LECTURE OUTLINE

- Key Concepts
  - What is a pest
  - Pesticides : Types and Uses
  - Pros and Cons of using pesticides
  - Pesticides regulations
  - Alternatives to chemical pests

- Pest and Pesticide
  - Unwanted organism, interferes with food production, human health, and peace and quietness of environment and causes economic harm
  - The word pesticide itself means “pest killer.” Pests include bacteria, fungi, insects, weeds, rodents, and other living things that affect humans, animals, or plants adversely. Depending on the kind of pest against which they are effective, pesticides are known as bactericides, fungicides, nematicides, insecticides, herbicides, and so on.

  - A pesticide is any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest. Pests can be insects and insect-like organisms, mice and other vertebrate animals, unwanted plants (weeds), or fungi, bacteria and viruses that cause plant diseases. Though often misunderstood to refer only to insecticides, the term pesticide also applies to herbicides, fungicides, and various other substances used to control pests.

  - Any material, whether naturally derived or not, that is sold or distributed with the intent to control or eliminate any pest (weeds, insects, microorganisms, etc.) is classified as a pesticide. By their very nature, pesticides create some risk of harm to humans, animals, or the environment because they are designed to kill or otherwise adversely affect living organisms. Many household products are pesticides

- An ideal pesticide:-
  - Kills target pest
  - Non-persistent, short lived
  - No adverse effects on other organisms.
  - No genetic resistance
  - Less costly than economic losses

- Types of Pesticides:-

Chemical, organism, facility or activity that kills pest organisms.

- Insecticides
- Herbicides
- Fungicides
- Bactericides
- Rodenticides

- Biopesticides

Biopesticides (also known as biological pesticides) are pesticides derived from such natural materials as animals, plants, bacteria, and certain minerals. For example, canola oil and baking soda have pesticidal applications and are considered biopesticides.

- Types of Biopesticides

  - Microbial pesticides
  - Plant pesticides
  - Biochemical pesticides

Microbial pesticides consist of a microorganism (e.g., a bacterium, fungus, virus, or protozoan) as the active ingredient. Microbial pesticides can control many different kinds of pests, although each separate active ingredient is relatively specific for its target pest[s]. For example, there are fungi that control certain weeds, and other fungi that kill specific insects.

The most widely used microbial pesticides are subspecies and strains of Bacillus thuringiensis, or Bt. Each strain of this bacterium produces a different mix of proteins, and specifically kills one or a few related species of insect larvae. While some Bt's control moth larvae found on plants, other Bt's are specific for larvae of flies and mosquitoes. The target insect species are determined by whether the particular Bt produces a protein that can bind to a larval gut receptor, thereby causing the insect larvae to starve.

Plant pesticides are pesticidal substances that plants produce from genetic material that has been added to the plant. For example, scientists can take the gene for the Bt pesticidal protein and introduce the gene into the plant's own genetic material. Then the plant, instead of the Bt bacterium, manufactures the substance that destroys the pest. Both the protein and its genetic material are regulated by EPA; the plant itself is not regulated.

Biochemical pesticides are naturally occurring substances that control pests by non-toxic mechanisms. Conventional pesticides, by contrast, are generally synthetic materials that directly kill or inactivate the pest. Biochemical pesticides include substances, such as insect sex pheromones, that interfere with mating, as well as various scented plant extracts that attract insect pests to traps.

Because it is sometimes difficult to determine whether a substance meets the criteria for classification as a biochemical pesticide, EPA has established a special committee to make such decisions.

Advantages of Biopesticides

- Biopesticides usually are inherently less harmful than conventional pesticides.
- Biopesticides generally affect only the target pest and closely related organisms, in contrast to broad-spectrum conventional pesticides that may affect organisms as different as birds, insects, and mammals.
- Biopesticides often are effective in very small quantities and often decompose quickly, thereby resulting in lower exposures and largely avoiding the pollution problems caused by conventional pesticides.
- When used as a component of Integrated Pest Management (IPM) programs, biopesticides can greatly decrease the use of conventional pesticides, while crop yields remain high.

- First Generation Pesticides (i.e. pre 1940s)
  - Natural substances
  - Sulphur, lead, arsenic, mercury
  - Plant extracts: nicotine, pyrethrum
    - Degradable

- Second Generation Pesticides
  - Synthetic organic compounds
    - 630 biologically-active compounds, 35,000 pesticide products
  - DDT – Dr. Mueller, Nobel Prize in 1948
  - Attributes : cheap, easy to produce, persistent, insoluble in water.

- Third Generation Pesticides (1985+)
  - Genetically engineered predators
  - Genetically engineered plants
    - Round-up ready corn, wheat, rice.

Pesticide Ingredients

· Pesticide products contain both "active" and "inert" ingredients. The terms "active ingredient" and "inert ingredient" have been defined by Federal law, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), since 1947.

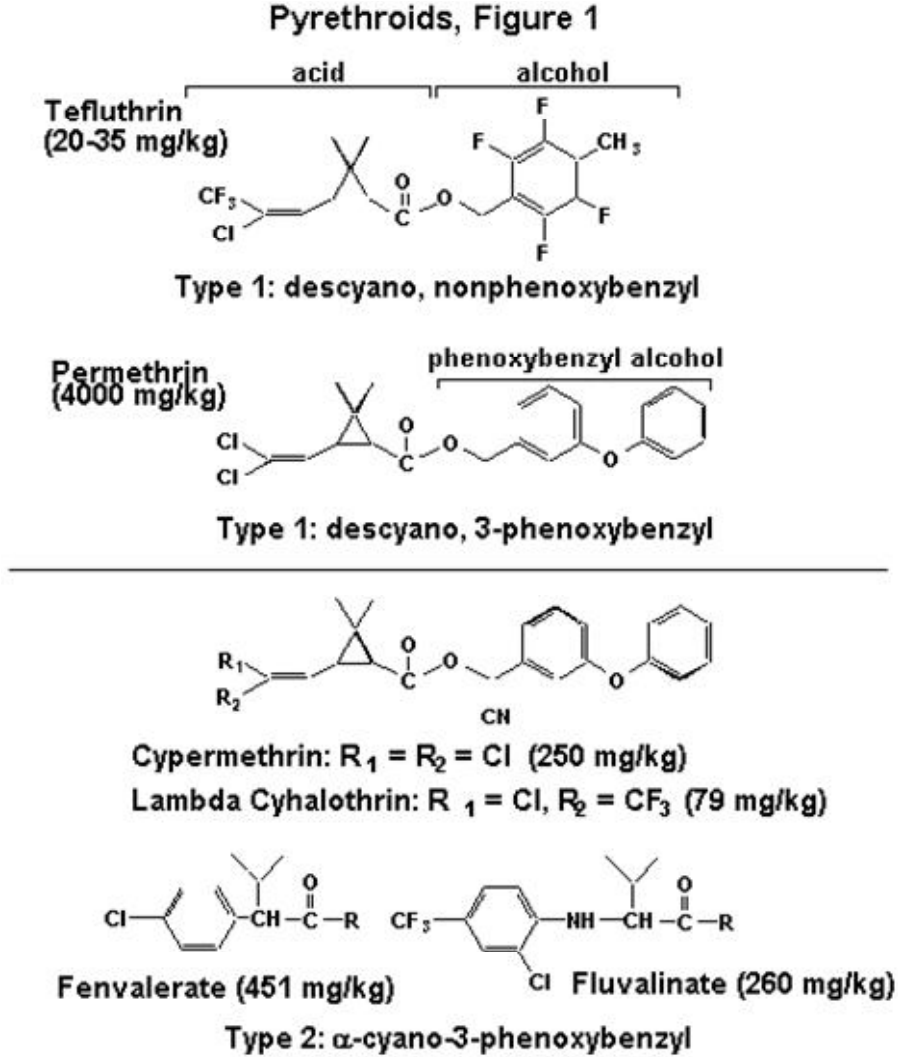
· Active Ingredients
An active ingredient is one that prevents, destroys, repels or mitigates a pest, or

is a plant regulator, defoliant, desiccant, or nitrogen stabilizer. By law, the active ingredient must be identified by name on the label together with its percentage by weight.

· Inert Ingredients
An inert ingredient is simply any ingredient in the product that is not intended to affect a target pest. For example, isopropyl alcohol may be an active ingredient and antimicrobial pesticide in some products; however, in other products, it is used as a solvent and may be considered an inert ingredient. The law does not require inert ingredients to be identified by name and percentage on the label, but the total percentage of such ingredients must be declared.

Chemistry and Mode of Action of Insecticides

(Source :- http://pesticide.umd.edu)
Compounds Affecting Voltage-Dependent Sodium Channels
Pyrethroids, Figure 1.



The pyrethroid insecticides are typically esters of chrysanthemic acid having a high degree of lipophilicity (fat solubility). The original compounds in this series were the natural pyrethrins, which are isolated from the flowers of chrysanthemum. Pyrethroid chemistry and action are classified as Type 1 or Type 2, depending on the alcohol substituent. The Type 1 group is rather broadly defined and includes pyrethroids containing descyano-3-phenoxybenzyl or other alcohols. Many of the older nonphenoxybenzyl Type 1 compounds (*e.g*., pyrethrins, allethrin, tetramethrin) are unstable in the environment and this characteristic prevented their use in row crops. Introduction of the phenoxybenzyl (*e.g*., permethrin) or certain halogenated alcohols (*e.g*., tefluthrin) improved chemical stability and allowed the use of pyrethroids in the field. The Type 2 pyrethroids are more narrowly defined in terms of their chemical structure. They specifically contain an a-cyano-3-phenoxybenzyl alcohol, which increases insecticidal activity about 10-fold. Moreover, some commercially important Type 2 pyrethroids have altered the acid portion of the molecule to include a phenyl ring (*e.g*., fenvalerate and fluvalinate). The stereoisomerism of pyrethroids is important for their toxic action, but a detailed discussion of this topic is beyond the scope of this course on IPM.

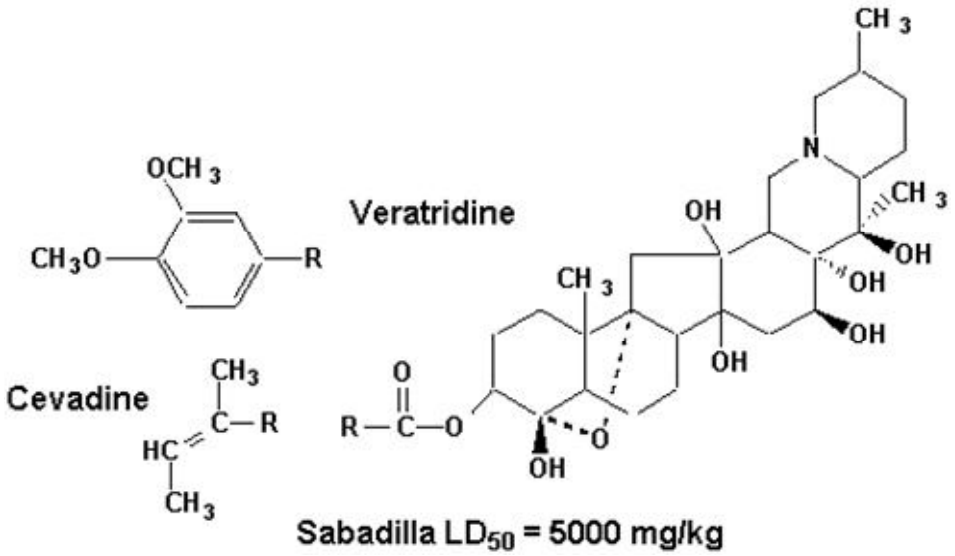
The signs of intoxication by pyrethroids develop rapidly and there exist different poisoning syndromes for the two types of compounds. Typical signs of intoxication by Type 1 pyrethroids include hyperexcitability and convulsions in insects and a whole body tremor in mammals. In insects, the Type 2 pyrethroids cause predominantly ataxia and incoordination, while in mammals they produce choreoathetosis (sinuous writhing) and salivation. In insects, the effects of pyrethroids (especially Type 1) can develop within 1-2 minutes after treatment and can result in knockdown, which is a loss of normal posture and locomotion. Human dermal exposure to either type of pyrethroid can cause paresthesia, a tingling or burning sensation of the skin, but this effect is more intense for Type 2 compounds.

Pyrethroid intoxication results from their potent effects on nerve impulse generation within both the central and peripheral nervous systems. Under normal conditions, neurons possess a transmembrane voltage of about -60 mV on the inside. The nerve impulse or action potential consists of a transient depolarization (positive wave) whose upstroke is driven by an influx of Na+ ions, followed by a downstroke from the efflux of K+ ions.

These ion fluxes occur due to the opening and closing of specific ion channel proteins embedded within the nerve membrane. The action potential is propagated down the axon until it reaches the nerve terminal, where it stimulates the release of chemical transmitters. Type 1 compounds induce multiple spike discharges in peripheral sensory and motor nerves, as well as interneurons within the central nervous system (CNS). In

contrast, Type 2 pyrethroids depolarize the axon membrane potential, which reduces the amplitude of the action potential and eventually leads to a loss of electrical excitability. All these effects occur because pyrethroids prolong the current flowing through sodium channels by slowing or preventing the shutting of the channels. The somewhat different actions observed for Type 1 and Type 2 compounds are due to differences in the degree of physiological effect: the duration of modified sodium currents by Type 1 compounds lasts tens or hundreds of milliseconds, while those of Type 2 compounds last for minutes or longer. These effects on the sodium current also cause a profound increase in the release of neurotransmitters from nerve terminals. The insect neuromuscular synapse is an especially important target for the pyrethroids, as well as other insecticides

Veratrum Alkaloids, Figure 3



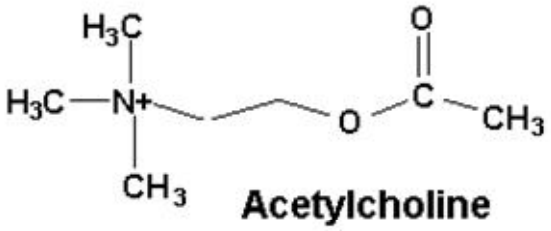
When used in organic farming or gardening, the veratrum alkaloids are usually applied as an extract (sabadilla) from the seeds of plants belonging to the genus *Schoenocaulon*. The insecticidal activity of sabadilla comes from the alkaloid fraction, which constitutes 3-6% of the extract. The two most important compounds are the lipophilic alkaloids veratridine and cevadine, with veratridine having greater insecticidal potency. Sabadilla breaks down rapidly in sunlight.

The major effects of sabadilla poisoning include muscle rigor in mammals and paralysis in insects. In addition, sabadilla strongly irritates mucous membranes in mammals and can cause violent sneezing. Sabadilla extract is much less toxic to mammals than most other insecticides and therefore is safe to use.

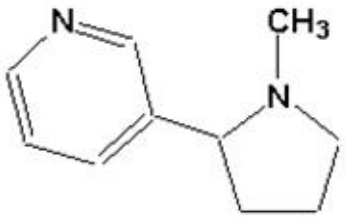
The mode of action of the veratrum alkaloids is similar to that of the pyrethroids. When applied to nerve, veratridine causes an increase in the duration of the action potential, repetitive firing, and a depolarization of the nerve membrane potential, due to effects on

the sodium channel (The Nerve Impulse, Neuromuscular Transmission and the Action of Insecticides, Figure 2). Veratridine prolongs the open state of the sodium channel by delaying channel shutting and by increasing the probability of channel opening.

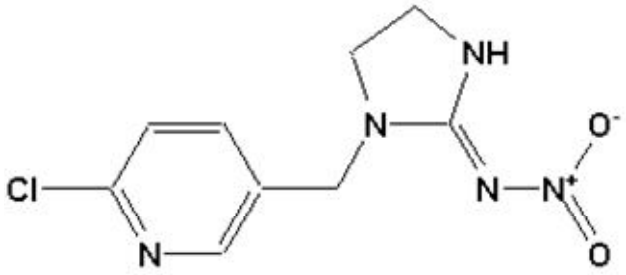
Acetylcholine Mimics, Figure 5



Acetylcholine



Nicotine (55 mg/kg)



Imidacloprid (424-475 mg/kg)

The tobacco alkaloid nicotine has been used as an insecticide since the middle of the 18th century. This compound is miscible with water and is often formulated as the sulfate salt. Nicotine has excellent contact activity, due to its ability to penetrate the integument of insects. This property increases the hazards of handling nicotine, as its contact toxicity to mammals is also significant. A newer compound in this class is the nitroguanidine, imidacloprid. This compound generally works best as a stomach poison, and has plant systemic activity as well. It is much less toxic to mammals than nicotine.

Nicotine and imidacloprid mimic the action of acetylcholine, which is a major excitatory neurotransmitter in the insect CNS. After acetylcholine is released by the presynaptic cell, it binds to the postsynaptic nicotinic acetylcholine receptor and activates an intrinsic cation channel.

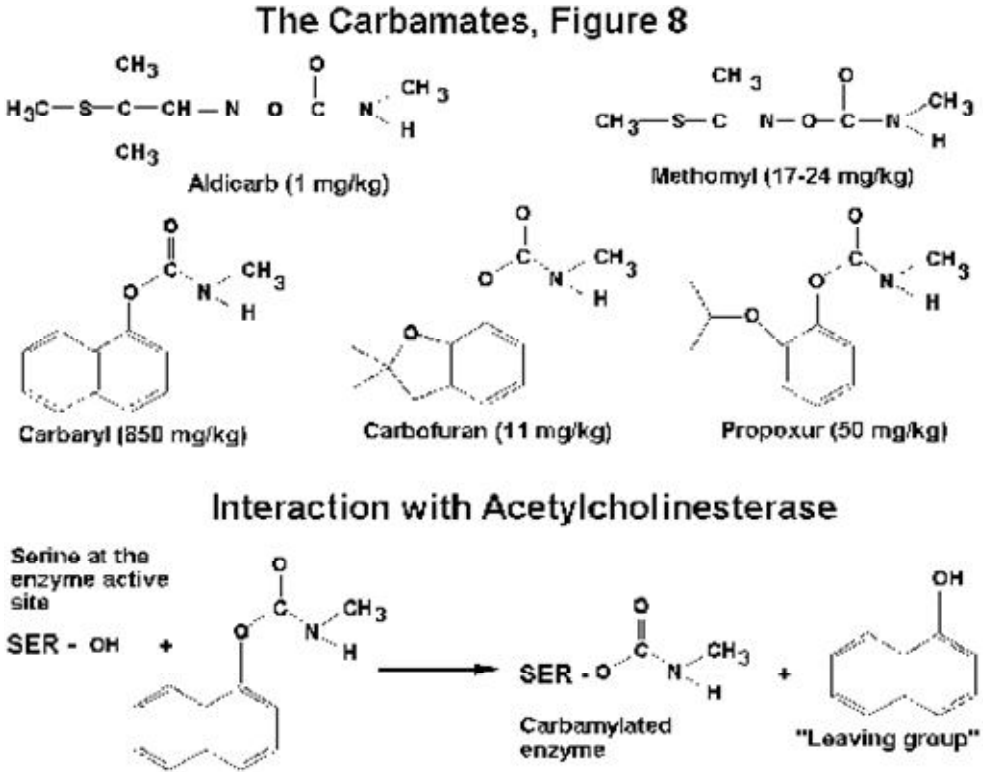
This results in a depolarization of the postsynaptic cell due an influx of sodium and calcium ions. The synaptic action of acetylcholine is terminated by the enzyme acetylcholinesterase, which rapidly hydrolyzes the ester linkage in acetylcholine. Nicotine and imidacloprid also activate the nicotinic acetylcholine receptor, but do so persistently, since they are insensitive to the action of acetylcholinesterase. This persistent activation leads to an overstimulation of cholinergic synapses, and results in hyperexcitation, convulsions, paralysis, and death of the insect.

Acetylcholinesterase Inhibitors

The organophosphorus insecticides (OPs) are a very important group of compounds that vary tremendously in chemical structure and chemical properties. These compounds can be miscible with water, but more typically are miscible in organic solvents. OPs can be classified into several groups depending on the atoms that are directly attached to the central phosphorus. Thus, the majority of OPs exist as phosphates, phosphonates, phosphorothionates, phosphorodithioates, phosphoramidothioates, etc (Organophosphorous Insecticides, Figure 7). An important bioactivation step occurs for OPs containing a sulfur atom attached to the phosphorus by a double bond (*e.g.,* phosphorothionates). For these compounds, oxidative desulfuration occurs via cytochrome P450 monooxygenases, which are enzymes that oxidase a wide variety of xenobiotics (Organophosphorous Insecticides, Figure 7). However, in this casethe oxidized metabolite possesses greater toxicity. The acute toxicity of the OPs varies substantially, but many of them have a high mammalian toxicity.

The primary target site for the OPs is the enzyme acetylcholinesterase. The OPs react with a serine hydroxyl group within the enzyme active site, phosphorylating this hydroxyl group and yielding a hydroxylated "leaving group" (Organophosphorous Insecticides, Figure 7). This process inactivates the enzyme and blocks the degradation of the neurotransmitter acetylcholine. The synaptic concentrations of acetylcholine then build up and hyperexcitation of the CNS occurs. The signs of intoxication include restlessness, hyperexcitability, tremors, convulsions, and paralysis. In insects, the effects of OPs are confined to the CNS, where virtually all of the cholinergic synapses are located. Because they often require bioactivation and must penetrate into the CNS, the OPs do not have a rapid action like that of the pyrethroids. The phosphorylation of acetylcholinesterase by OPs is persistent; reactivation of the enzyme can take many hours or even days.

Carbamates, Figure 8



The carbamate insecticides exist as esters of carbamic acid, typically having some kind of aryl (ring) substituent as the leaving group. These compounds are most soluble in organic solvents. Other carbamates are more aliphatic in nature and may possess sufficient miscibility with water to act as effective plant systemic insecticides (e.g., aldicarb). The carbamates are often highly toxic to mammals, and must be handled carefully. Among insects, they are particularly toxic to beneficial hymenoptera such as honeybees.

The mode of action of the carbamates is similar to that of the OPs. In this case, the reaction yields a carbamylation of the serine hydroxyl group (Carbamates, Figure 8). An hydoxylated leaving group is also generated. The CNS is the site of action of carbamates and the signs of intoxication are also similar to those of the OPs. Compared to phosphorylation, the carbamylated enzyme complex is relatively less stable; it will typically hydrolyze over a time course of minutes.