UNIVERSITY OF MARYLAND EXTENSION
Solutions in your community

Pesticide Information Leaflet

Department of Entomology
College Park, MD 20742
(301) 405-3913

College of Computer, Mathematical & Natural Sciences
College of Agriculture & Natural Resources

Check out the Pesticide Education and Assessment Program web site at http://pesticide/umd.edu

No. 41: Mode of Action of Structural Pest Control Chemicals

Amy E. Brown, Ph.D., Coordinator
Elizabeth Ingianni, M.S., Program Assistant
Pesticide Education and Assessment Programs
Orig. 2005; Last rev. August 2013

INTRODUCTION

To understand how insecticides and rodenticides work (their mode of action), it is necessary to understand how the pests' targeted physiological systems normally function. Insecticides used in structural pest control operations generally target the nervous system, growth and development, energy production, or water balance. Most rodenticides used in pest control interfere with blood clotting. A general description of these processes is presented in this leaflet, followed by a table listing the mode of action of pesticides (insecticides and rodenticides) used by structural pest control operators. Throughout the text, italics are used to indicate important physiological processes or terms, and bold text is used to identify pest control chemicals or classes of chemicals.

PHYSIOLOGICAL SYSTEMS AND PROCESSES TARGETED

THE NERVOUS SYSTEM

The nervous system functions as a fast-acting means of transmitting important information throughout the body. The nervous system has two components:

1. The *peripheral nervous system* receives and transmits incoming signals (taste, smell, sight, sound, and touch) to the central nervous system, and transmits outgoing signals to the muscles and other organs, effectively telling them how to respond.

2. The *central nervous system (CNS)* interprets the signals and coordinates the body's responses and movements. The CNS is composed of the brain and spinal cord in humans and a series of ganglia, or nerve bundles, in insects.

A *neuron* is a single nerve cell. It connects with other neurons and with muscle fibers (the basic units of muscles). These connecting neurons (or connecting neuron and muscle fiber) do not touch, however, and instead have a slight gap between them called a *synapse*.

Incoming signals (the pain from a sharp object, the sight of a predator, the odor of food, etc.) are transformed by the neuron into an electrical charge that travels down the length of the neuron. When the electrical charge reaches the end of the neuron, it stimulates a chemical messenger, called a *neurotransmitter*, to be released into the synapse. This neurotransmitter crosses the synapse and binds to a *receptor* on the receiving end of the next neuron. Binding to the receptor causes the signal to be converted back into an electrical charge in the second neuron, and the signal is transmitted along the length of that neuron. After transmitting its message across the synapse, the neurotransmitter is resorbed back into its originating neuron, and the nerve cell is then in a resting stage until the next signal is received.

This process repeats over and over until the signal has reached the CNS to be interpreted. Impulses from the CNS to the peripheral nervous system continue in the same way until the signal reaches the appropriate muscles or organs.

Both humans and insects have many different neurotransmitters that work at different sites throughout the nervous system. Some neurotransmitters are *excitatory*: they result in the signal being sent on through the synapse to a connecting neuron. Others are *inhibitory*: they result in the signal being blocked from traveling to a connecting neuron. In this way, the body ensures that the signal has the desired effect in each muscle or organ, since many different reactions are involved in even a simple movement.

Of the many neurotransmitters that both insects and humans have, *acetylcholine (ACh)* and *gamma-aminobutyric acid (GABA)* are important targets of some insecticides. ACh can either excite or inhibit its target neurons. Depending on the particular neuron and the specific receptors at the site, ACh can cause particular neurons to "fire," continuing the nerve impulse transmission, or it can cause the nerve impulse to stop at that particular site. In contrast, GABA is strictly an inhibitory neurotransmitter. When GABA is activated at a synapse, the nerve impulse stops.

Some insecticides interfere with the normal action of these neurotransmitters. Other insecticides attacking the nervous system work by other means. The most common mechanisms are explained below.

<u>Cholinesterase inhibitors</u>

Organophosphate and **carbamate** insecticides are known as **cholinesterase inhibitors**. They bind to the enzyme *cholinesterase*, which is normally responsible for breaking down ACh after it has carried its message across the synapse. Cholinesterase inhibitors control insects by binding to their cholinesterase, making the insect's cholinesterase unavailable to break down the ACh. As a result, the neurotransmitter continues to cause the neuron to "fire," or send its electrical charge. This causes overstimulation of the nervous system, and the insect dies.

Like insects, humans also use ACh as a neurotransmitter, and we use cholinesterase to break it down once the signal has been transmitted. Cholinesterase poisoning in

humans can be very severe. Upon each exposure to an organophosphate or carbamate insecticide, more cholinesterase becomes bound and is unavailable to do its job. Although cholinesterase inhibition by carbamates is somewhat reversible, organophosphate poisoning is not reversible. This means the insecticide does not release the bound cholinesterase. Fortunately, the body continually produces cholinesterase, although it may take several weeks to again reach the desirable circulating level.

Applicators using cholinesterase-inhibiting pesticides regularly should consider having their cholinesterase level monitored. A simple blood test performed in the preseason and again at intervals throughout the application season predicts whether an applicator is being exposed to too much organophosphate or carbamate. For more information, refer to *Pesticide Information Leaflets* **No. 7: Cholinesterase Testing** and **No. 30: Cholinesterase Monitoring - A Guide for the Health Professional**.

Acetylcholine Mimics

Imidacloprid, a nicotinoid insecticide, mimics the action of the neurotransmitter acetylcholine (ACh). Although cholinesterase is not affected by this insecticide, imidacloprid itself directly and continually stimulates the nerve, and the end result is similar to that caused by cholinesterase inhibitors – overstimulation of the nervous system leading to poisoning and death. Fortunately, imidacloprid is a closer mimic for the insect's ACh than for human ACh, giving this insecticide more specificity for insects and less ability to poison humans.

Chloride Channel Modulators

Avermectins are derived from a soil microorganism and belong to a group called the macrolactones. **Fipronil** is a member of the class of insecticides known as phenylpyrazoles. Avermectins and fipronil both bind to the GABA-gated chloride channel. This channel, when activated, normally blocks reactions in some nerves, preventing excessive stimulation of the CNS.

Avermectins activate the chloride channel, causing an inhibitory effect: the activated channel blocks or inhibits normal reactions, which, when excessive, results in the insect's death. Fipronil has the opposite effect on the chloride channel; this insecticide blocks the channel from activating and performing its normal inhibitory action. Thus, when fipronil binds to the channel, the nerve is overstimulated, and death eventually occurs.

Sodium Channel Modulators

Pyrethrins are naturally-occurring compounds derived from members of the chrysanthemum family. While they have a quick knock-down effect against insects, they are unstable in the environment, so may not last long enough to kill the pest.

Pyrethroids are synthetic versions of pyrethrins, specifically designed to be more stable in the environment (although still lasting only days or weeks), and thus provide longer-lasting control.

Pyrethrins and pyrethroids act on tiny channels through which sodium is pumped to cause excitation of neurons. They prevent the sodium channels from closing, resulting in continual nerve impulse transmission, tremors, and eventually, death.

Pyrethrins and pyrethroids are well-known irritants of humans' respiratory systems as well as of the skin and eyes. Applicators who have an allergic reaction to these insecticides must either increase the amount of personal protective equipment worn during handling, or stop working with this class of insecticides.

GROWTH AND DEVELOPMENT

Unlike humans, insects must shed their skin in order to grow and develop into their next life stage. Insects' skin is a hard *exoskeleton*, also called the *cuticle*, which provides both protection and structure. Molting is necessary not only for the insect to grow, but also for the insect to reach the adult stage so that it can reproduce. Some insecticides target the insect's growth and development processes.

Chitin Synthesis Inhibitors (CSIs)

Chitin is an important component of the insect's cuticle. Some insecticides, called **chitin synthesis inhibitors**, block the production of chitin. An insect poisoned with a CSI cannot make chitin and so cannot molt. Because molting must take place for the insect to reach the adult stage, a CSI-poisoned insect also cannot reproduce. Eventually, the insect dies.

Because humans do not make chitin, CSIs are not considered toxic to humans. However, CSIs are very toxic to any organism that has an exoskeleton, such as crustaceans (shellfish), and should be used with great care, if at all, in areas where they could contaminate the environment.

Insect Growth Regulators (IGRs)

Insects produce a special protein called *juvenile hormone*, which is circulated throughout the insect's body and "tells" the insect to stay in its current life stage. After a certain amount of time, the insect stops producing juvenile hormone, and the insect *metamorphoses*, or changes, into its next life stage.

Some insecticides, called **insect growth regulators (IGRs)**, mimic juvenile hormone. Insects poisoned with IGRs act as if they have not stopped making juvenile hormone. They cannot molt or reproduce, and eventually they die.

Like chitin synthesis inhibitors, IGRs can affect molting in closely-related organisms. Humans do not make or use juvenile hormone; therefore IGRs are considered to have little human toxicity.

METABOLISM AND ENERGY PRODUCTION

Interference with Water Balance

Insects have a thin covering of wax on their bodies that helps prevent water loss. Silica aerogels and diatomaceous earth are tiny, sharp particles that scratch through this protective layer and absorb the protective oils, leaving the insect's body vulnerable to water loss, or dehydration.

Boric acid also disrupts water balance in insects, but its mode of action is not completely understood. It appears to disrupt digestion, causing the insect to starve to death. Boric acid is also toxic to humans and can harm the stomach, intestines, blood, and brain, and can irritate the respiratory tract and skin.

Interference with Energy Production

All organisms must generate energy from the food they take in. Several classes of

insecticides inhibit or disrupt energy production. Exactly how they work differs, but the end result is the same. Initially, the insect has enough stored energy to continue its basic functions. While it can eat and digest food in the initial stages after being poisoned, it cannot produce energy from the food. Eventually, the insect "runs out of steam," stops eating and moving, and dies.

Hydramethylnon, sulfuryl fluoride, chlorfenapyr, and sulfluramid are all in different classes of insecticides, and work through different mechanisms, but all disrupt energy production. Chlorfenapyr and sulfluramid must be converted to an active form before they can cause this effect. Fortunately, humans do not seem to be as able to produce the activated form as insects, so are less affected by chlorfenapyr and sulfluramid. Hydramethylnon also is much less toxic to humans than to insects.

Sulfuryl fluoride is considered moderately toxic to humans. However, it poses a unique hazard because it is used as a fumigant in enclosed spaces and is odorless and colorless, meaning it has a potential for higher exposure. Labels of this product specify time and concentration limits during which people must stay out of the treated area until the gas has dissipated below the level that would cause any acute effects for humans.

Interference with Micronutrient Balance

Micronutrients are substances that the body needs in relatively small amounts in order to function properly; however, excessive amounts of micronutrients can be toxic. Vitamins and elements such as phosphorus, potassium, selenium, calcium, and other inorganic compounds are examples of micronutrients.

Cholecalciferol is the activated form of vitamin D, and this substance has a use as a rodenticide. Cholecalciferol pulls calcium and phosphorus from the bones into the blood stream. Too much calcium in the blood causes calcification (hardening) of soft tissues. Eventually, death occurs, usually from heart failure. While poisoning is very rare in humans, calciferol can affect pets if eaten.

THE CIRCULATORY SYSTEM

Anticoagulants

Several rodenticides are considered anticoagulants, meaning they interfere with the production of vitamin K, which is necessary for blood clotting. The anticoagulants also increase the permeability of the capillaries, allowing blood to seep out of the vessels and into the organs and surrounding body cavity. When poisoned with an anticoagulant, the rodents bleed internally and, since the blood will not clot, the animal eventually bleeds to death.

There are two classes of anticoagulants: **coumarins** and **inandiones**. Coumarins are usually effective in only a single dose, while inandiones must be eaten in several doses to cause death. These anticoagulants are considered to have low toxicity to humans, but other animals and pets may be more sensitive.

Table 1: Modes of Action for Pesticides Commonly Used for Control of Structural Pests. Derived from data developed and organized by the Insecticide Resistance Action Committee (IRAC). For a more comprehensive list, and to be sure the information is most current, access the IRAC website directly at **www.irac-online.org**. The table can be found under Tools at **www.irac-online.org/eClassification/**

Common name (examples of trade names[1])	Class of pesticide	Targeted system/process	Mode of action
abamectin B1 (Advert)	Avermectin insecticide	Nervous system	Chloride channel activator
acephate (Orthene)	Organophosphate insecticide	Nervous system	Cholinesterase inhibitor (irreversible)
bendiocarb (Ficam)	Carbamate insecticide	Nervous system	Cholinesterase inhibitor
bifenthrin (Brigade, Capture, Empower, Talstar)	Pyrethroid insecticide	Nervous system	Sodium channel modulator
boric acid	Inorganic insecticide	Metabolic processes/ water balance	Water balance disruptor/ starvation inducer
brodifacoum (Havoc, Talon)	Coumarin rodenticide	Circulatory system	Anticoagulant (single dose)
bromadiolone (Contrac)	Coumarin rodenticide	Circulatory system	Anticoagulant (single dose)
carbaryl (Sevin)	Carbamate insecticide	Nervous system	Cholinesterase inhibitor
chlorfenapyr (Pirate)	Pyrrole insecticide	Metabolic processes/ Energy production	Oxidative phosphorylation uncoupler
chlorophacinone (Rozol)	Inandione rodenticide	Circulatory system	Anticoagulant (multiple dose)
chlorpyrifos (Dursban)	Organophosphate insecticide	Nervous system	Cholinesterase inhibitor (irreversible)
cholecalciferol (Muritan, Quintox, Rampage)	Activated vitamin D; used as an insecticide	Micronutrient balance	Calcium mobilizer
cyfluthrin (Baythroid, Laser, Tempo)	Pyrethroid insecticide	Nervous system	Sodium channel modulator
cypermethrin (Ammo)	Pyrethroid insecticide	Nervous system	Sodium channel modulator
deltamethrin (Flythrin, DeltaDust, DeltaGard, Suspend)	Pyrethroid insecticide	Nervous system	Sodium channel modulator
diatomaceous earth	Mineral product mined from fossilized algae; used as an insecticide	Metabolic processes	Water balance disruptor
diazinon	Organophosphate insecticide	Nervous system	Cholinesterase inhibitor (irreversible)

Common name (examples of trade names[1])	Class of pesticide	Targeted system/process	Mode of action
diphacinone (Diphacin, DiTrac, Promar, Ramik)	Inandione rodenticide	Circulatory system	Anticoagulant (multiple dose)
fenoxycarb (Insegar, Logic, Pictyl, Torus, Varikill)	Insect growth regulator (IGR)	Growth and development	Juvenile hormone mimic
fipronil (Combat, FrontLine, Maxforce)	Phenylpyrazole insecticide	Nervous system	Chloride channel modulator
hexaflumuron (Sentricon)	Benzoylurea insecticide	Growth and development	Chitin synthesis inhibitor (CSI)
hydramethylnon (Amdro, Combat, MaxForce, Siege)	Amidinohydrazone insecticide	Metabolic processes/ Energy production	Electron transport inhibitor
hydroprene (Gentrol)	Insect growth regulator (IGR)	Growth and development	Juvenile hormone mimic
imidacloprid (Advantage, Merit)	Nicotinoid insecticide	Nervous system	Acetylcholine agonist (mimic)
lambda-cyhalothrin (Karate, Matador, Warrior)	Pyrethroid insecticide	Nervous system	Sodium channel modulator
lufenuron (Program)	Benzoylurea insecticide	Growth and development	Chitin synthesis inhibitor (CSI)
methoprene (Precor)	Insect growth regulator (IGR)	Growth and development	Juvenile hormone mimic
permethrin (Flee)	Pyrethroid insecticide	Nervous system	Sodium channel modulator
propetamphos	Organophosphate insecticide	Nervous system	Cholinesterase inhibitor (irreversible)
propoxur (Baygon)	Carbamate insecticide	Nervous system	Cholinesterase inhibitor
pyriproxyfen (Archer, Esteem, Flea Fix, Nylar)	Insect growth regulator (IGR)	Growth and development	Juvenile hormone mimic
silica gels and dusts	Inorganic insecticide	Metabolic processes	Water balance disruptor
sulfluramid (Enforcer, First-Line, Fluorgard, Raid Max)	Halogenated alkyl sulfonamide insecticide	Metabolic processes/ Energy production	Oxidative phosphorylation uncoupler
sulfuryl fluoride (Vikane)	Fumigant	Metabolic processes/ Energy production	Disruption of the glycolysis and fatty acid cycles

[1] Trade names are provided solely as an aid to the reader. No assurance is made that the list is inclusive of all trade names for a given active ingredient.

SOURCES

EXTOXNET Pesticide Information Profiles. Various. National Pesticide Telecommunication Network Fact Sheets. extoxnet.orst.edu/pips/ghindex.html, accessed 01/25/2005.

Gilkeson, LA and RW Adams. (Undated.) *Integrated Pest Management Manual for Structural Pests in British Columbia*. Ministry of Environment, Lands and Parks, Pollution Prevention and Pesticide Management Branch, British Columbia, Canada. www.env.gov.bc.ca/epd/ipmp/publications/manuals/structural_pests/toc.htm, accessed 01/24/2005.

Insecticide Resistance Action Committee. 2012. *Mode of Action Classification Scheme v 7.2*. http://www.irac-online.org/content/uploads/MoA-classification.pdf, accessed 8/20/2013.

Valles, SM and PG Koehler. (Undated.) School IPM. *Technical Information – Pesticides*. University of Florida, Gainesville, FL. schoolipm.ifas.ufl.edu/index.html accessed 01/24/2005.

Ware, GW and DM Whitacre. 2004. *An Introduction to Insecticides, 4th Ed*. MeisterPro Information Resources, Willoughby, OH.

Sulfuryl Fluoride Technical Fact Sheet. National Pesticide Information Center, Oregon State University Extension Services, 2000. http://npic.orst.edu/factsheets/sftech.pdf accessed 08/21/2013.

Hydramethylnon Technical Fact Sheet. National Pesticide Information Center, Oregon State University Extension Services, 2002. http://npic.orst.edu/factsheets/hydratech.pdf accessed 08/21/2013.

Rodenticides Topic Fact Sheet. National Pesticide Information Center, Oregon State University Extension Services, 2011. http://npic.orst.edu/factsheets/rodenticides.pdf accessed 08/21/2013.

US Environmental Protection Agency. 2013. *Recognition and Management of Pesticide Poisonings*: Sixth Edition. Ch 17. http://npic.orst.edu/RMPP/rmpp_ch17.pdf