E X T O X N E T

Extension Toxicology Network

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Pesticide
Information
Profile

Deet

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TRADE OR OTHER NAMES

Deet is found in a variety of commercial insecticides. Trade names for products containing Deet include Autan, Delphene, Detamide, Deltamid, Flypel, m- Delphene, Meta-Delphene, Naugatuck Det, and Off (1).

REGULATORY STATUS

There are 53 registrants of Deet-containing insect repellents (3).

INTRODUCTION

Deet is the common name for N,N-diethyl-m-toluamide, a multipurpose insect repellent registered for direct application to human skin, clothing, household pets, tents and bedrolls and screens. Deet is a unique pesticide, because it is applied directly to the human body for purposes of repelling insects. It was developed and patented by the U. S. Army in 1946 for use by military personnel in insect-infested areas. Because Deet was recognized as one of the few products effective against mosquitoes and biting flies, it was registered for use by the general public in the U. S. in 1957 (8).

Technical Deet is 95% m-isomer. The o- and p-isomers are highly repellent but less effective than the m-isomer. The compound is also known as detamide, diethylbenzemide, diethyl toluamide, m-delphene, metadelphene, and by the acronyms DET, DETA, and M-DET (1).

Products containing N,N-diethyl-m-toluamide and isomers (Deet) are beneficial as insect repellents, but have also been associated with dermal and neurological reactions in humans (3).

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

Different preparations of Deet with different proportions of the misomer produced oral LD50 (the amount of a chemical that is lethal to one-half (50%) of experimental animals fed the material is referred to as its acute oral lethal dose fifty, or LD50) values varying from 1,800 to 2,700 mg/kg in male rats and from 1,750 to 1,800 mg/kg in females. Rats killed by dosages in the LD50 range

showed lacrimation, chromodacryorrhea, depression, prostration, tremors, and asphyxial convulsions. Respiratory failure usually preceded cardiac failure (1, 9).

In rabbits, an intravenous dosage of 75 mg/kg was rapidly fatal, but 50 mg/kg was not. Five doses at the rate of 25 mg/kg/day produced no cumulative effect, except for injury of the intima of some veins used for injection. Single dermal applications to rabbits at rates of 2 or 4 ml/kg produced no systemic effect, but did produce mild to moderate erythema. Repeated dermal application of 50% solutions for 13 weeks at the rate of 2 ml/kg/day produced no evidence of systemic toxicity but did produce desquamation, coriaceousness, dryness, and fissuring in the same species. Except for some scarring, these lesions cleared within 3 weeks. Instillation of Deet into the eyes of rabbits produced mild to moderate edema of the nictitating membrane, lacrimation, conjunctivitis, and some corneal injury, as revealed by fluorescein staining. After 5 days, all eyes appeared normal. No sensitization was seen in guinea pigs (1, 9).

Animals topically exposed to Deet have developed dermal and ocular reactions. Dermal effects including erythema, desquamation and scarring in rabbits (9) and profuse sweating, irritation and exfoliation in horses (Blume et al, 1971) (10) have been reported following repeated applications of Deet at concentrations of 50 percent or greater. Direct ocular application of either diluted (30 or 40 percent Deet) or undiluted Deet in rabbits has produced edema, tearing, conjunctivitis, pus and clouding in the eyes (3, 9).

Repeated dermal application to horses produced hypersteatosis, an overactivity of the selacious glands, when the solution of Deet was 15% or higher (10).

Dermal application in humans of insect repellents containing Deet can produce a variety of skin reactions in humans. Cases of localized skin irritation, large painful blisters and permanent scarring of skin at the crease of the elbow have been reported in soldiers who applied solutions of 50 or 75 percent Deet (11) (Reuveni and Yagupsky, 1982). Results from questionnaire surveys conducted by the National Institute for Occupational Safety and Health (NIOSH) among Everglades National Park Employees indicated a variety of dermal reactions including rashes, irritation of skin and mucous membranes, and numb or burning sensations of the lips among park workers who were highly exposed to Deet-containing repellents (McConnell et al., 1986). Urticaria or dermatitis, resulting from topical Deet exposure has been noted in both children and adults (Maibach and Johnson, 1975; Mayenburg and Rakoski, 1983; Miller, 1982; Oransky et al., 1989; Roland et al., 1985). In one instance involving only limited Deet exposure, the urticaria was accompanied by an anaphylactic reaction (Miller, 1982) (3).

Controlled human exposure studies using 50 or 75 percent Deet have reproduced many of the dermal effects noted in field studies (9, 11). The U.S. Army conducted an investigation in volunteers using 75 percent Deet applied to the upper arm and elbow's crease. Of the 77 volunteers, 37 (48%) had severe dermal reactions at the crease of the elbow. No dermal reactions were observed on the upper arm or in the control group of men tested with ethanol solvent alone (3, 11).

Several cases of toxic encephalopathy associated with the use of Deet in children have been reported in the medical literature. The first reported case involved a 3.5 year old girl whose body, bedclothes and bedding were sprayed each night for two weeks with an insect repellent containing 15 percent Deet (12). Since then, five additional cases of toxic encephalopathy have been temporally associated with the use of Deet products in children, all of whom were females (Edwards and Johnson, 1987; de Garbino et al., 1983; Heick et al., 1980; Roland et al., 1985; Zadikoff, 1979). The toxic encephalopathy was characterized by agitation, weakness, disorientation, ataxia, seizures, coma and in three cases resulted in death. Autopsies conducted on two fatalities (Heick et al., 1980; Zadikoff, 1979) indicated edema of the brain, with one case

presenting necrotic lesions in the cerebellum and spinal cord and an enlarged liver accompanied by microscopic changes (Heick et al., 1980). One child was reported to be heterozygous for ornithine carbamoyl transferase deficiency (a sex linked enzyme deficiency which may produce effects similar to those reported above) and it has been hypothesized that children with this enzyme disorder may be at greater risk of adverse reactions to Deet (Heick et al., 1980). This enzyme deficiency which usually causes infant death in males is of variable severity in females (Stanbury et al., 1983). Accidental and deliberate ingestion of Deet-containing products has produced neurotoxic effects similar to those described following dermal exposure (Tenenbein 1987, Zadikoff, 1979) (3).

Generalized seizures have also been temporally associated with the use of Deet-containing insect repellent on skin (Oransky et al 1989). These cases differ from those described above in that they involved males (four boys aged 3-7 years and one 29-year-old adult), had few associated neurotoxic effects and resolved rapidly. Lower exposure to Deet in these males (four of five males had either one or two dermal applications) may have accounted for the effects being less severe than in females. That the majority of identified neurotoxic cases involved children raises concerns that this subpopulation is at greater risk of adverse reaction following exposure to Deet than are adults (3).

Signs and symptoms of more subtle neurotoxicity have also been associated with extensive dermal application of Deet in adults. Questionnaire results indicate that Everglades National Park employees having extensive Deet exposure were more likely to have insomnia, mood disturbances and impaired cognitive function than were lesser exposed co-workers (McConnell et al., 1986). A young male who repeatedly applied Deet to his skin prior to spending prolonged periods in a sauna was reported to develop acute manic psychosis characterized by aggressive behavior, delusions and hyperactivity (Snyder et al., 1986) (3).

Either o-DET or p-DET, or both occur as impurities in commercial m-DET (Deet). A thorough study of the o-and p-isomers showed that the o-isomer is slightly more toxic than the others (oral LD50 1,210 mg/kg in rats). However, no alarming difference was found, and it was concluded that the presence of 5% of o-DET or p-DET as impurities in the insect repellent is not a serious health problem (1, 14).

CHRONIC TOXICITY

When rats were fed Deet at a dietary level of 10,000 ppm for about 200 days, their growth rate was decreased without a decrease in food intake. There was a significant increase in the relative weight of the testes and liver in males, of the liver and spleen in females, and the kidneys of both males and females. Some of these changes were seen in lesser degree at a dietary level of 1,000 ppm. No gross or significant histological changes were seen at any dietary level and no changes of any kind were noted at 100 ppm or 500 ppm (about 25 mg/kg/day) (1, 9).

Essentially identical results were found in other subacute dermal and feeding studies each carried out on rats, rabbits, and dogs. In these oral studies, 2,000 ppm proved to be a no-effect-level. Oral administration of Deet to dogs at rates of 100 and 300 mg/kg/day caused tremor and hyperactivity and occasional vomiting, but no other effects. Blood studies (hemoglobin, hematocrit, sedimentation rate, platelet counts, total and differential white cell counts) on dogs receiving 300 mg/kg orally or dermally or on rabbits receiving 300 mg/kg dermally revealed no effect on the hematopoetic system. Gross and microscopic examination of the organs of all three species revealed only slight kidney damage in rabbits typical of that associated with burns of the skin. Thirteen other organs, including liver, spleen, and bone marrow, were normal in the three species (1, 13).

No systemic toxicity was observed in rats exposed 8 hours/day, 5 days/week for 7 weeks to air saturated with Deet. No toxic effects were observed in rats exposed for 6 hours to an aerosol of Deet. No gross or significant histological changes were seen (1, 9).

Reproductive Effects

When Deet was applied to the skin of rats at the rate of 1,000 mg/kg/day throughout pregnancy, implantation was reduced significantly. Prenatal mortality was 34.1%, compared with 20.9% in the control. Mortality between birth and weaning was 44.0%, compared to 15.7% in the control. Injury was less (but probably significant) at a dosage of 100 mg/kg/day throughout pregnancy (1, 15).

Teratogenic Effects

A dermal teratology study was conducted on rabbits. Groups of 20 pregnant rabbits received daily dermal applications of 0, 50, 100, 500, 1000, or 5000 mg Deet/kg/day in ethanol on shaved backs from day 0 through day 29 of gestation. There were no significant differences between control and treated animals with respect to the fertility index, number of implantations per animal, or number of fetuses per animal. In addition, treatment did not change fetal weight, fetal length or placental weights and no increases in the incidence of skeletal or soft tissue anomalies were observed in treated groups when compared with untreated controls. This study demonstrated that Deet has no teratogenic or embryotoxic effects in rabbits exposed dermally to technical Deet (8).

An additional supplementary teratology study was conducted on rats. Groups of 20 pregnant rats were daily administered 10 ml of peanut oil containing 0, 8, 20 or 80 mg/kg/Deet by gavage from day 5 through day 15 of gestation. No significant differences were reported between control and treated mothers with respect to fertility, fetuses per litter, fetal weight or fetal survival. However, the study did show decreases in number of implantation sites per dam and number of fetuses per animal. In addition, a related increase was observed in the number of resorptions per dam (8).

Mutagenic Effects

Sperm--Rat inhalation 1,500 mg/m3 (6).

Carcinogenic Effects

No carcinogenic effects were reported (6).

Organ Toxicity

Hypertrophy of the kidneys and liver and effects of mild central nervous system stimulation including tremors and hyperactivity were noted in animals following repeated exposure. Significant testicular hypertrophy was observed in male rats repeatedly fed a diet containing from 48 to 531 mg/kg/day of Deet (6).

Fate in Humans and Animals

Deet is absorbed promptly from the skin and distributed to all organs including the brain and the fetus. The compound is excreted in the milk but primarily in the urine (1, 15, 16).

Using radioautography following intravenous injection of 14C-Deet, high tissue levels were found at first in the liver, kidney, lacrimal gland, and nasal mucosa. Very soon, concentrations higher

than that in the blood were found in the thyroid and brown fat. Concentrations were highest and most persistent in the lacrimal gland. Concentrations in the fetus remained lower than those in the mother. Excretion was rapid and mainly by way of the kidney. By 4 hours after injection, very little radioactivity remained in any tissue, except the lacrimal gland (17). An essentially similar picture was seen following dermal application. However, low levels of excretion continued during the entire one-month period of observation. Direct measurement of the skin indicated that persistent excretion depended mainly on continuing absorption from the skin (18).

After 14C-carboxylabeled Deet was applied to the skin of guinea pigs at rates of 1.08 to 1.10 mg/cm2 (rates similar to those used for human skin under practical conditions), over 98% of the total dose was recovered in different experiments. Within 6 hours, 0.149 to 0.152 mg/cm2 was lost by measured evaporation, and this amounted to 13.8 to 13.9% of the applied dose. At the end of this 6hour period, it was possible to recover a further 38.4 to 67.3% of the applied dose by washing the skin with ethanol until no further radioactivity could be removed. Similar proportions of nonradioactive Deet were measured chemically after evaporation and washing. Calculated by difference, the remainder, which had already been absorbed or was still in the skin presumably available for absorption, amounted to 18.9 to 47.8% of the applied dose. In spite of the washing, considerable radioactivity was detected in the skin by an instrument held 2.54 cm above the surface. Activity measured in the same way was 50% after 72 hours and 10% after 216 hours, counting the reading just after washing as 100%. This indicated considerable retention in the skin. When urine was sampled frequently, the highest concentration of radioactivity was found 6.5 hours after application, and considerable radioactivity was still present in 24 hours. Excretion then decreased rapidly but was still detectable 216 hours after application. Of the remainder mentioned above, >93% was measured in the urine, 0.75% was measured in the feces, and activity measured in skin and hair brought the proportion of the remainder actually measured to >94.90% of that determined by difference (1, 19).

Excretion of 14C reached a high level 5 hours after application and remained high until 21 hours after application in a volunteer who had received a single application of a 25% solution of 14CDeet in absolute alcohol on two occasions. The treated skin was washed 8 hours after application, and 8 and 15% of the applied dose were recovered in the two experiments. Smaller total amounts (5.5 and 3.8%) were recovered in the urine (18).

ECOLOGICAL EFFECTS

Effects on Birds

No information was found.

Effects on Aquatic Organisms

One study on the acute toxicity of technical Deet to fish reported a 24-hour LC50 of 125 ppm and a 96-hour LC50 of 172 ppm for rainbow trout. These results are sufficient to characterize Deet as slightly toxic to coldwater fish (8).

Effects on Other Animals (Nontarget Species)

Recently, numerous cases of neuro-toxicity in cats and dogs have been associated with the topical use of a product containing both Deet and the pyrethroid fenvalerate (Dorman et al., 1990; Mount et al., 1991; U.S. EPA, 1988). Because of coapplication, the role of Deet in the development of these effects is not certain (3).

ENVIRONMENTAL FATE

Breakdown of Chemical in Soil and Groundwater

Registered outdoor uses of Deet are not expected to result in the introduction of significant amounts of this pesticide into the environment (8).

Breakdown of Chemical in Surface Water

Registered outdoor uses of Deet are not expected to result in the introduction of significant amounts of this pesticide into the environment (8).

Breakdown of Chemical in Vegetation

No information was found.

PHYSICAL PROPERTIES AND GUIDELINES

Technical Deet is colorless to amber in color and has a faint odor (6).

Physical Properties:

CAS #:	134-62-3
Chemical name:	N,N-diethyl-3-methyl-benzamide or N,N-diethyl-m-toluamide
Chemical Class/Use:	insect repellent
Specific gravity:	0.996 @ 25[ring] C (6)
Solubility in water:	practically insoluble in water (1, 6)
Solubility in other solvents:	Soluble in ethanol, ether, isopropanol, chloroform, carbon disulfide, alcohol, benzene, propylene glycol, cotonseed oil, ketones, petroleum distillates; sparingly soluble in petroleum ether and glycerin (1, 6)
Boiling point:	111[ring] C at 1 torr (1); 111[ring] C at 1.3 mbar (5); 320[ring] F (160[ring] C) at 19 mmHg (6)
Vapor pressure:	0.0019 mmHg @ 160[ring] C (6)

BASIC MANUFACTURERS

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