

**COMBAT OF DOMESTIC CULPRIT BY PROPOXUR: THE
ACETYLCHOLINESTERASE INHIBITOR**

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ABSTRACT

Propoxur is an insecticide used to control cockroaches, flies, mosquitoes and lawn and turf insects. Acute (short-term) exposure of humans to propoxur by ingestion leads to cholinesterase inhibition of red blood cells, with mild cholinergic symptoms including blurred vision, nausea, vomiting, sweating and tachycardia; however, the effects are transient. Chronic (long-term) inhalation exposure has resulted in depressed cholinesterase levels, headaches, vomiting, and nausea in humans. Chronic ingestion studies in animals have reported depressed cholinesterase levels, depressed body weight, effects to the liver and bladder and a slight increase in neuropathy. No information is available on the reproductive, developmental, or carcinogenic effects of propoxur in humans. Mixed results are available from cancer studies of propoxur in animals. EPA has not classified propoxur for carcinogenicity.

KEYWORDS: Insecticide, Propoxur, Carbamate, Acetyl cholinesterase inhibitor, Neurotoxicity.

OVERVIEW

Although insects and bugs are God’s very own intricate creation, it is hard to accept that they are to live along with us. In this civilized world, everyone wants those buggy insects to be in their eco-system and not creep into our system. But that doesn’t happen. Man himself has somehow distorted the equilibrium and thus making way for insects to disturb him day-in day-out. Among all the insects, it is the Cockroach that is most pestering of all. Being one of the oldest creatures to walk the earth, they find place everywhere in a house. I hate cockroaches. Those nasty creatures, although harmless look annoying. What annoys me most is their number. They increase in number within no time. Sometimes, cockroaches increase in numbers in such a way so as to pose a threat for the record holder for population, i.e., the beloved Homo-Sapiens lot. Anyway, cockroaches are unwanted in any house. They pester a lot by hiding in places where we don’t want them to and create a lot of mess. One or two is okay but too much is too bad and this is where the question of getting rid of this creature comes into picture. Well if you ask me, the best way to keep cockroaches away is by having a cockroach repellent, especially the Hit Cockroach Repellent that has proven to be an effective tool against cockroaches.

Manufactured by Godrej, Hit is the most effective cockroach repellent around. It is a propoxur household insecticide, which is a ready to use Aerosol for spot applications against cockroaches and other insects. The repellent proves to be really effective for it can keep the cockroaches away for weeks. Hit basically contains

Propoxur, Isopropyl Alcohol, Petroleum distillate with Petroleum gas that has proven to be very strict against cockroaches. The application of this cockroach makes the cockroach numb, unconscious and kills it after breathing it. Thus it has proven to be very effective.^[1]

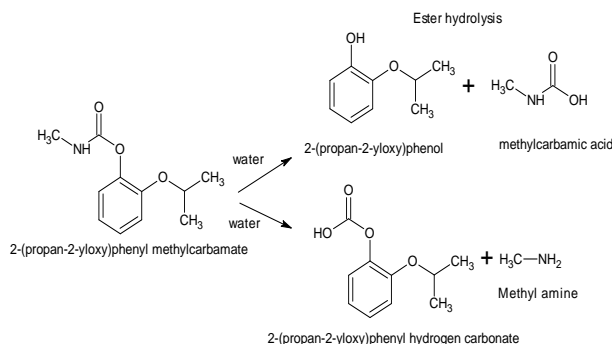


Figure-1: Carbamate hydrolysis

Propoxur (Baygon) is a carbamate insecticide and was introduced in 1959. Propoxur is a non-systemic insecticide with a fast knockdown and long residual effect used against turf, forestry and household pests and fleas. It is also used in pest control for other domestic animals, Anopheles mosquitoes, ants, gypsy moths and other agricultural pests. It can also be used as a molluscicide. Several U.S. states have petitioned the Environmental Protection Agency (EPA) to use propoxur against bedbug infestations, but the EPA has been reluctant to approve indoor use because of its potential toxicity to children after chronic exposure. Application

of the spray is an important procedure. Firstly certain precautions are to be taken. One should never ever spray this on utensils and animal food. Also one should avoid direct contact and inhalation. So it is better to clear off utensils from the places of application. Then tie a scarf or some cloth around your nose covering your mouth so that you wouldn't inhale any of the stuff. But then yes, you definitely would look like a hijacker but never mind. Now slowly spray the substance to the required levels.

Mechanism of action of Propoxur

As all carbamate insecticides propoxur acts on the nervous system of the parasites (but also of mammals, birds, fish and many organisms!) as inhibitor of acetylcholinesterase (also known as AchE), an enzyme that hydrolyzes acetylcholine (Ach). Ach is a molecule involved in the transmission of nervous signals from nerves to muscles (so-called neuromuscular junctions) and between neurons in the brain (so-called cholinergic brain synapses). AchE's role is to terminate the transmission of nervous signals where Ach is the neurotransmitter (there are several other neurotransmitters). By inhibiting the activity of AchE, carbamates prevent the termination of those nervous signals, i.e. the neurons remain in constant activity and excitation, massively disturbing the normal movements of the parasites. The bottom line for the parasites is that they are paralyzed and die more or less quickly. Carbamates bind reversibly to AchE, in contrast with organophosphates, another chemical class of parasiticides, which bind irreversibly to AchE. Acetylcholine is cationic quaternary ammonium compound which has ester (-CO-O-) linkage which is bioisosteres with propoxur which has carbamate (-NH-CO-O-) which have both ester (-CO-O-) and amide (-NH-CO-) linkages. In ester (-CO-O-: 12+16+16=44) and in amide (-NH-CO-: 14+1+12+16=43), so both linkages are bioisosteres.^[2]

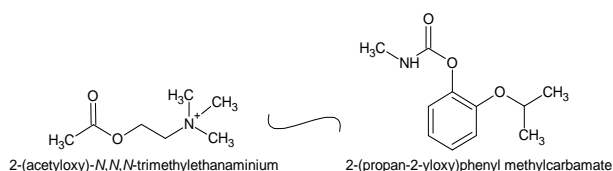


Figure-2: Acetylcholine and Propoxur.

Acetylcholinesterase (HGNC symbol ACHE), also known as AChE or acetylhydrolase, is the primary cholinesterase in the body. It is an enzyme that catalyzes the breakdown of acetylcholine and of some other choline esters that function as neurotransmitters. AChE is found at mainly neuromuscular junctions and in chemical synapses of the cholinergic type, where its activity serves to terminate synaptic transmission. It belongs to carboxylesterase family of enzymes. It is the primary target of inhibition by organophosphorus compounds such as nerve agents and pesticides. After application, close the lid in an air-tight manner and store it in a cool, dry place away from heat and open flame.

Most important of all, keep the repellent out of reach of children.



Figure-3: Hit to beat cockroach

Acute Toxicity and Tolerance of Propoxur

LD₅₀ acute, rats, p.o. 50 mg/kg; LD₅₀ acute, mice, p.o. ~100 mg/kg; LD₅₀ acute, rats, dermal 4000 mg/kg; LD₅₀ acute, rabbits, dermal 4000 mg/kg. Dogs tolerated daily oral doses of 20 mg/kg/day during months without toxic symptoms. In chickens delayed neurotoxic effects with degeneration of the spinal cord has been reported. As a general rule, dogs, cats and livestock tolerate topically applied propoxur very well (shampoos, soaps, baths, aerosols, lotions, creams, dusts, collars, etc.).

Now, the countdown begins. Preferably, if you spray the repellent before you go to sleep, you can catch the cockroaches as they are mostly nocturnal. Get up in the morning and a whole lot of dead cockroaches will await you. All you are left to do is, clean them up and forget cockroach nuisance for another 4-5 weeks. Even after complete use, dispose the bottle safely because it is flammable. So, this cockroach repellent, manufactured in

consultation with Enichem Synthesis Spa (Italy) proves to be the biggest enemy of Cockroaches. So, definitely HIT Cockroach Repellent is a good buy. And priced at 63 rupees for a 160 ml spray-can, this cockroach repellent is certainly affordable. In my opinion, HIT is the best around and the slazzy red can speak volumes. So, I would like to strongly recommend this cockroach repellent to all those who are troubled by the mess created by the most hated insects on Planet Earth, Cockroaches.

Toxic Symptoms caused by Propoxur Poisoning

Toxic symptoms caused by carbamate intoxications are the same as those of organophosphate intoxication, but are usually less severe and recovery is faster because carbamates bind reversibly to acetylcholinesterase, whereas organophosphate binding is irreversible. This means that the organism can hydrolyze carbamates, which allows the enzyme to retake its normal function in a few hours. However, in case of massive overdose the organism cannot break down the poisonous substance fast enough. Ingested propoxur affects mainly the nervous system and the liver. Acute intoxication. Is caused by inhibition of the acetylcholinesterase: as a consequence acetylcholine accumulates in the neuromuscular synapses (including those in skeletal, smooth and cardiac muscles), in the neuroglandular connections, and in the CNS (Central Nervous System). This causes hyperexcitation in all the muscarinic and nicotinic cholinergic receptors, which disturbs the normal functioning of the affected organs. After accidental ingestion or massive dermal overdose, intoxication follows an acute development. Ingested propoxur is vastly and quickly absorbed into blood. The symptoms appear a few minutes to 2 hours after ingestion, often dramatically. If the patient survives the first 24-48 hours, prognosis is favorable.

Usually muscarinic symptoms are the first to manifest, followed by hyperexcitation of the nicotinic receptors of vegetative ganglions and motor end plates. If the intoxication crosses the blood-brain barrier the CNS becomes hyperexcited as well.

Main muscarinic symptoms: **Exocrine glands:** salivation (drooling), lacrimation (excessive secretion of tears), sudoration (excessive sweating). **Eyes:** miosis (constriction of the pupil), in swine nystagmus (uncontrolled eye movements). **Digestive system:** nausea, vomit (particularly in dogs), diarrhea, tenesmus (need for imperative defecation), fecal incontinence. **Cardiovascular system:** bradycardia (low heart rate), low blood pressure. **Respiratory system:** bronchoconstriction, bronchospasms, cough, tachypnea (low breathing rate), dispnea (shortness of breath). **Urinary system:** frequent urination.

Main nicotinic symptoms

Muscles: anxiety followed by depression, trembling, ataxia (uncoordinated movements), muscular stiffness, generalized muscular spasms, paralysis.

Main CNS symptoms: Lethargy, fatigue, trembling, spasms and coma with respiratory paralysis. Death is mostly a consequence of paralysis of the respiratory muscles, of the inhibition of the respiratory center and of excessive bronchial constriction and secretion. In swine death can follow within 15 to 30 minutes after exposure to the lethal dose.

Diagnosis

An important diagnostic parameter is the global acetylcholinesterase (AChE) activity in blood. A drop below 25% of the normal value indicates intoxication with an AChE inhibitor (not necessarily an organophosphate or carbamate pesticide).

Propoxur Side Effects, Adverse Drug Reactions (ADRs) and Warnings

After slight overdose the following effects have been reported: reduced heart rate and vascular dilatation, increase of bronchial secretion and contraction, salivation (drooling), sphincter relaxation (gastrointestinal and urinary), miosis. In case of large skin injuries topical treatment with propoxur can lead to excessive cutaneous absorption with development of parasympathetic symptoms. Propoxur-impregnated collars for dogs and cats can cause local skin irritation. During the first 3 days after getting the collar, a reduction in the number of red blood cells and of the plasmatic cholinesterase levels has been reported. Propoxur should not be administered to animals suffering digestive (particularly mechanical intestinal or urinary obstruction), respiratory (mainly bronchial asthma) and cardiovascular disturbances. Propoxur should not be administered to pregnant dams during the last third of gestation. Certain solvents in the formulation can enhance the toxicity of Propoxur because they accelerate its cutaneous or mucosal absorption. Carbamates must not be administered together with other acetylcholinesterase inhibitors such as organophosphates, levamisole, morantel, pyrantel and neostigmine.

Antidote and Treatment of Propoxur Intoxication

Atropine (a parasympatholytic drug) is the antidote for the acute muscarinic symptoms, the most dangerous ones. It is an antagonist of acetylcholine in the muscarinic receptors of the nervous system. Recommended atropine dosing (one third i.v. the rest s.c.), or otherwise at the physician's discretion.

Cattle: 0.6 mg/kg, Sheep: 1.0 mg/kg, Horses: 0.1 mg/kg, Dogs: 0.3 mg/kg, Cats: 0.3 mg/kg. Atropinization efficacy peaks when the pupils dilate and salivation stops. If necessary treatment can be repeated every 4 to 6 hours up to a max. dose of 6 mg/kg. Causal antidotes that act upon the toxic mechanisms can also be used.

Pralidoxime (2 to 5 mg/kg i.v., maybe i.m.) and obidoxime (20 to 100 mg/kg) can reactivate the cholinesterase but not later than 24 hours after ingestion, and treatment should not be repeated more than once or twice. Both should be administered after atropine. Retreatment not earlier than 20 minutes, usually after 2 hours. **WARNING:** obidoxime can also act as a cholinesterase inhibitor! Symptomatic and support measures may be advisable.

Breathing support: artificial respiration and aspiration of bronchial secretions. **After oral poisoning:** vomit or stomach lavage, administration of active charcoal or mineral oil. **After dermal poisoning:** rinse the injury with abundant water with alkaline detergent. **Treatment of acidosis and spasms:** Administration of electrolytes and multivitamins to support the hepatic metabolism.

Pharmacokinetics of Propoxur

- Topically administered propoxur remains mostly on the hair-coat of the treated animals and is very poorly absorbed through the skin. Treated animals can ingest propoxur through licking or grooming.
- Absorption of ingested propoxur into blood is very fast. It is also quickly excreted through urine. Rats eliminated up to 85% of the administered dose within 16 hours.

Environmental Toxicity of Propoxur

Propoxur is highly to moderately toxic to birds, depending on the species, Propoxur is only slightly toxic to fish and many aquatic invertebrates, but is highly toxic to numerous insects, Propoxur is unlikely to bioaccumulate in the aquatic food chain, Propoxur is moderately persistent in the soil. Half-life in soil is 14 to 50 days. It hardly binds to soil particles. For these reasons and because it is quite soluble in water it has potential for contaminating groundwater. In aqueous environment propoxur degrades at a speed of ~1.5%/day.^[3]

CONCLUSION

Propoxur is a non-systemic insecticide which was introduced in 1959. Propoxur is not used on food crops. It is used against mosquitoes in outdoor areas, for flies in agricultural settings, for fleas and ticks on pets, as an acaricide, on lawns and turf for ants, on flowering plants, and in private dwellings and public buildings. It is also used as a molluscicide, a chemical that kills snails. It is effective against cockroaches, aphids and leafhoppers. Propoxur is one of the chemicals that have, to a large extent, replaced DDT in the control of black flies and mosquitoes. It is a nonsystemic insecticide with contact and stomach action that has longstanding residual poisonous, or toxic activity when it is in direct contact with the target pest. Many formulations are available including ready-to-use liquids and aerosols, emulsifiable concentrates, wettable powders, granular baits, dusts and impregnated pet collars and strips. Propoxur is one of a family of insecticides called carbamates. These

chemicals block the production and action of cholinesterase, an essential nervous system enzyme. These materials quickly paralyze the nervous systems of insects, gaining them a reputation of having a rapid "knockdown" effect. Please refer to the Toxicology Information Brief on cholinesterase-inhibition for a more detailed discussion of cholinesterase inhibition.

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