumulation of acetylcholine at nerve synapses and myoneural junctions causes the toxic effects.
- 2.1.3 **Excretion products:** Bromophos is excreted rapidly via the urine, the major metabolites found are dichloro-bromophenol and monodesmethyl bromophos. Extremely low levels of bromoxon may also occur in blood. Approximately 63% of a 10 mg/kg oral dose of bromophos was excreted in urine and 16% in faeces over a 24 hour period.
- 2.1.4 **Toxicity, single dose:**

Oral LD₅₀

Rat (M,F)	3750 - 6100 mg/kg b.w.
Rat (M,F)	1600-1730 mg/kg b.w.
Mouse	2829-5850 mg/kg b.w.
Guinea pig	1500 mg/kg b.w.
Rabbit	720 mg/kg b.w.

Dermal LD₅₀

Rat (M, F)	5000 mg/kg b.w.
Rabbit	2181 mg/kg b.w. (scarified skin)

Intraperitoneal LD₅₀

Rat	1625-3125 mg/kg b.w.
Mouse	1040 mg/kg b.w.

2.1.5 **Toxicity, repeated dose:** Rats given bromophos by gavage at doses from 188 to 1250 mg/kg b.w. for 100 days displayed signs of poisoning for approximately one hour after each administration. Observed compound related adverse effects were: depression of body weights, depressed food consumption at the high dose level and depression of brain, liver and plasma esterase at all doses.

2.1.6 **Dietary studies:**

Short term: Rats were fed bromophos at 0, 1500, 6000 and 10000 mg/kg/diet for a period of 100 days. Animals at the 2 higher doses showed a marked decrease in weight gain. Some minor pathological changes were observed in liver and kidney at the highest dose.

Groups of male and female beagle dogs were fed bromophos at levels of 0, 20, 80, 320 and 1280 mg/kg/diet for one year. Reduced body weight and food consumption occurred at 1280 mg/kg/diet and females in this group had less frequent oestrus. Plasma cholinesterase inhibition occurred at 80, 320, 1280 mg/kg/diet, erythrocyte cholinesterase inhibition occurred at 320 and 1280 mg/kg/diet and brain cholinesterase inhibition occurred at 1280 mg/kg/diet.

Long term: Male and female dogs were given bromophos at 11, 44 and 87.5 and 175 mg/kg/b.w./day, by gavage for two years. One dog at 87.5 mg/kg b.w. and three at 175 mg/kg b.w. died after developing respiratory difficulties, hoarseness, salivation, tremors followed by ataxia and then paresis of the hind limbs. Two other dogs at 175 mg/kg b.w. developed the same signs but recovered. Plasma, erythrocytes, liver and brain cholinesterases were depressed at all doses.

2.1.7 **Supplementary studies of toxicity:**

Carcinogenicity: Male and female rats were administered 87.5, 175 and 350 mg/kg b.w. of bromophos by gavage for two years. Cholinesterase was inhibited in plasma, erythrocytes, brain and liver at all dose levels. No tumours were reported to have occurred at any dose level.

Albino mice fed bromophos at 0, 85, 350 and 1400 mg/kg/diet for 18 months did not reveal any carcinogenic potential. Erythrocyte and brain cholinesterase inhibition occurred at 350 and 1400 mg/kg/diet.

Mutagenicity: No mutagenic activity was seen using *Drosophila melanogaster* as a test organism.

Neurotoxicity: In early studies in hens administered bromophos, either as a single oral dose of 10 g/kg b.w./day, or as 1 g/kg/day for periods of 12-56 days, incoordination and ataxia associated with demyelination were observed. These studies were considered unsatisfactory.

In later studies hens were given 5.5 g/kg b.w. over a period of 7 weeks, or 2 oral doses of 2 g/kg b.w. 3 weeks apart. No neuropathological changes were observed in the CNS or peripheral nerves.

In order to reinvestigate the paralysis described in dogs in the 2 year feeding study described under Section 2.1.6. Long term dietary studies, dogs were administered 87.5 and 175 mg/kg b.w./day orally for 270 days. An extensive neuropathological examination of the central nervous system, spinal ganglia and peripheral nerves failed to reveal any pathological changes.

Teratogenicity: Female rabbits were administered 25, 50, 100, 200 or 400 mg/kg b.w. of bromophos from day 6 to 18 of pregnancy. In no group did the type or number of malformations observed differ from that of the controls.

Reproduction: No effect was seen in a three generation study at 5 and 20 mg/kg of bromophos. At 80 mg/kg, reduced weanling weight and increased stillbirths were seen in F1a generation. In this study the cholinesterase activity of liver and plasma was significantly depressed in animals receiving five mg/kg/day. The threshold dose for erythrocyte enzyme inhibition was between 5 and 30 mg/kg/day and for brain enzyme between 5 - 30 mg/kg/day for males and 20-80 mg/kg/day for females.

- 2.1.8 **Modification of toxicity:** Potentiation of the acute toxicity of bromophos occurred with, bromophos-ethyl, diazinon, dichlorvos, dimethoate, malathion, mevinphos, naled, parathion and carbaryl.

2.2 TOXICOLOGY - MAN

- 2.2.1 **Absorption route:** Bromophos is absorbed through the intact skin as well as by the respiratory and gastrointestinal tracts.

- 2.2.2 **Dangerous doses:**

Single: Not known.

Repeated: Not known.

- 2.2.3 **Observations on occupationally exposed workers:** A group of workers applied bromophos to house interiors for malaria control, for 4 hours on one day and for 2.5 hours on the following day. No clinical effects were seen in spraymen or villagers. Spraymen plasma cholinesterase activities the day after spraying were 94.9% of the pre-exposure levels. One week after spraying villagers had plasma cholinesterase activities 92% of pre-exposure value rising to 94.4% four weeks later.

- 2.2.4 **Observations on exposure of the general population:** See section 2.2.3.

- 2.2.5 **Observations on volunteers:** The no effect level for bromophos was found to be 0.4 mg/kg b.w./day after a 28 day period of administration. At 0.8 mg/kg/b.w./day, plasma cholinesterase was inhibited.

- 2.2.6 **Reported mishaps:** No information available.

2.3 TOXICITY TO NON-MAMMALIAN SPECIES

- 2.3.1 **Birds:**

Oral LD₅₀	Chickens	9700 mg/kg
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- 2.3.2 **Fish:** Mosquito fish, at 0.5 - 1.0 mg/L, no mortality.

LC₅₀	Guppies	0.5 mg/L
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2.3.3 **Other species:** Slightly toxic to honey bees.

3.0 FOR REGULATORY AUTHORITIES - RECOMMENDATIONS ON REGULATION OF COMPOUND

3.1 RECOMMENDED RESTRICTIONS ON AVAILABILITY

[For definition of categories see the 'Introduction to Data Sheets'].

All available liquid formulations, Category 4.

All available solid formulations, Category 5.

3.2 TRANSPORT AND STORAGE

Formulations in category 4: Should be transported in clearly labelled, rigid and leakproof containers out of reach of children, away from food and drink. Storage should be under lock and key and secure from access by children and other unauthorized persons. Avoid contact with metals other than aluminium and tin.

Formulations in category 5: Should be transported and stored in clearly labelled, leakproof containers out of reach of children, away from food and drink. Avoid contact with metals other than aluminium and tin.

3.3 HANDLING

Formulations in category 4: Full protective clothing should be used by all handling the compound. Adequate washing facilities should be available at all times during handling and they should be close to the site of handling. Eating, drinking and smoking should be prohibited during handling and before washing hands and face.

Formulations in category 5: No facilities other than those needed for the handling of any chemical are required.

3.4 DISPOSAL AND/OR DECONTAMINATION OF CONTAINERS

All formulations: Containers must be decontaminated (for method see paragraph 4.3 of part 4). Decontaminated containers should not be used for food and drink. Containers that are not decontaminated should be burned or crushed and buried below topsoil (at least 0.5 m). Care must be taken to avoid subsequent contamination of water sources.

3.5 SELECTION, TRAINING AND MEDICAL SUPERVISION OF WORKERS

Formulations in category 4: Pre-employment medical examination for workers desirable. Special account should be taken of the workers' ability to comprehend and follow instructions.

Formulations in category 5: Warning of workers to minimize contact is essential.

3.6 ADDITIONAL REGULATIONS RECOMMENDED IF DISTRIBUTED BY AIRCRAFT

All formulations: Pilots and loaders should have special training in application methods and recognition of early warning symptoms of poisoning, and they must wear a suitable respirator. Flagmen should wear overalls and a broad brimmed hat and, be well away from the dropping zone.

3.7 LABELLING

Formulations in category 4 - minimum cautionary statement:

WARNING - POISON (Skull and cross bones insignia)

Bromophos is an organophosphorous compound which inhibits cholinesterase. It is of slight toxicity. Contact with the skin, inhalation of dust or spray, or swallowing may be hazardous. Wear protective gloves, clean protective clothing. Bathe immediately after work. Ensure that containers are stored under lock and key. Empty containers must be disposed of in such a way as to prevent all possibility of accidental contact with them. Keep the material out of reach of children and well away from foodstuffs, animal feed and their containers.

In case of contact, immediately remove contaminated clothing and wash the skin thoroughly with soap and water; for eyes, flush with water for 15 minutes.

If poisoning occurs, call a physician. Atropine sulphate is a pharmacological antidote. Repeated doses may be necessary. Artificial respiration may also be needed.

Formulations in category 5 - minimum cautionary statement: This formulation contains bromophos, it is poisonous if swallowed. Keep the material out of reach of children and well away from food stuffs, animal feed and food containers.

3.8 RESIDUES IN FOOD

Maximum Residue Limits (MRLs) have been recommended by the Joint FAO/WHO Meeting on Pesticide Residues. In 1977 an Acceptable Daily Intake (ADI) for bromophos was set at 0.04 mg/kg b.w.

4.0 PREVENTION OF POISONING IN MAN AND EMERGENCY AID

4.1 PRECAUTIONS IN USE

- 4.1.1 **General:** Bromophos is an organophosphorus pesticide of slight mammalian toxicity. It is readily absorbed through the intact skin, from the gastrointestinal tract, and by inhalation of dust or spray mist. Repeated exposure may have a cumulative effect on acetylcholinesterase activity.
- 4.1.2 **Manufacture and formulation - TLV:** Closed systems and forced ventilation may be required to reduce as much as possible the exposure of workers to the chemical.
- 4.1.3 **Mixers and applicators:** When opening the container and when mixing, protective impermeable boots, clean overalls, gloves and a suitable respirator should be worn. Mixing, if not mechanical, should always be carried out with a paddle of appropriate length. When spraying tall crops or during aerial application, a face mask should be worn, as well as an impermeable hood, clothing, boots, and gloves. The applicator should avoid working in spray mist and avoid contact with the mouth. Particular care is needed when equipment is being washed after use. All protective clothing should be washed separately from other laundry immediately after use, including the insides of gloves. Splashes must be washed immediately from the skin, or eyes with large quantities of water. Before eating, drinking, or smoking, hands and other exposed skin should be washed.

4.1.4 **Other associated workers:** Persons exposed to bromophos and associated with its application should wear protective clothing and observe the precautions described above in 4.1.3. under "Mixers and Applicators".

4.1.5 **Other populations likely to be affected:** With good application practice subject to 4.2 below, other persons are not likely to be exposed to hazardous amounts of bromophos.

4.2 ENTRY OF PERSONS INTO TREATED AREAS

Unprotected persons should be kept out of tall crops for four days and out of other crops for 24 hours.

4.3 DECONTAMINATION OF SPILLAGE AND CONTAINERS

Residues in containers should be emptied in a diluted form into a deep dry pit (depth >0.5 m) taking care to avoid contamination of ground waters. The empty container may be decontaminated by rinsing two or three times with water and scrubbing the sides. An additional rinse should be carried out with 5% sodium hydroxide solution which should remain in the container overnight. Impermeable gauntlets should be worn during this work, and a soakage pit should be provided for the rinsings. Decontaminated containers should not be used for food, feed or water storage. Spillage of bromophos and its formulations should be removed by washing with 5% sodium hydroxide solution and then rinsing with large quantities of water.

4.4 EMERGENCY AID

4.4.1 **Early symptoms of poisoning:** Early symptoms of poisoning may include excessive sweating, headache, weakness, giddiness, nausea, vomiting, increased salivation, stomach pains, blurred vision, diarrhoea, slurred speech and muscle twitching. Later there may be shortness of breath, convulsions and coma.

4.4.2 **Treatment before person is seen by physician, if these symptoms appear following exposure:** The person should stop work immediately, remove contaminated clothing and wash contaminated skin with soap and water and flush the area with large quantities of water. If swallowed, and if the person is conscious, vomiting should be induced. In the event of collapse, artificial respiration should be given bearing in mind that if mouth-to-mouth resuscitation is used, vomit may contain toxic amounts of bromophos.

5.0 FOR MEDICAL AND LABORATORY PERSONNEL

5.1 MEDICAL DIAGNOSIS AND TREATMENT IN CASES OF POISONING

5.1.1 **General information:** Bromophos is an organophosphorus pesticide of slight mammalian toxicity which is active against a variety of agricultural and public health pests. It is readily absorbed from the gastrointestinal tract, through the intact skin, and by inhalation of dust or spray mist. It is converted *in vivo* to the oxygen analogue of bromophos which inhibits acetylcholinesterase. It does not accumulate in body tissues.

- 5.1.2 **Symptoms and signs:** Symptoms of poisoning are due to excessive stimulation by acetylcholine of all cholinergic innervation. Thus initial symptoms and signs of poisoning may include excessive sweating and salivation, headache, weakness, miosis, dyspnoea, nausea, vomiting and diarrhoea, blurred vision and muscle fasciculations. More severe poisoning leads to respiratory failure due to a combination of bronchorrhea, bronchoconstriction (muscarinic effects), paralysis of respiratory muscles (nicotinic effects) and respiratory centre paralysis (central effects). Central nervous system effects include, in severe cases, coma and convulsions.
- 5.1.3 **Laboratory:** Diagnosis is confirmed by finding inhibition of erythrocyte or whole blood acetylcholinesterase. However, treatment must start immediately and cannot be delayed until confirmation from the laboratory. This test cannot be used to control the effectiveness of the treatment nor is it of help for prognosis.
- 5.1.4 **Treatment:** Patients with respiratory failure must be given artificial ventilation, then diazepam (10 mg intravenously) to control convulsions. When vital functions are controlled, atropine sulfate is given (initial dose is usually 2 mg intravenously) followed by pralidoxime (1000 mg) or toxogonin (250 mg) by slow intravenous infusion.

If the pesticide has been ingested, gastric lavage might be needed or vomiting induced. Protection of airways (intubation) is required if inducing vomiting in unconscious patients.

For skin contact, the skin should be washed with soap and large amounts of water. Precautions should be taken by medical personnel during these decontamination procedures to prevent their own overexposure. If the compound has entered the eyes, they should be washed with large quantities of saline or water.

Atropine treatment might be required for several days after poisoning. Only clinical assessment determines atropine dose, i.e. evident signs of atropinization (dry mouth, tachycardia, vasodilation, mydriasis) should be maintained. Total amounts of atropine given to these patients might be extremely high because they are tolerant to the effects of atropine.

Caution should be taken when doses of atropine are reduced because reappearance of symptoms might occur, due to redistribution processes in the body. Cholinesterase reactivators such as pralidoxime and toxogonin are usually only effective during the first few days of poisoning, unless the slow disposal of the chemical within the body suggests that some acetylcholinesterase is newly inhibited. Indications for the continuing use of reactivators might derive from measurements of erythrocyte cholinesterase before and after treatment with such reactivators.

5.1.5 **Prognosis:** Unless brain hypoxia has occurred, full recovery is expected.

5.1.6 **References to previously reported cases:** No information available.

5.2 SURVEILLANCE TESTS

Any fall of erythrocyte cholinesterase activity to 70% of pre-exposure values requires an investigation of working methods and hygiene and more frequent cholinesterase tests. Symptoms of poisoning may appear when the erythrocyte cholinesterase activity is less than 35% of normal. If erythrocyte cholinesterase activity is less than 50% of normal, the worker must be suspended from all contact with organophosphorus or carbamate pesticides until the level rises above 70% of normal. Pseudocholinesterase activity in the plasma can fall to very low levels without evidence of symptoms. This only indicates undesirable exposure.

5.3 LABORATORY METHODS

5.3.1 Detection and assay of compound:

Thin-layer chromatography and gas liquid chromatography methods have been used to analyze bromophos in technical products and in its formulations. Analysis of residues in plant and animal tissues is by gas chromatography and flame photometry methods.

Weeren RD & Eichler D (1978), Anal Methods Pestic Plant Growth Regul 10: 31-40.

5.3.2 Other tests in case of poisoning: Activity of cholinesterase in the blood provide the most useful diagnosis of poisoning.

Ellman GL et al (1969) Biochem pharmacol 7: 88-95.

Wilhelm K & Reiner E (1973), Bull Wld Health Org, 48: 235-238.

Measurement of urine metabolites such as dialkylthiophosphates may also be determined in order to give an indication of exposure for methods. See section 5.3.1, Detection and Assay.

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