

Mode of Action of Landscape Insecticides and Miticides

Pesticide Information Leaflet No. 42

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Revised January 2006 (Orig. Pub. April 2005)

Introduction

To understand how pesticides work (their mode of action), it is necessary to understand how the pests' targeted systems normally function. It is also helpful to understand how human systems function in order to see similarities and differences between humans and the pests we try to control.

Another reason it is important to understand the modes of action of the pesticides we use is to prevent development of pesticide resistance in the target pest(s). Using pesticides with the same modes of action contributes to this problem by killing the susceptible pests and leaving only those with resistance to the entire class of

pesticides that work through similar mechanisms. Development of pest resistance can be avoided or delayed by rotating pest control chemicals that work through different modes of action

Insecticides and miticides used in landscape management generally target the nervous system, growth and development, or energy production of the pest. A description of these processes is presented in this leaflet, followed by a table listing the mode of action of insecticides and miticides used by landscape managers. 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.

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* to receive and transmit incoming signals (taste, smell, sight, sound, and touch) and to transmit outgoing signals to the muscles and other organs, effectively telling them how to respond, and 2.) the *central nervous system (CNS)* that interprets the signals and coordinates the body's responses and movements.

A *neuron* is a single nerve cell. It connects with other neurons and with muscle fibers (the basic units of muscles) through gaps at the end of each neuron. The gap between neurons, or between a neuron and a muscle fiber, is called a *synapse*.

Incoming signals (the pain from a sharp object, the sight of a predator, or the odor of food, etc.) are transformed by the neuron into an *electrical charge* which then travels down the length of the neuron. The charged particles (called ions) that deliver the charge move through *channels* in the membrane of the neurons. There are four main types of channels to allow different ions to move along the neuron: *sodium channels*, *potassium channels*, *calcium channels*, and *chloride channels*. Many of the channels have gates that open or close in response to a certain stimulus, which is an important mechanism through which some pesticides work, as explained later in this leaflet.

When an electrical charge reaches the end of the neuron, it stimulates a chemical messenger, called a *neurotransmitter*, to be

released from the end of the neuron. 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 (the brain and spinal cord in humans and a series of ganglia, or nerve bundles, in the insect) 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), and some are *inhibitory* (they result in the reaction 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 an inhibitory neurotransmitter – when GABA is the neurotransmitter 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.

Cholinesterase Inhibition

Organophosphate and carbamate insecticides are known as *cholinesterase inhibitors*. They bind to the enzyme that is normally responsible for breaking down ACh after it has carried its message across the synapse. When an insect has been poisoned by a cholinesterase inhibitor, the cholinesterase is not available to help break down the ACh, and 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 cholinesterase to break it down, and 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 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 Leaflet No. 7: Cholinesterase Testing and No. 30: Cholinesterase Monitoring -- A Guide for the Health Professional.

Acetylcholine Receptor Stimulation

Neonicotinoid insecticides act as agonists of the acetylcholine receptor. That is, they mimic the action of the neurotransmitter, acetylcholine (ACh). Although cholinesterase is not affected by these insecticides, the nerve is continually stimulated by the neonicotinoid itself, and the end result is similar to that caused by cholinesterase inhibitors – overstimulation of the nervous system leads to poisoning and death. Fortunately, the neonicotinoids are a closer mimic for the insect’s ACh than for human ACh, giving this class of insecticides more specificity for insects and less ability to poison humans.

Spinosad is also an acetylcholine receptor agonist. The exact mechanism of spinosad is somewhat different than that of the neonicotinoid class, but the end result is the same.

Chloride Channel Regulation

Avermectins are derived from a soil microorganism and belong to a group called the macrolactones. Avermectins bind to the chloride channel. This channel normally blocks reactions in some nerves, preventing excessive stimulation of the central nervous system (CNS). Avermectins activate the chloride channel, causing an inhibitory effect, which, when excessive, results in the insect's death.

Organochlorine insecticides of the cyclodiene type affect the chloride channel by inhibiting the GABA receptor. As explained above, the GABA receptor has an inhibitory function at its site. When a cyclodiene insecticide binds to the GABA molecule, the neurotransmitter can no longer close the chloride channel for which it acts as a gate. Thus there is nothing to stop the electrical charge from continuing down the neuron. The end result is overstimulation of the nervous system.

Bifenazate affects the GABA-gated chloride channel as an agonist. That is, it causes the gate to have the same action as GABA would cause, which closes the gate. Nerve impulses are then unable to travel down the chloride channel.

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 to 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.

Hormones play various roles in molting. Disruption of, or interference with, any of these hormones inactivates the molting process. Some insecticides target the insect's growth and development processes through interfering with hormones, and others through blocking the production of a structural component of the exoskeleton.

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)

_____ **Insect Growth Regulators, or IGRs**, attack the insect's endocrine system, which produces the hormones needed for growth and for development into an adult form. Insects poisoned with IGRs cannot molt or reproduce, and eventually they die.

Many of the currently available IGRs mimic a special protein called *juvenile hormone*. In a normal insect, juvenile hormone is circulated throughout the insect's body and "tells" the insect to stay in its current stage. After a certain amount of time, the insect stops producing juvenile hormone, and the insect *metamorphoses*, or changes, into its next life stage. When an insect is poisoned by an IGR that mimics juvenile hormone, the insect doesn't receive the signal to metamorphose because, even though the insect may have stopped producing juvenile hormone, the IGR is still

circulating throughout its body and sending the signal to stay in the current stage.

Another hormone important in metamorphosis is *ecdysone*. The insecticide **tebufenazide** interferes with the production of ecdysone, causing the insect to be unable to molt.

Prothoracicotropic hormone (PTTH) is another insect development hormone. The insecticide **azadirachtin**, which is derived from neem oil, interferes with synthesis of PTTH. Besides its ability to kill through interfering with growth and development, azadirachtin also acts as a feeding deterrent, as discussed later in this leaflet.

Humans do not make or use the hormones insects use in molting. Because of this, IGRs are considered to have little human toxicity.

Nonspecific Growth Regulators

The exact mode of action of the **mite growth regulator** hexythiazox is not well-understood. Hexythiazox kills the eggs before the mites hatch and also some immature mites. Adult mites are not killed, although adults exposed to residues may lay eggs that are not viable.

Energy Production

All organisms must generate energy from the food they take in. As organisms digest the nutrients in the food they consume, they store the energy from those nutrients in molecules known as *adenosine triphosphate (ATP)*. The energy stored in

the ATP molecules can then be used to do the body's work such as thinking, moving, growing, or synthesizing chemicals and structures that the body needs.

Some insecticides inhibit or disrupt energy production. Initially, the insect can mobilize 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 more energy from the food. Eventually, the insect "runs out of steam," stops eating and even moving, and dies.

Electron Transport Inhibition

Electron transport is an important process in the production of energy in plants and animals. When this process is disrupted, the energy cannot be stored for later use, and is simply lost. **Organo-chlorine insecticides of the aliphatic type** interfere with electron transport, effectively shutting down the target organism's ability to produce energy from its food.

Metabolism

Some insecticides block feeding. Different classes of insecticides work through different mechanisms, as described below.

Bacillus thuringiensis (Bt) is a microbe that produces a crystal with a toxic effect against some insects. When Bt is eaten by a larva, it attacks the lining of the insect's midgut and causes it to stop feeding and ultimately to die. Different strains, or varieties, of Bt produce slightly different crystals which have selective toxicity against various insects.

Azadirachtin acts as both a feeding deterrent and a growth regulator. In this case, feeding is affected through azadirachtin's interference with *phagostimulants*, which play a role in normal feeding behavior of insects and related arthropods.

Cryolite, an inorganic insecticide, is a non-specific feeding blocker. Its exact mechanism of action is not yet well understood.

Common name and examples of trade names¹	Class of pesticide	Targeted system/process	Mode of action
abamectin B1 (Abacide, Avid, Greyhound, Vivid II)	Avermectin	Nervous system	Chloride channel activator
acephate (Orthene)	Organophosphate	Nervous system	Cholinesterase inhibitor
azadirachtin (Azatin, Bioneem, Triact)	Botanical from neem oil	Growth and development / Metabolic processes	Prothoracicotropic hormone (PTTH) inhibitor and Phagostimulant disruptor
Bacillus thuringiensis (Bt, Dipel)	Microbial	Metabolic processes	Insect midgut membrane disruptor
bifenazate (Acramite)	Hydrazine carboxylate	Nervous system	GABA-gated chloride channel agonist
bifenthrin (Talstar)	Pyrethroid	Nervous system	Sodium channel modulator
carbaryl (Sevin)	Carbamate	Nervous system	Cholinesterase inhibitor
cinnamaldehyde (Cinnacure, Cinnamite)	Botanical	Energy production	Exact mode of action not well understood; possibly interference with glucose uptake or utilization
cryolite (Prokil)	Inorganic – sodium aluminofluoride	Metabolic processes	Non-specific feeding blocker
cyfluthrin (Tempo)	Pyrethroid	Nervous system	Sodium channel modulator
cypermethrin (Cynoff)	Pyrethroid	Nervous system	Sodium channel modulator
deltamethrin (DeltaGard)	Pyrethroid	Nervous system	Sodium channel modulator
dicofol (Kelthane)	Organochlorine (Diphenyl aliphatic type)	Energy production	Electron transport inhibitor – Site II
diflubenzuron (Dimilin)	Benzoylurea	Growth and development	Chitin synthesis inhibitor (CSI)
dimethoate (Rebelate)	Organophosphate	Nervous system	Cholinesterase inhibitor
fluvalinate (Mavrik)	Pyrethroid	Nervous system	Sodium channel modulator
halofenazide (Mach 2)	Diacylhydrazine	Growth and development	Ecdysone agonist/disruptor

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.

Common name and examples of trade names¹	Class of pesticide	Targeted system/process	Mode of action
hexythiazox (Hexygon,)	Carboxamide mite growth inhibitor	Growth and development	Unknown or non-specific mode of action
horticultural oils	Petroleum-based products	Metabolic processes	Mechanical suffocation by blocking the breathing apparatus, or by disruption of cellular membranes
imidacloprid (Admire, Advantage, Gaucho, Merit, Provado)	Neonicotinoid	Nervous system	Acetylcholine agonist
insecticidal soap (M-Pede, Safer's Insecticidal Soap)	Fatty Acids	Metabolic processes	Membrane disruption
lambda-cyhalothrin (Scimitar)	Pyrethroid	Nervous system	Sodium channel modulator
malathion	Organophosphate	Nervous system	Cholinesterase inhibitor
methoxychlor	Organochlorine (Cyclodiene type)	Nervous system	GABA-gated chloride channel antagonist
neem oil extract (Azatin, Neemix, Trilogy) – see azadirachtin			
permethrin (Astro)	Pyrethroid	Nervous system	Sodium channel modulator
phosmet (Imidan)	Organophosphate	Nervous system	Cholinesterase inhibitor
pyrethrins (Pyrenone)	Pyrethrins	Nervous system	Sodium channel modulators
pyriproxyfen (Distance)	Insect growth regulator (IGR)	Growth and development	Juvenile hormone mimic
rotenone	Botanical	Energy production	Electron transport inhibitor – Site I
spinosad (Entrust, Success)	Spinosyn	Nervous system	Nicotinic acetylcholine receptor agonist
tebufenoxide (Confirm)	Diacylhydrazine	Growth and development	Ecdysone agonist/disruptor

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References

- EXTOXNET Pesticide Information Profiles. Various. National Pesticide Telecommunication Network Fact Sheets. <http://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. <http://wlapwww.gov.bc.ca/epd/ipm/docs/tablcont.html> accessed 01/24/2005.
- Goodell, PB. 2004. "Insecticide resistance management and quality cotton." UC Statewide IPM Project. 3 pp.
- Insecticide Resistance Action Committee. 2004. "Mode of action classification v 3.3.2." <http://www.irac-online.org/resources/moa.asp>, accessed 01/24/2005; 04/06/2005.
- Larson, LL. 2001. "Mergers, regulation, resistance management, and new product approaches: the odyssey continues for industry." Informal Conference during the Annual Meeting of Entomological Society of America; San Diego, CA, December 10, 2001. <http://www.entsoc.org/Protected/AMT/AMT27/Text/Other/ConferenceReport.html>, accessed 04/06/2005.
- McKinley, N, S Kijima, G Cook, and D Sherrod. 2002. "Avaunt (indoxacarb): A new mode of action insecticide for control of several key orchard pests." *Proc. 76th Ann. W. Orchard Pest & Disease Mgt. Conf.* Portland, OR. 2 pp.
- Meister, RT. 2005. Crop Protection Handbook. Meister Media Worldwide, Willoughby, OH. 1242 pp.
- Pesticide Action Network (PAN). Pesticide Database. <http://www.pesticideinfo.org/Index.html>, accessed 04/06/2005.
- Robertson, CT. 2005. Greenbook. Turf and Ornamental Reference for Plant Protection Products. Vance Communications Corp., New York, NY. 1320 pp.
- Sclar, DS. 1994. "Neem: Mode of action of compounds present in extracts and formulations of *Azadirachta indica* seeds and their efficacy to pests of ornamental plants and to non-target species." Colorado ST. Univ., Ft. Collins, CO. http://www.colostate.edu/Depts/Entomology/courses/en570/papers_1994/sclar.html, accessed 04/06/2005.
- US Environmental Protection Agency (EPA). 1998. "Pymetrozine pesticide tolerance filing." *Fed. Reg.* 63(194):53902-53911.
- US Environmental Protection Agency (EPA). 2000. Kaolin (100104) Registration Eligibility Document. US EPA, Washington, DC. http://www.epa.gov/pesticides/biopesticides/ingredients/tech_docs/red_100104.htm, accessed 04/06/2005.
- US Environmental Protection Agency (EPA). 2000. "Pyridaben; pesticide tolerance related material." *Fed. Reg.* 65(136):43704-43713.
- Valles, SM and PG Koehler. (Undated.) "School IPM. Technical information – Pesticides." University of Florida, Gainesville, FL. <http://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.
- Whalon, ME and BA Wingerd.. 2003. "Bt: Mode of action and use." *Arch. Ins. Biochem. Physiol.* 54:200-211.