Insecticide chemistry must be rotated to prevent and/or delay resistance.

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Most pesticides including insecticides have what is know as "single site" activity. The pesticide affects one very specific target site which results in death of the pest. Knowing the exact mechanism(s) responsible for control of insects is critically important in IPM programs. Insecticide chemistry must be rotated effectively to prevent and/or delay the onset of resistance. The Insecticide Resistance Action Committee (IRAC) has developed a classification system which groups insecticides by their mode of action. Insecticides with the same group number work at the same target site. There may be subgroups within groups which are designated with a letter after a number, i.e. 2A. Insecticides within subgroups work at the same target site but by different mechanisms. IRAC group numbers are listed for the compounds discussed. Due to size limitations, not all insecticides and their mode of action are discussed in this article.

**Disruption of the Nervous System**

To understand how insecticides that disrupt the nervous system work, one must understand how the nervous system works. Cells in the nervous system are called neurons which are responsible for signal transmission. Signals are transmitted along neurons by sequential pumping of sodium and potassium ions in and out of cells through sodium channels in the membrane. Sequential pumping of sodium and potassium forces unidirectional signals along neurons. Between neurons there is a gap called a synapse. When a signal transmitted down neurons reaches the synapse, there are chemical molecules (neurotransmitters) released which bind to the next neuron and turn on OR turn off signal transmission down that neuron.

Carbamate [Group 1A] and organophosphate [Group 1B] insecticides work by disrupting processes which occur at synapses. When "on" signals reach the end of neurons, acetylcholine an excitatory neurotransmitter is released and binds to the acetylcholine receptor site of the next neuron effectively turning on signal transmission down that neuron. The "off switch" is the enzyme acetylcholinesterase (AChE) which degrades acetylcholine to produce acetate and choline. Carbamate and organophosphate insecticides bind to AChE changing its shape so that it can not degrade acetylcholine. The switch does not get turned off. There is repetitive firing of signals which results in tremors, uncoordinated movement and death.

Fipronil insecticides such as ethiprole and fipronil [Group 2B] block the function of chloride channels. When gamma aminobutyric acid (GABA) an inhibitory neurotransmitter binds to the terminus of neurons after crossing synapses, chloride channels are turned on. Chloride ions are released which effectively turns signals off. Fiprole insecticides bind to the same site as GABA which blocks GABA from binding. Chloride channels are not activated and no chloride is released to dampen the "on signal". This results in hyper-excitation and convulsions with resultant death. The old cyclodiene insecticides [Group 2A] such as aldrin chlorordane and dieldrin work by the same mechanism.

Pyrethrins and pyrethroids [Group 3A] bind to sodium channels in membranes of neurons where sodium and potassium ions are pumped in and out. Binding of pyrethrins or pyrethroids to sodium channels prevents closure of individual channels and prevents normal flow of sodium out of cells. Neurons are in a permanent "on" state which results in tremors, then paralysis and death. The old organochlorine insecticides [Group 3B] such as DDT also bind to sodium channels.

Nicotine [Group 4B], sulfoxaflor [Group 4C], and the neonicotinoid [Group 4A] insecticides such as imidacloprid mimic acetylcholine and bind to acetylcholine receptors. The enzyme acetylcholinesterase has no activity on this group of compounds so there effectively is no "off switch". The result is over stimulation of nerve signals with hyperexcitation, paralysis and death.

Spinosyn [Group 5] compounds such as spinosad and spinetoram work by binding to nicotinic acetylcholine receptors at a site different than nicotine or neonicotinoid insecticides. The binding causes a change in shape of the nicotinic acetylcholine receptors which results in prolonged acetylcholine responses. This prolonged "on" signal results in involuntary muscle contraction, tremors, paralysis and death.

Avermectin [Group 6] insecticides such as abamectin and emamectin work by mimicking gama aminobutyric acid which results in uncontrolled release of chloride from chloride channels. The release of chloride effectively stops signal flow to muscles. The result is paralysis followed by death.

Indoxacarb [Group 22A] and metaflumizone [Group 22B] are oxadiazine insecticides which work by binding to sodium channels at a location different than pyrethroids and blocking inflow of sodium into nerve cells. This blocking of sodium inflow disrupts
signal flow which results in paralysis and death. This mode of action is different than pyrethrins or pyrethroids.

Chlorantraniliprole, cyantraniliprole, flubendiamide and ryanodine, are anthanilic diamide insecticides [Group 28] that cause death of insects by disruption of calcium flow within muscle tissue. When nerve signals reach muscle tissue, events occur which results in the influx of calcium ions into muscle tissues which causes muscle contraction. Ryanodine receptors are responsible for the release of calcium into muscle tissue. The anthanilic diamide insecticides bind to the ryanodine receptors locking them partially open. Calcium leaks out of muscle tissues which results in the inability to regulate muscle function which causes paralysis and death.

**Disrupting of Energy Production**

Adenosine triphosphate (ATP) is an energy rich molecule used by all organisms. When ATP is converted to adenosine diphosphate (ADP), a phosphate molecule and energy are released. The energy released is used by cells to drive cellular processes. ADP then is converted back to ATP by the enzyme ATP synthase. The cycling of ATP to ADP and conversion of ADP to ATP is continuous in organisms.

Chlorfenapyr and sulfluramid [Group 13] prevent the formation of ATP by inhibiting flow of protons which is necessary for the enzyme ATP synthases to convert ADP back to ATP. Hydramethylnon [Group 20A] and rotenone [Group 21B] work by slightly different mechanisms, however both prevent flow of electrons which is needed to convert ADP to ATP. Although the insecticides which operate by disruption of energy production are slow to cause symptoms, the result is inactivity, paralysis and death.

**Insect Growth Regulators**

Insects pass through developmental stages from egg to adult. Since insects have no bones, structural support is from an exoskeleton which is composed of about 50% chitin. Insect exoskeletons are basically a suit of armor. In order for insects to proceed to the next development stage, the old exoskeleton must be removed and a new exoskeleton laid down. Removal of the old exoskeleton and replacement with a new exoskeleton is called a molt. There are two insect hormones which control insect development. Juvenile hormones control the stage of development of the insect. Molting hormone (ecdysome) is responsible for triggering molts at the appropriate time.

One group of insect growth regulators inhibit synthesis of chitin. Buprofezin [Group 16] diflubenzuron, lufenuron and noviflumuron [Group 15] are examples of insecticides which prevent production of chitin. This causes problems for insects when they molt.

Juvenile hormone mimics such as fenoxycarb [Group 7B] hydroprene, methoprene, [Group 7A] and pyriproxyfen [Group 7C] mimic the natural juvenile hormone compounds in insects. Effects of juvenile hormone mimics include malformed insects after molts which is usually lethal. There are often reproductive problems in adults exposed to juvenile hormone mimics. These materials perform best when levels of juvenile hormone are low; later larval or early pupal stages.

Halofenozide and tebufenozide [Group 18] mimic the molting hormone and force a premature molt which is often lethal.

**Disruption of Insect Guts**

These insecticides are derived from the bacteria Bacillus thuringiensis (B.t.) [Group 11A] and Bacillus sphaericus [Group 11B] and are host specific. These bacteria produces toxins made of proteins. When the proteins are consumed by a susceptible insect, they bind to specific sites on the membrane of the mid-gut. The mid-gut is where digestion of food and absorption of nutrients occurs. Binding of the toxins causes disruption of this membrane which ultimately ruptures which leads to paralysis of the gut and death.

References:

Insecticide Resistance Action Committee. April 2012. IRAC MoA Classification Scheme.