THE TOXICITY OF SEVERAL CHLORINATED HYDROCARBON AND ORGANIC PHOSPHORUS INSECTICIDES TO FIELD MICE BELONGING TO THE GENERA PEROMYSCUS AND MICROTUS

by

THEODORE LOUIS HOPKINS

A THESIS

submitted to

OREGON STATE COLLEGE

in partial fulfillment of
the requirements for the
degree of

MASTER OF SCIENCE

June 1956

APPROVED:

Redacted for privacy

Associate Professor of the Department of Fish and Game Management

In Charge of Major

Redacted for privacy

Head of Department of Fish and Game Management

Redacted for privacy

Chairman of School Graduate Committee

Redacted for privacy

Dean of Graduate School

Date thesis is presented May 3, 1956

Typed by Colleen Hopkins

ACKNOWLEDGMENTS

To the personnel of the Corvallis research station, United States Department of Agriculture, Entomology Research Branch, Section of Insects Affecting Man and Animals, sincere appreciation is expressed for having made this thesis possible through the use of facilities, equipment, and materials.

To Associate Professor Lee W. Kuhn and Professor R. E. Dimick of the Department of Fish and Game Management, Oregon State College, grateful acknowledgment is made for their interest and encouragement in this study and for the time and help spent in preparation of the manuscript.

Special thanks are also due my wife, Colleen A. Hopkins, for the invaluable assistance rendered in editing and typing the manuscript.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF TABLES

THE TOXICITY OF SEVERAL CHLORINATED HYDROCARBON AND ORGANIC PHOSPHORUS INSECTICIDES TO FIELD MICE BELONGING TO THE GENERA *PEROMYSCUS* AND *MICROTUS*

INTRODUCTION

This experimental study was conducted to obtain data concerning the toxic effects of several of the chlorinated hydrocarbon and organic phosphorus insecticides to two species of native mice commonly associated with forest and agricultural lands of the Willamette Valley in Oregon. Data of the type reported may serve a twofold purpose: as the basis for evaluating toxicants as control agents for destructive mouse populations, and to gain a better understanding of the potential toxicity such compounds may exert on native mammal populations.

The widespread application of organic chemicals for the control of destructive insects has created several problems concerning their possible toxic effects to wild and domestic animals and to man. Since a number of these insecticides have been demonstrated to be highly poisonous to warm-blooded animals as well as to the arthropods for which their use was originally intended, toxicological information is necessarily the basis for determining the hazards of employing these compounds. Subsequent to the development of the organic insecticides, a large amount of experimental work has been conducted to measure the acute and chronic toxicity, pathology, and symptomatology produced

by these compounds on laboratory animals such as white mice, rats, and rabbits. Field observations on wildlife following large-scale insecticide applications to their habitat for the control of insects constitute the greater part of the knowledge concerning the toxicity of these chemicals to native species. Recently a few of the more potent organic insecticides have been used experimentally with varying degrees of success for the control of destructive field mouse populations.

Because of the increasing contact of native mammals with the organic insecticides, whether accidental or as directed control agents, basic information is needed concerning the actual toxicities of these compounds to the species of mammals involved.

TERMINOLOGY

The following toxicological terms and abbreviations are defined as used throughout this thesis.

Acute Toxicity: Toxic effects which are attended with symptoms of some severity and rapidly culminating in a crisis; limited to a short duration of a few minutes to several days, as opposed to chronic toxicity; usually referring to the effects produced by single doses by any of the various routes of administration.

Approximate Lethal Dose: The lowest dosage rate resulting in mortality.

Dermal Toxicity: The effects produced by application of the test material to bare skin.

LD-0: The largest dosage that will cause no mortality.

LD-50: The lethal dose that will theoretically result in 50 percent mortality.

LD-100: The smallest dosage that will cause 100 percent mortality.

Lethal Range: The dosage range extending from the upper limit of survival for all animals tested to the lower limits of doses that proved fatal to all animals tested.

Median Lethal Dose: Another means of expressing the LD-50.

Mg./Kg.: Milligrams of toxicant per kilograms of body weight of the test animal.

Minimum Lethal Dose (MLD): The lowest dosage rate that will cause mortality.

Oral Toxicity: The effects produced by administration of the test material by mouth, or more specifically, intragastric injection by stomach tube or needle.

REVIEW OF LITERATURE

The development and greatly expanded usage of the chlorinated hydrocarbon and organic phosphorus insecticides within the last few years has ultimately required information concerning the poisonous effects of these compounds to animals as the basis for their safe employment. The literature covering these investigations is voluminous and, therefore, only pertinent references on the toxicity of these chemicals to small mammals of both native and laboratory species were selected.

DDT (2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane).

DDT has been the subject of numerous investigations concerning its toxicity to wild mammals when applied to various land areas for insect control. Couch, 1946, studied the effects of an aerial application of 0.2 and 0.5 pounds of DDT in oil per acre on various small mammals inhabiting a Mississippi river-bottom forest and could detect no direct losses due to the insecticide, although food chains were disrupted for some species (6, p.327). Stickel, 1946, reports no adverse effects to a deer mouse, Peromyscus leucopus noveboracensis (Fischer), population when DDT in oil was applied at the rate of two pounds per acre over forest lands in Maryland (27, p.217). Erickson, 1947, measuring cotton rat, Sigmodon hispidus Say and Ord, and house mouse, Mus musculus Linnaeus, populations in South

Carolina by live-trapping on sprayed and unsprayed areas, could find no population changes resulting from 17 weekly applications of DDT at 0.1 pound per acre applied by airplane for mosquito control. Daily sight records on cottontail rabbits, cotton rats, and raccoons also yielded no positive information of population shifts due to the DDT applications (10, pp.8-10). Adams et al., 1949, studied the effects on wild mammals when extensive forest areas in Wyoming were sprayed twice in eight days with DDT in oil. In areas treated with a total of five and 7.5 pounds per acre, no population changes of the following small mammals could be correlated with the application of the DDT by live-trapping methods: red-backed mice, Clethrionomys gapperi saturatus (Rhoads); field mice, Microtus longicaudus (Merriam); white-footed mice, Peromyscus maniculatus artemisiae (Rhoads); jumping mice, Zapus princeps Allen; chipmunks, Eutamius amoenus luteiventris (Allen); and pine squirrels, Tamiasciurus douglasii (Bachman). In areas treated with five pounds per acre, several chipmunks and one shrew, Sorex palustris navigator (Baird), showed tremors characteristic of DDT poisoning (1, p.252). Benton, 1951, recorded some mortality among grey squirrels, Sciuris carolinensis Gmelin, and red bats, Lasiuris borealis Muller, in New Jersey when up to three pounds of DDT were applied as an emulsion to individual trees for Dutch elm disease (4, p.22). Stickel, 1951, observed a

deer mouse population in a Maryland forest sprayed annually for five years with DDT in oil at two pounds per acre and reported no population changes could be related to the treatment (28, p.162). Jackson, 1952, studied populations of deer mice living in the edge of forests in New Jersey that had been contaminated by drift from routine airplane dust applications of DDT at 1.75 to 2.25 pounds per acre. No population changes or pathological effects could be found in these mice (17, pp.277-278).

These studies indicate that DDT has no measurable effect on small mammal populations when applied over various types of habitats at rates up to 7.5 pounds per acre. Individuals of some species may show symptoms of poisoning at the higher rates of application and mortality may occur where heavy applications are made over limited areas such as in tree spraying.

The acute oral and dermal toxicity of DDT to small laboratory and wild mammals has been determined by various workers and is summarized in tables 1 and 2 respectively.

TOXAPHENE (Chlorinated camphene).

This chlorinated insecticide has recently become the subject of experimental studies for the control of field mouse infestations. In Oregon it was first observed to kill meadow mice when applied as a ground spray at four pounds per acre for the control of cutworms on alfalfa

TABLE 1. Acute oral toxicity of DDT to small mammals as reported by various authors.

Animal	Formulation	Mg./Kg.	Mortality	Reference
White mouse	aqueous suspension	1600	LD-50	32, p.109
			dead/total	
	corn oil solution	142	0 / 10	34, p.153
		200	1 / 10	
		282	0 / 10	
		399	8 / 10	
		502	10 / 10	
			dead/total	
White-footed mouse	aqueous suspension	1000	0 / 4	5, p.214
		1500	3 / 6	
		2000	5 / 6	
White rat	aqueous suspension	500	LD-50	32, p.107
	olive oil solution	150	LD-50	26, p.988
	olive oil solution	225-250	LD-50	16, p.264
	pure compound in innocuous solvent	250	LD-50	20, p.129
	corn oil solution	200	LD-100	24, p.24
		115	LD-50	
		70	LD-0	
			dead/total	
	corn oil solution	140	2 / 5	34, p.153
		180	3 / 5	
		220	4 / 5	
		260	1 / 5	
		300	9 / 15	
Domestic rabbit	aqueous suspension	275	LD-50	32, p.275
	olive oil solution	300	LD-50	26, p.988
Cottontail rabbit	aqueous suspension	Lethal dose greater than 2500 mg./kg.		5, p.212

TABLE 2. Acute dermal toxicity of DDT to small mammals as reported by various authors.

Animal	Formulation	Mg./Kg.	Mortality	Reference
White mouse	aqueous suspension	250-500	LD-50	32, p.109
White rat	aqueous suspension	1000	LD-50	32, p.109
Domestic rabbit	aqueous suspension	250-500	LD-50	32, p.109
	dry technical grade microtized powder 50% wettable powder	-	no effect	21, p.4
	30% in dimethyl phthalate	2820	slight symptoms, no mortality	21, p.4

(22, p.52). Further tests in Washington on experimental plots in orchards with cover crops demonstrated that toxaphene at six pounds per acre is a marginal dose for the control of meadow mice, Microtus montanus canescens Bailey, while 12 pounds per acre gave good control as a ground spray. Rabbits were also killed in these plots (18, p.80). Additional tests the following year with toxaphene applied to orchard lands at rates varying from six to 30 pounds per acre gave erratic mouse control due partially to the heaviness of ground cover (33, p.90). When toxaphene was applied experimentally to acreages of alfalfa in California at four pounds per acre, satisfactory control

of meadow mice, Microtus californicus aestuarinus Kellogg, was reported (23, p.61). Wolfe and Johansen, 1953, exposed captive meadow mice, Microtus montanus canescens Bailey, to excelsior litter soaked previously in a toxaphene spray solution. All mice died within five days after previously being observed licking the material from their skin. No mortality occurred after five days among another group of mice fed apple slices soaked with toxaphene spray (33, pp.92-93).

The acute toxicity of toxaphene in corn oil solutions to white rats when administered orally has been determined as follows: LD-0, 73 mg./kg.; LD-50, 120 mg./kg.; LD-100, 145 mg./kg. (24, p.24). The oral LD-50 for rats has also been reported 69 mg./kg. (20, p.130). The dry technical product produced slight symptoms, but no deaths at 4000 mg./kg. when applied to the skin of domestic rabbits (21, p.5). The dermal LD-50 of toxaphene to domestic rabbits dipped in wettable powder suspensions was between 1025 and 1075 mg./kg. (19, p.703).

DIELDRIN (1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,-4a,5,6,7,8,8a-octahydro-1,4-endo,exo-5,8-dimethanonaphthalene).

Dieldrin is relatively toxic to warm-blooded animals and is readily absorbed through the skin (13, p.519). Ryckman et al., 1953, sprayed dieldrin on a field in California at the rate of 1.04 pounds per acre for the control

of rodent fleas. Seven dead squirrels and rabbits were discovered four days later, presumably poisoned by this compound (25, p.598).

The acute oral LD-50 of dieldrin for white rats has been calculated as 87 mg./kg. (20, p.130), and as 38.3 mg./kg. (30, p.403). The acute dermal toxicity is reviewed in table 3.

TABLE 3. Acute dermal toxicity of dieldrin to small mammals as reported by various authors.

Animal	Formulation	Mg./Kg.	Mortality dead/total	Reference
White rat	technical powder	400 100	20 / 20 7 / 10	13, p.520
	25% concentrate	400	42 / 43	13, p.520
	6.25% solution	100	17 / 25	13, p.520
Domestic rabbit	4% in dimethyl phthalate	<150	LD-50	21, p.5
	dry recrystallized powder	250-360	MLD	30, p.404
	wettable powder aqueous suspension	400-450	LD-50	19, p.702

ALDRIN (1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4-endo,exo-5,8-dimethanonaphthalene).

The acute toxicity of aldrin appears to be several times greater than that of DDT to laboratory mammals. The median lethal dose for white rats has been assessed as 67 mg./kg. when given orally in an innocuous solvent

(20, p.130). When recrystallized aldrin was administered in peanut oil to young female rats, the LD-50 was calculated to be 45.9 mg./kg. (30, p.403). In dermal treatments rats receiving 200 mg./kg. of aldrin on shaved skin died in 48 to 72 hours (31, p.423). The LD-50 for domestic rabbits dipped in wettable powder suspensions was estimated to lie between 15 and 25 mg./kg. (19, p.702). The minimum lethal dose of dry recrystallized aldrin maintained in contact with the skin of rabbits for 24 hours was between 600 and 1250 mg./kg. (30, p.404). The LD-50 of aldrin in dimethyl phthalate applied to the skin of rabbits was less than 150 mg./kg. (21, p.5).

CHLORDANE (1,2,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene).

Chlordane has approximately the same degree of oral toxicity to laboratory mammals as has DDT, table 4. The LD-50 by dermal application on rabbits has been estimated to be less than 780 mg./kg. (21, p.5).

LINDANE (γ-1,2,3,4,5,6-hexachlorocyclohexane).

When white mice were given oral dosages of lindane as an aqueous suspension, no mortality occurred among those receiving 80 mg./kg. while two out of six mice died that received 200 mg./kg. (11, p.519). The oral LD-50 for white rats was estimated to be 125 mg./kg. (20, p.130). Lindane, when applied dermally to domestic rabbits in the dry form

TABLE 4. Acute oral toxicity of chlordane to small mammals as reported by various authors.

Animal	Formulation	Mg./Kg.	Mortality	Reference
White rat	olive oil solution	225-250	LD-50	16, p.264
	olive oil solution	200-250	LD-50	29, p.14
	innocuous solvent	457	LD-50	20, p.130
	cottonseed oil solution	590	LD-50	2, p.198
Domestic rabbit	olive oil solution	300	LD-50	29, p.16

was calculated to have an LD-50 greater than 4000 mg./kg. (21, p.5). The following LD-50 values were reported when lindane was applied to the skin of laboratory mammals as acetone solutions: mouse, 300 mg./kg.; rat, 500 mg./kg.; rabbit, 300 mg./kg. (32, p.510).

PARATHION (O,O-diethyl O-p-nitrophenyl thiophosphate).

This organic phosphorus compound is one of the most toxic insecticides to be used in large scale applications. Jackson, 1951, studied populations of deer mice living in forested areas in New Jersey that were contaminated by parathion dusts applied to adjacent fields at rates varying from 0.35 to 0.45 pounds per acre. No harmful effects could be attributed to these treatments (17, pp.277-278). When parathion was administered to male and female rats

in single oral doses, the LD-50 was found to be 15 and 6 mg./kg. respectively (8, p.80). Three mg./kg. has also been reported as the oral LD-50 for rats (20, p.131). The median lethal oral dose for commercial and purified parathion in corn oil to female white rats was 3.50 and 4.03 mg./kg. respectively (7, p.49). The dermal LD-50 of technical parathion for domestic rabbits was calculated to be between 40 and 50 mg./kg. (21, p.5). The approximate lethal dose of commercial and purified parathion when applied to the skin of male rabbits for six hours was 150 to 710 and 870 mg./kg. respectively (7, p.47).

MALATHION (O,O-dimethyl-S-(1,2-dicarboxyethyl) dithiophosphate).

Among the organic phosphorus insecticides, malathion has a relatively low order of toxicity to mammals. The acute oral toxicity to laboratory mammals is summarized in table 5. In these studies it is of note that the toxicity of malathion is inversely proportional to the purity of the compound. When 90 percent technical malathion was applied to the closely clipped abdomens of domestic rabbits, the animals exhibited no toxic symptoms suggestive of dermal absorption at dosages as high as four ml./kg. or approximately 4920 mg./kg. (14, p.401).

TABLE 5. Acute oral toxicity of malathion to small mammals as reported by various authors.

Animal	Formulation	Mg./Kg.	Mortality	Reference
White mouse	90% technical in vegetable oil	886	LD-50	14, p.400
	99+% in vegetable oil	3,321	LD-50	14, p.400
	99+% undiluted	4,059	LD-50	14, p.400
White rat	90% technical in vegetable oil	480	LD-50	14, p.400
	99+% in vegetable oil	1,845	LD-50	14, p.400
	99+% undiluted	5,843	LD-50	14, p.400
	99% undiluted	1,400	LD-50	9, p.352

EPN (O-ethyl O-p-nitrophenylbenzenethiophosphonate).

The acute oral LD-50 of EPN for white rats has been determined as 14.5 mg./kg. (20, p.131). Hodge et al, 1954, found a substantial difference in the susceptibility of male and female white rats to EPN. When the crystalline form was administered orally in peanut oil, the median lethal doses were 14 and 42 mg./kg. for female and male rats respectively. Technical liquid EPN was slightly more toxic (15, p.30). The approximate LD-50 of EPN when applied to domestic rabbits as a single dermal application for 24 hours was between 30 and 50 mg./kg. (21, p.5).

MATERIALS AND METHODS

EXPERIMENTAL ANIMALS.

The white-footed mouse, Peromyscus maniculatus rubidus Osgood, was used for determining the toxic range of the chemicals tested. The meadow mouse, Microtus montanus canicaudus Miller was utilized only in a limited number of experiments primarily because of the difficulties encountered in securing sufficient numbers of this species for test purposes.

Distribution and Economic Status.

Members of the genus Peromyscus are widely distributed in North America and occur in almost all types of habitat. P. m. rubidus occupy a range in western Oregon and California extending from San Francisco Bay to the Columbia River (3, p.183). They are nocturnal dwellers of brush and forest land but are commonly found in other situations. White-footed mice do not make burrows of their own but frequent those of other mice, gophers, and moles. Concentrations of this species have been captured around rock and brush piles and along well-vegetated fencerows. They are of economic importance primarily in cut-over forest lands where their destruction of conifer seed may retard reforestation.

Figure 1. White-footed mouse, Peromyscus maniculatus rubidus Osgood.

Figure 2. Meadow mouse, Microtus montanus canicaudus Miller.

Meadow mice are also one of the most abundant and widespread groups of mammals in North America and are generally of far greater economic importance than white-footed mice. The species of Microtus used in these experiments has a range that extends throughout the Willamette Valley and eastward through northern Oregon as far as Hood River and Wapinitia (12, p.414). Its principal habitat consists of open fields, meadows, and waste land where it constructs intricate systems of surface runways and underground tunnels. Large populations have been observed in irrigated clover and alfalfa fields and on undisturbed lands with a heavy grass cover. Its destructiveness to grain and forage crops is usually proportional to population numbers which appear to increase and decline with cyclic regularity. Some damage may also be sustained by orchard trees due to trunk and root girdling.

Trapping.

All wild mice utilized in the experiments were live-trapped or raised from parent stock obtained from the field. The live-traps employed were the common type manufactured from one-quart oil cans and mouse-sized snap-traps. They were simple in construction and operation and were very effective for capturing white-footed mice. The traps were made as follows: the wooden base was fastened by half its length to the inside wall of the can with two

small stove bolts, one on each side of the trigger. The hardware cloth door was cut slightly larger than the open end of the can and was wired to the guillotine. The pedal was also made of hardware cloth and was attached to the trigger with the metal bait retainer. For taking white-footed mice, peanut butter was used for bait. Each trap was furnished with waste cotton for nesting material which helped keep the mice alive on cold nights.

The only successful method found for live-trapping meadow mice was to bury the trap in a vertical position with its opening below one of their tunnels. The hole was constructed to allow for unimpeded closing of the door and was covered with sod or other material to exclude all light. Mice running along the tunnel in darkness would fall into the trap and release the mechanism for closing the door. Grain and nesting material were provided in each trap. Usually more than one mouse could be taken from the tunnel over a period of days before the trap would have to be moved.

Maintenance and Rearing.

In the laboratory mice were kept in glass battery jars with hardware cloth tops or in wire cages of various types. Cotton and fir shavings or excelsior were utilized for bedding in which the mice rapidly constructed nests and tunnels.

Figure 3. Live-trap of the type used for collecting white-footed mice.

Figure 4. Close-up of live-trap mechanism in the "set" position.

The laboratory diet consisted of chicken scratch feed which contained a variety of grains, high protein dog pellets, and fresh carrots. Water was supplied in beakers or inverted drinking bottles. All captured mice were conditioned a week or more to laboratory conditions prior to testing to eliminate any unhealthy or abnormal specimens. A certain number of white-footed mice were also obtained from a colony established from pregnant females collected in trapping operations. It was found that the young mice could be successfully reared and mated under laboratory conditions.

ORGANIC INSECTICIDES.

Chlorinated Hydrocarbons.

DDT or Dichloro-diphenyl-trichloroethane of the technical grade used in these experiments is a white- to cream-colored amorphous powder which contains approximately 70 percent of the p,p' isomer, 2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane. The vapor pressure of DDT is exceedingly low, resulting in its long residual properties as an insecticide. It is almost completely insoluble in water but soluble to varying degrees in organic solvents and oils. DDT has been used for the control of many insect pest species, particularly those involved in the transmission of diseases.

Toxaphene is a chlorinated camphene containing 67 to 69 percent chlorine. The technical product is an amber waxy solid with a mild piney odor, and has been used effectively for the control of grasshoppers, crop pests, and livestock parasites.

Dieldrin contains not less than 85 percent of 1,2,-3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-endo,exo-5,8-dimethanonaphthalene in the technical product. It is a white crystalline solid with potent insecticidal properties and a long residual effectiveness. It has been used to control a variety of agricultural insects and disease vectors.

Aldrin is an insecticidal product containing not less than 95 percent of 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,-8a-hexahydro-1,4-endo,exo-5,8-dimethanonaphthalene. It is a white crystalline solid that is insoluble in water but very soluble in a number of organic solvents. Aldrin has been used against grasshoppers and other crop pests and soil insects.

Chlordane of the technical grade contains not less than 60 percent of 1,2,4,5,6,7,8,8-octachloro-2,3,3a,4,-7,7a-hexahydro-4,7-methanoindene with the remainder consisting of related dicyclopentadiene derivatives. It is a viscous, dark amber-colored liquid that is miscible with organic solvents but insoluble in water. Chlordane is an effective insecticide for household pests, livestock

parasites, and crop insects.

Lindane contains not less than 99 percent of γ-1,2,3,-4,5,6-hexachlorocyclohexane, a colorless crystalline solid with a relatively high vapor pressure that results in a fumigant action on insects. It is relatively insoluble in water but soluble in organic solvents. Lindane has been used successfully for the control of household, animal, plant and soil insects.

Organic Phosphates.

Parathion is the commercial name for O,O-diethyl O-p-nitrophenyl thiophosphate. The technical material is a dark brown liquid with an odor of garlic. The sample used in these experiments had a purity of 98.8 percent. Parathion is very slightly soluble in water but highly miscible in organic solvents and oils except the paraffinic hydrocarbons. It has a wide application of use for the control of insects and mites.

Malathion or O,O-dimethyl-S-(1,2-dicarboxyethyl) dithiophosphate is a dark brown liquid with a strong garlic odor. The technical product utilized in these experiments was 95 percent pure. It is slightly soluble in water, moderately so in petroleum oils, and miscible in most organic solvents. It is a highly effective insecticide and acaricide for several species of arthropods as well as having a low order of toxicity to mammals.

EPN is the code name for O-ethyl O-p-nitrophenylbenzenethiophosphonate. A purified grade of the technical product, consisting of light buff crystals, was used to assess the toxicity of this compound. EPN has a slight degree of solubility in water and is very soluble in the organic solvents. This phosphonate is very effective for the control of mites and certain species of insects including aphids and the larvae of mosquitos.

TESTING PROCEDURES.

Two methods were employed for determining the range of acute toxicity.

Dermal Application.

All of the materials were first tested for toxic action by single dermal applications of acetone solutions. The dorsal region of each mouse extending from the pelvis to the nape was clipped of hair to allow for complete contact between the chemical and skin. The mice were held immobile in hardware cloth cylinders, weighed to the nearest 100 mg., and the calculated dosage applied over the bare area with a graduated 0.1 ml. pipette. The percent of toxicant in solution was adjusted so that the applied volume never exceeded 0.15 ml. Acetone at the rates employed is an innocuous solvent and volatilizes rapidly leaving only the chemical adhering to the skin. By this method the

chemical could gain entrance into the body by either direct penetration of the dermal surface or by oral ingestion during the grooming process.

Oral Administration.

The second method was used to evaluate a few selected insecticides for acute oral toxicity. The mice were weighed and anesthetized with ether prior to treatment. The materials in corn oil solutions were delivered directly into the stomach with a curved and blunted No. 18 gauge hypodermic needle attached to a glass 0.25 ml. syringe. The percent of toxicant in solution was adjusted so that the administered volume never exceeded 0.125 ml. Control mice treated with equal volumes of corn oil showed no ill effects.

Holding and Observation.

Following treatment by both methods the mice were held for a 10-day observation period in which mortality and symptoms, if any, were noted. The holding containers for white-footed mice were one-quart, wide-mouth glass jars. Cotton and fir shavings were used for nesting material and the regular diet was provided. The water supply for each jar was contained in a medicine dropper inserted through the screen top. Meadow mice were held in glass battery jars because of their larger size. All experiments were

conducted in a constant-temperature room maintained at approximately 70°F.

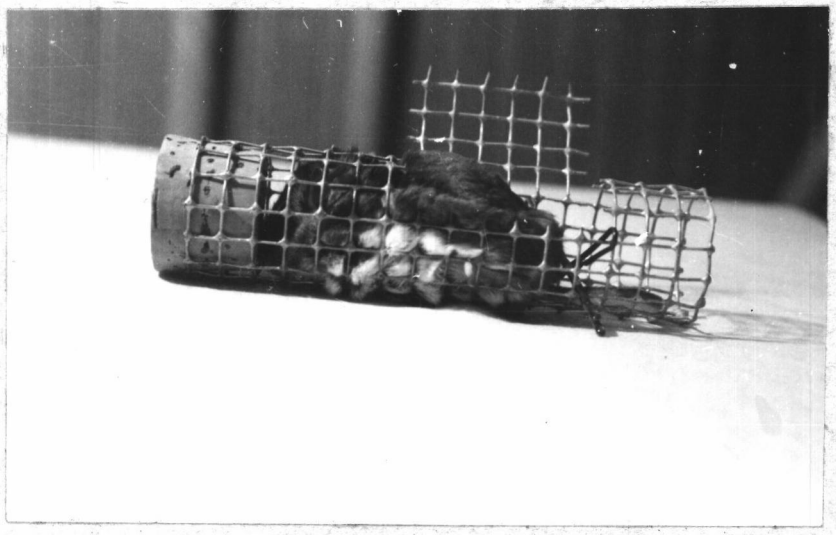

Figure 5. White-footed mouse confined in a wire cylinder prior to dermal treatment.

Figure 6. Equipment utilized in the toxicity experiments with field mice.

A. Wire holding cylinder.

B. Post-treatment holding cage.

C. Rubber-tipped forceps for handling mice.

D. Screw-type pipettor used for pipetting toxic materials.

E. Syringe and needle for oral treatments.

F. Graduated pipette for dermal treatments.

RESULTS

DDT TOXICITY.

DDT when applied to the skin of white-footed mice had a lethal range of 700 to 1,000 mg./kg. Of the animals subjected to doses of 800 mg./kg., two died within 48 hours, while three survived and appeared normal when observations were terminated at the end of 10 days (table 6). Mortality occurred primarily within 24 hours but as long as three days following treatment. Symptoms were manifest from one to two days. These included mild tremors and hyperexcitability at the lower dosages to severe tremors and convulsions at the higher levels of treatment. DDT appeared to produce some irritation at the upper dosages as mice were observed biting and scratching in an effort to remove the material from their skin.

The median lethal dose of DDT administered orally to white-footed mice was approximately 700 mg./kg. The compound also had a lethal range of 600 to 800 mg./kg. by the oral route (table 7). Mortality usually occurred within 24 hours, while symptoms from sublethal doses have been noted two to three days following treatment.

TABLE 6. Acute toxicity of DDT to white-footed mice by dermal application.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	Mortality : percent
500	male	16.0	survived	0 / 1	0
600	male	20.3	survived	0 / 2	0
	male	20.0	survived		
700	male	13.4	survived	0 / 2	0
	female	19.2	survived		
800	male	17.2	two days	2 / 5	40
	male	16.2	one day		
	female	17.2	survived		
	female	13.0	survived		
	female	17.7	survived		
1,000	male	17.0	one day	2 / 2	100
	female	14.7	one day		
2,000	female	13.3	one day	1 / 1	100
2,500	female	13.2	one day	1 / 1	100
3,000	male	15.5	three days	1 / 1	100

TABLE 7. Acute toxicity of DDT to white-footed mice by oral administration.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	Mortality percent
200	male	14.4	survived	0 / 2	0
	female	16.4	survived		
300	male	19.7	survived	0 / 3	0
	female	13.6	survived		
	female	16.9	survived		
400	female	14.5	survived	0 / 1	0
500	male	17.7	survived	0 / 1	0
600	female	21.0	survived	0 / 2	0
	female	17.6	survived		
700	male	16.0	survived	2 / 4	50
	male	14.6	survived		
	female	14.8	two days		
	female	14.0	one day		
800	male	15.8	one day	2 / 2	100
	female	14.9	one day		

TOXAPHENE TOXICITY.

Toxaphene displayed nearly the same level of toxicity to white-footed mice as did DDT when applied to the dermal surfaces. It had an approximate LD-50 of 800 mg./kg. and a lethal range of 700 to 1,100 mg./kg. (table 8). Mice treated with lethal doses were usually dead within 48 hours, although mortality has been delayed as long as the fifth day. Few symptoms were observed in most cases of poisoning.

Toxaphene was approximately three times as toxic to white-footed mice when administered orally than it was when applied to the skin. The LD-50 appears to be between the dosage rates of 200 and 300 mg./kg. with a lethal range of 70 to 300 mg./kg. The minimum lethal dose was 80 mg./kg. (table 9). Most of the mice were killed in one to two days with some deaths occurring as early as two to three hours. Symptoms exhibited were nervousness and hyperactivity followed by convulsions and periods of rest. Death usually ensued after several reoccurrences of the convulsions.

Meadow mice showed approximately the same susceptibility to oral doses of toxaphene as did white-footed mice (table 10). All mice receiving treatments of toxaphene in corn oil as high as 200 mg./kg. survived, while complete mortality occurred among those subjected to dosages of 300 and 400 mg./kg. Mortality occurred over a period of two to three days. Mice showed few symptoms other than inactivity and loss of appetite.

TABLE 8. Acute toxicity of toxaphene to white-footed mice by dermal application.

Dosage, Mg./Kg.	Sex	Weight, grams	Survival period	Mortality dead/total	: percent
400	female	16.1	survived	0 / 1	0
600	male	17.6	survived	0 / 2	0
	male	15.4	survived		
700	male	14.9	survived	0 / 1	0
800	male	18.8	survived	2 / 4	50
	male	22.6	one day		
	male	18.0	one day		
	female	20.6	survived		
1,000	male	16.1	five days	3 / 5	60
	male	23.1	three days		
	male	21.5	three days		
	male	16.0	survived		
	female	16.1	survived		
1,100	male	16.2	one day	2 / 2	100
	female	14.1	one day		
1,200	male	16.2	one day	2 / 2	100
	female	17.3	two days		
1,300	male	15.9	two days	2 / 2	100
	female	16.7	two days		
1,500	male	16.8	one day	1 / 1	100
2,000	male	17.7	one day	1 / 1	100

TABLE 9. Acute toxicity of toxaphene to white-footed mice by oral administration.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	Mortality : percent
70	male	17.2	survived	0 / 2	0
	male	16.8	survived		
80	male	16.8	ten days	1 / 3	33
	female	19.1	survived		
	female	16.5	survived		
90	male	16.7	one day	1 / 3	33
	male	24.1	survived		
	male	19.3	survived		
100	male	15.0	two hours	1 / 4	25
	female	24.0	survived		
	female	16.5	survived		
	female	14.1	survived		
200	male	18.0	survived	0 / 5	0
	male	16.7	survived		
	female	15.3	survived		
	female	16.2	survived		
	female	19.6	survived		
300	male	15.1	one day	3 / 3	100
	male	17.4	one day		
	female	15.0	three hours		
400	female	19.3	two days	3 / 3	100
	female	16.3	one day		
	female	16.4	two days		

TABLE 10. Acute toxicity of toxaphene to meadow mice by oral administration.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	percent
100	male	32.4	survived	0 / 1	0
200	male	34.2	survived	0 / 2	0
	female	27.8	survived		
300	female	30.0	two days	2 / 2	100
	female	28.2	two days		
400	female	26.8	three days	1 / 1	100

DIELDRIN TOXICITY.

Dieldrin appeared to be nearly eight times as toxic to white-footed mice by dermal application as did DDT. The LD-50 was within a lethal range of 100 to 125 mg./kg. with symptoms and mortality manifest from one to four days (table 11). Intermittent nervousness and convulsions were noted in some cases of fatal poisoning. At least partial abstinence from food and water by mice receiving sublethal doses resulted in some loss of weight prior to their recovery. This has been reported as a common sign of dieldrin poisoning and is attributed to starvation rather than to physiological disorders (13, p.519).

TABLE 11. Acute toxicity of dieldrin to white-footed mice by dermal application.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	: percent
100	male	16.1	survived	0 / 2	0
	male	16.7	survived		
125	male	22.7	one day	3 / 3	100
	male	17.0	two days		
	female	17.6	one day		
150	male	22.9	two days	2 / 2	100
	female	19.1	two days		
175	male	16.2	two days	1 / 1	100
200	male	15.5	four days	1 / 1	100
250	female	13.2	two days	1 / 1	100

ALDRIN TOXICITY.

The acute toxicity of aldrin by skin application to white-footed mice was slightly greater than that of dieldrin. The LD-50 was estimated to lie within the dosage rates of 75 to 100 mg./kg. with the lethal range 50 to 200 mg./kg. (table 12). Symptoms and mortality similar to those described for dieldrin were evident one to five days following treatment.

TABLE 12. Acute toxicity of aldrin to white-footed mice by dermal application.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	percent
50	female	15.4	survived	0 / 2	0
	male	18.4	survived		
75	male	22.8	survived	1 / 3	33
	male	18.7	survived		
	male	17.7	two days		
100	male	16.1	two days	2 / 3	67
	female	20.4	survived		
	female	15.5	five days		
200	female	17.3	one day	2 / 2	100
	female	16.2	two days		
250	female	14.0	two days	1 / 1	100

CHLORDANE TOXICITY.

Chlordane was approximately three to four times as toxic by skin application to white-footed mice as was DDT. The lethal range was found to be 100 to 600 mg./kg. and the minimum lethal dose 200 mg./kg. (table 13). Deaths occurred over a span of one to eight days following treatment. Symptoms similar to those produced by several of the other chlorinated hydrocarbons tested consisted of intermittent convulsions accompanied by grinding of the teeth and shrill squeaks.

TABLE 13. Acute toxicity of chlordane to white-footed mice by dermal application.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	Mortality percent
100	male	16.2	survived	0 / 2	0
	female	15.4	survived		
200	male	19.8	survived	1 / 3	33
	male	15.7	survived		
	female	15.1	six days		
400	male	18.9	two days	2 / 3	67
	male	20.0	survived		
	female	16.0	two days		
600	male	18.2	eight days	3 / 3	100
	male	16.9	one day		
	female	15.0	two days		
800	male	16.7	two days	2 / 2	100
	female	14.0	three days		
1,000	male	14.1	two days	2 / 2	100
	female	17.4	four days		
1,200	female	16.8	four days	1 / 1	100
1,400	female	19.3	four days	1 / 1	100

LINDANE TOXICITY.

The median lethal dose of lindane by skin application to white-footed mice was found to be approximately 600 mg./kg., which made this compound about one-fourth to one-third times more toxic than DDT (table 14). The lethal range was determined as 400 to 800 mg./kg. with mortality occurring in a period of one to three days. Mice showed symptoms of intermittent convulsions accompanied by shrill squeaking prior to death.

TABLE 14. Acute toxicity of lindane to white-footed mice by dermal application.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	percent
300	male	16.6	survived	0 / 1	0
400	male	16.6	survived	0 / 2	0
	female	17.1	survived		
500	male	21.2	survived	1 / 3	33
	male	21.5	survived		
	male	16.1	one day		
600	male	14.4	two days	2 / 4	50
	male	23.9	survived		
	female	14.7	one day		
	female	19.8	survived		
700	male	15.5	one day	2 / 3	67
	female	21.0	survived		
	female	13.3	three days		
800	male	18.2	three days	2 / 2	100
	female	12.7	one day		

PARATHION TOXICITY.

Parathion, one of the more toxic organic insecticides, was also the most toxic compound evaluated by skin application to white-footed mice. It had a lethal range of 30 to 40 mg./kg. which made it nearly 25 times as toxic as DDT (table 15). Few symptoms were evident except depression and inactivity. All deaths occurred within a period of two to three days.

TABLE 15. Acute toxicity of parathion to white-footed mice by dermal application.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	: percent
25	female	14.2	survived	0 / 2	0
	female	15.0	survived		
30	male	20.8	survived	0 / 4	0
	male	19.9	survived		
	male	25.3	survived		
	female	17.4	survived		
40	male	15.4	two days	4 / 4	100
	male	20.1	three days		
	male	15.4	two days		
	female	16.3	two days		
50	male	15.9	two days	2 / 2	100
	male	15.4	two days		

MALATHION TOXICITY.

Limited tests with malathion applied to the skin of white-footed mice demonstrated the low mammalian toxicity of this compound (table 16). Mice treated with doses of 3,000 mg./kg. survived and appeared normal at the end of the test period. Of two mice subjected to doses of 6,000 mg./kg., one died within four days following treatment while the other survived.

TABLE 16. Acute toxicity of malathion to white-footed mice by dermal application.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	Mortality percent
3,000	male	15.4	survived	0 / 2	0
	male	16.0	survived		
6,000	male	21.0	four days	1 / 2	50
	female	14.0	survived		

EPN TOXICITY.

EPN was about eight to nine times as toxic as DDT to white-footed mice by dermal treatment. It had an approximate LD-50 of 100 mg./kg. and a lethal range of 50 to 200 mg./kg. (table 17). Mice died within one to three days following treatment with the compound. Animals subjected to fatal doses displayed symptoms of depression and inactivity prior to death. Lacrimation with the accumulation of white matter around the eyes was evident in a few cases of poisoning.

TABLE 17. Acute toxicity of EPN to white-footed mice by dermal application.

Dosage, Mg./kg.	Sex	Weight, grams	Survival period	Mortality dead/total	Mortality percent
25	male	17.4	survived	0 / 1	0
50	male	17.1	survived	0 / 2	0
	female	14.2	survived		
100	male	15.2	one day	3 / 6	50
	male	15.6	survived		
	male	15.0	survived		
	male	15.5	survived		
	female	14.3	one day		
	female	14.7	two days		
200	male	19.6	one day	3 / 3	100
	female	18.1	three days		
	female	16.2	one day		
300	female	15.6	two days	1 / 1	100

DISCUSSION

Toxicological data pertaining to the lethal effects of several of the newer organic insecticides on white-footed mice have been obtained and the results summarized in table 18. Direct comparison of this information with that found in the literature on the various species of small mammals may not be entirely valid but certain interesting similarities and observations can be speculated upon.

DDT as a dry powder or in various dry formulations demonstrated little or no toxicity when applied to the skin of rabbits. In these same studies percutaneous absorption was facilitated with an increase in toxicity when DDT was dissolved in the oily solvent dimethyl phthalate (21, p.4) and 26, p.990). In the present work the acute toxicity of DDT was only slightly less by dermal application than by intragastric injection, probably due to the fact that the mice were not prevented from cleaning their skin. It is not known whether the fleeting contact of acetone with the dermal surface had any effect on insecticide penetration. The dermal toxicity of lindane applied as an acetone solution to laboratory animals (32, p.510) was generally similar to the range found in the present study for white-footed mice, but was much higher than that reported when the dry powder was applied to the skin of rabbits (21, p.5). It was not stated whether the

TABLE 18. A summary of the acute toxicity of several of the newer organic insecticides to white-footed mice.

Insecticide	Site of application	MLD, mg./kg.	Lethal Range, mg./kg.
Parathion	skin	40	30-40
Aldrin	skin	75	50-200
EPN	skin	100	50-200
Dieldrin	skin	125	100-125
Chlordane	skin	200	100-600
Lindane	skin	500	400-800
Toxaphene	skin stomach	800 80	700-1,100 70-300
DDT	skin stomach	800 700	700-1,000 600-800
Malathion	skin	6,000	3,000-6,000

animals were restrained during the tests to prevent oral ingestion of the compound.

Toxaphene has also been reported to have a very low toxicity when applied to the skin of rabbits in the technical waxy form (21, p.5). Wolfe and Johansen, 1953, indicate that toxaphene in commercial spray preparations is lethal to meadow mice wholly or partially by skin contact (33, p.92-93). The solvents and emulsifiers incorporated in such formulations undoubtedly facilitate penetration of the toxicant and may even exert some toxic action of their own. Xylene, a common constituent in spray concentrates,

has been found to be lethal to white-footed mice in doses as small as 0.1 ml. by dermal application. The percutaneous absorption of aldrin and dieldrin has also been demonstrated to be enhanced by the use of oily solvents (30, p.404).

Solvent vehicles appear to play a similar role in the gastrointestinal absorption of several insecticides. Coburn and Treichler, 1946, found the acute oral LD-50 of an aqueous suspension of crystalline DDT for white-footed mice to be approximately 1,500 mg./kg. (5, p.214). In the present study the same determination of DDT dissolved in corn oil was approximately 700 mg./kg. indicating an increased absorption of the oil solution. Smith and Stohlman, 1944, state that aqueous suspensions of DDT are much less toxic to rats than are olive oil solutions, and attribute the differential to the poor gastrointestinal absorption of the former (26, p.988). The acute oral toxicity of malathion to rats and mice has also been significantly increased when the compound was administered in vegetable oil (14, p.400).

These data serve to indicate that the toxicity of an insecticide to mammals in its technical or pure state may be profoundly influenced by the nature of the materials used for its formulation. Such factors are not only of importance when initially evaluating the toxic properties of an insecticide but must be taken into consideration when the formulated product is applied in the field.

SUMMARY AND CONCLUSIONS

An investigation of the acute toxicity of several chlorinated hydrocarbon and organic phosphorus insecticides to the white-footed mouse, Peromyscus maniculatus rubidus Osgood, has been conducted. Limited toxicological data were also obtained for the meadow mouse, Microtus montanus canicaudus Miller.

Experimental animals were collected from the field by live-trapping techniques or reared from parental stock from the same source. The mice were maintained on a standard diet, supplied with adequate water and nesting material, and held under these conditions for at least one week prior to testing.

Six chlorinated hydrocarbon insecticides: DDT, toxaphene, dieldrin, aldrin, chlordane, and lindane; and three organic phosphorus compounds: parathion, malathion, and EPN, were evaluated for acute toxicity.

Two testing procedures were utilized. Single dermal applications of the toxicants in acetone solutions were made to the dorsal skin area of mice after the removal of hair by clipping. Intoxication by this method could result from percutaneous absorption and/or oral ingestion of the toxicant when the animals groomed their skin and fur. The acute oral toxicity was assessed for DDT and toxaphene by administration of corn oil solutions intragastrically with a blunt hypodermic needle attached to a glass syringe.

Observations on mortality and symptoms were conducted for a period of ten days.

DDT appears to be a compound with a relatively low order of toxicity to white-footed mice by either dermal application or oral administration. Forty percent of the mice subjected to skin treatments succumbed to doses of 800 mg./kg., while fifty percent of the orally-treated animals died from the effects of 700 mg./kg. of DDT. Symptoms characteristic of DDT intoxication ranging from hyperexcitability to severe tremors and convulsions were manifest as long as two days after treatment. Mortality usually occurred within 24 hours.

The acute toxicity of toxaphene was about equal to that of DDT by skin application to white-footed mice, with the LD-50 and MLD approximately 800 mg./kg. By the oral route the MLD was as low as 80 mg./kg. and the LD-50 was estimated to be between 200 and 300 mg./kg. Symptoms exhibited by poisoned mice were nervousness and intermittent convulsions prior to death.

The acute oral toxicity of toxaphene to meadow mice was about the same range as that found for white-footed mice, with the LD-50 estimated to lie between 200 and 300 mg./kg.

Aldrin and its oxygen derivative dieldrin displayed nearly the same levels of toxicity to white-footed mice and were the most poisonous compounds of the group of

chlorinated hydrocarbons tested. The minimum lethal doses observed for aldrin and dieldrin were 75 and 125 mg./kg. respectively.

Chlordane was three to four times as toxic to white-footed mice as was DDT. The minimum lethal dose was 200 mg./kg. while two out of three mice succumbed to dosages of 400 mg./kg. Symptoms were manifest in fatal cases as intermittent convulsive spasms, squeaking, and tooth grinding.

Lindane was slightly more poisonous to white-footed mice than were either toxaphene or DDT. The approximate LD-50 was 600 mg./kg. and the MLD 500 mg./kg.

Parathion, the most potent insecticide tested, demonstrated a toxicity to white-footed mice of nearly 25 times that of DDT. The MLD was found to be 40 mg./kg. when the compound was applied to the integument.

Malathion was the least toxic of any of the chemicals tested. White-footed mice treated with doses of 3,000 mg./kg. survived the treatment and displayed no signs of poisoning, while one out of two mice died at the 6,000 mg./kg. level.

The toxicity of EPN to white-footed mice was very close to that of aldrin and dieldrin. The approximate LD-50 was determined as 100 mg./kg. The symptoms of intoxication produced by all three of the organic phosphorus insecticides were essentially depression and inactivity. Lacrimation

with the accumulation of matter around the eyes of mice was evident in some cases of EPN poisoning.

BIBLIOGRAPHY

1. Adams, Lowell et al. The effects on fish, birds, and mammals of DDT used in the control of forest insects in Idaho and Wyoming. Journal of wildlife management 13:245-254. 1949.

2. Ambrose, Anthony M. et al. Toxicological and pharmacological studies on chlordane. A.M.A. archives of industrial hygiene and occupational medicine 7:197-210. 1953.

3. Bailey, Vernon. The mammals and life zones of Oregon. North American fauna 55:1-416. 1936.

4. Benton, Allen H. Effects on wildlife of DDT used for control of Dutch elm disease. Journal of wildlife management 15:20-27. 1951.

5. Coburn, Don R. and Ray Treichler. Experiments on toxicity of DDT to wildlife. Journal of wildlife management 10:208-216. 1946.

6. Couch, Leo K. Effects of DDT on wildlife in a Mississippi river bottom woodland. Transactions of the North American wildlife conference 11: 323-329. 1946.

7. Deichmann, William B., William Pugliese, and James Cassidy. Effects of dimethyl and diethyl paranitrophenyl thiophosphate on experimental animals. A.M.A. archives of industrial hygiene and occupational medicine 5:44-51. 1952.

8. DuBois, Kenneth P. et al. Studies on the toxicity and mechanism of action of p-nitrophenyl diethyl thionophosphate (parathion). The journal of pharmacology and experimental therapeutics 95: 79-91. 1949.

9. DuBois, Kenneth P. et al. Studies on the toxicity and mechanism of action of some new insecticidal thionophosphates. A.M.A. archives of industrial hygiene and occupational medicine 8:350-358. 1953.

10. Erickson, Arnold B. Effects of DDT mosquito larviciding on wildlife. II. Effects of routine airplane larviciding on bird and mammal populations. Public health reports 62:1254-1262. 1947.

11. Furman, Deane P. Toxicity of benzene hexachloride to mammals. Journal of economic entomology 40:518-521. 1947.

12. Hall, E. Raymond, and E. Lendell Cockrum. A synopsis of the North American microtine rodents. University of Kansas museum of natural history publications 5:373-498. 1953.

13. Hayes, Wayland J., Jr., Frederick F. Ferguson, and Jules S. Cass. The toxicology of dieldrin and its bearing on field use of the compound. The journal of tropical medicine 31:519-522. 1951.

14. Hazleton, Lloyd W. and Emily G. Holland. Toxicity of malathon. Summary of mammalian investigations. A.M.A. archives of industrial hygiene and occupational medicine 8:399-405. 1953.

15. Hodge, Harold C. et al. Studies of the toxicity and of the enzyme kinetics of ethyl p-nitrophenyl thionobenzene phosphonate (EPN). The journal of pharmacology and experimental therapeutics 112:29-39. 1954.

16. Ingle, Lester. Toxicity of chlordane to white rats. Journal of economic entomology 40:264-268. 1947.

17. Jackson, William B. Populations of the wood mouse (Peromyscus leucopus) subjected to the applications of DDT and parathion. Ecological monographs 22:259-281. 1952.

18. Johansen, Carl. Mouse control in Yakima and Wenatchee valley orchards with toxaphene. Washington state horticultural association proceedings 48:80-82. 1952.

19. Johnston, Barbara L. and W. G. Eden. The toxicity of aldrin, dieldrin, and toxaphene to rabbits by skin absorption. Journal of economic entomology 46:702-703. 1953.

20. Lehman, Arnold J. Chemicals in foods: a report to the association of food and drug officials on current developments. II. Pesticides. Association of food and drug officials of the United States of America, quarterly bulletin 25:122-133. 1951.

21. Lehman, Arnold J. Chemicals in foods: a report to the association of food and drug officials on current developments. II. Pesticides. Section 2. Dermal toxicity. Association of food and drug officials of the United States of America, quarterly bulletin 26:3-9. 1952.

22. Marsh mice bow to toxaphene. Farm management 1:52. Nov.-Dec., 1951.

23. Morrison, A. E. The meadow mouse (Microtus californicus) problem in Sacramento county. California department of agriculture, bulletin 42:59-62. 1953.

24. Parker, W. Leroy and John H. Beacher. Toxaphene, a chlorinated hydrocarbon with insecticidal properties. Newark, University of Delaware, 1947. 26p. (University of Delaware. Agricultural experiment station. Bulletin no. 264).

25. Ryckman, Raymond E., Charles T. Ames, and Chester C. Lindt. A comparison of aldrin, dieldrin, heptachlor, and DDT for control of plague vectors on the California ground squirrel. Journal of economic entomology 46:598-601. 1953.

26. Smith, M. I. and E. F. Stohlman. The pharmacologic action of 2,2,-bis (p-chlorophenyl) 1,1,1 trichloroethane and its estimation in the tissues and body fluids. Public health reports 59:984-993. 1944.

27. Stickel, Lucille F. Field studies of a Peromyscus population in an area treated with DDT. The journal of wildlife management 10:216-218. 1946.

28. Stickel, Lucille F. Wood mouse and box turtle populations in an area treated annually with DDT for five years. The journal of wildlife management 15:161-164. 1951.

29. Stohlman, E. F., W. T. S. Thorp and M. I. Smith. Toxic action of chlordan. A.M.A. archives of industrial hygiene and occupational medicine 1:13-19. 1950.

30. Treon, Joseph F., and Frank P. Cleveland. Toxicity of certain chlorinated hydrocarbon insecticides for laboratory animals, with special reference to aldrin and dieldrin. Agriculture and food chemistry 3:402-408. 1955.

31. Waud, R. A. A study of the toxicology of the insecticide aldrin (hexachloro-hexahydro-dimethano naphthalene). The journal of pharmacology and experimental therapeutics 106:423. 1952.

32. West, T. F., and G. A. Cambell. DDT and newer persistent insecticides. New York, chemical publishing co., 1952. 632p.

33. Wolfe, Homer and Carl Johansen. Toxaphene spray for mouse control in Washington orchards. Washington state horticultural association proceedings 49:89-93. 1953.

34. Woodard, Geoffrey, Arthur A. Nelson and Herbert O. Calvery. Acute and subacute toxicity of DDT (2,2,-bis (p-chlorophenyl) 1,1,1-trichloroethane) to laboratory animals. The journal of pharmacology and experimental therapeutics 82:152-158. 1944.