(Ent-714) Insecticide Toxicology Credit Hours 3(2-1)

Lecture # 6 Delivered by Dr. Hassan Yasoob

Topic- Chemistry and Comparative Toxicology of Some Common Insecticides

What are common insecticides?

Insecticides are commonly used in agricultural, public health and industrial applications, as well as household and commercial uses (e.g., control of roaches and termites). The most commonly used insecticides are the **organophosphates**, **Organochlorides, pyrethroids** and **carbamates**

Organophosphates (OP) are chemical substances that are produced by the process of esterification between phosphoric acid and alcohol. Organophosphates can undergo hydrolysis with the liberation of alcohol from the esteric bond. These chemicals are the main components of herbicides, pesticides, and insecticides.

Organophosphate pesticides (OPPs), like some nerve agents, inhibit this neuromuscular enzyme, which is broadly essential for normal function in insects, but also in humans and many other animals. OPPs affect this enzyme in varied ways, a principle one being through irreversible covalent inhibition, and so create potentials for poisoning that vary in degree. The brain sends out neurotransmitters to the nerve endings in the body; organophosphates disrupt this process from occurring.This chemical, organophosphate works by disrupting the enzyme acetylcholinesterase. Acetylcholinesterase break down the acetylcholine neurotransmitter, which sends out signals to other nerve endings in the body.

For instance, parathion, one of the first OPPs commercialized, is many times more potent than malathion, an insecticide used in combating the Mediterranean fruit fly (Med-fly) and West Nile virus-transmitting mosquitoes. Human and animal exposure to them can be through ingestion of foods containing them, or via absorption through the skin or lungs.

The human and animal toxicity of OPPs make them a societal health and environmental concern; the EPA banned most residential uses of organophosphates in 2001, but their agricultural use, as pesticides on fruits and vegetables, is still

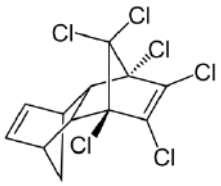
permitted, as is their use in mosquito abatement in public spaces such as parks. For instance, the most commonly used OPP in the U.S., malathion, sees wide application in agriculture, residential landscaping, and pest control programs (including mosquito control in public recreation areas). As of 2010, forty such OPPs were registered for use in the U.S., with at least 73 million pounds used in one time period in agricultural and residential settings. Commonly used organophosphates have included:

(1)parathion (2)malathion (3)methyl parathion (4)chlorpyrifos (5)diazinon

(6)dichlorvos (7)phosmet (8)fenitrothion (9)tetrachlorvinphos,

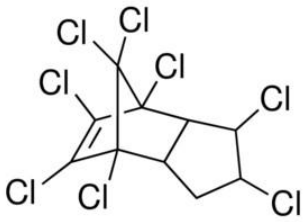
(10)azamethiphos (11)azinphos-methyl (12)terbufos

►Organochlorides



(1)Aldrin.

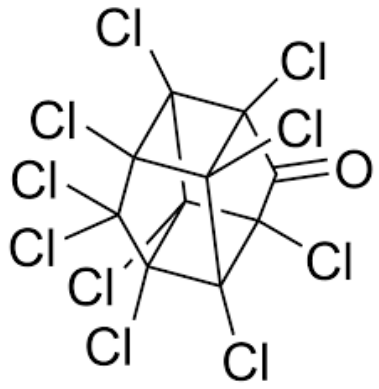
Aldrin is an organochlorine insecticide that was widely used until the 1990s, when it was banned in most countries. Aldrin is a member of the so-called "classic organochlorines" group of pesticides. COCs enjoyed a very sharp rise in popularity during and after The Second World War.



(2)Chlordane.

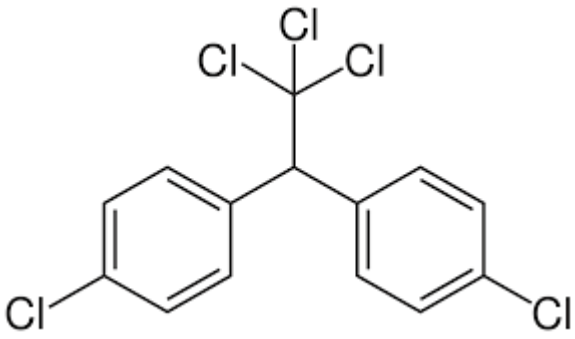
Chlordane, or chlordan, is an organochlorine compound used as a pesticide. It is a white solid. In the United States, chlordane was used for termite-treatment of approximately 30 million homes until it was banned in 1988.

(3)Chlordecone.



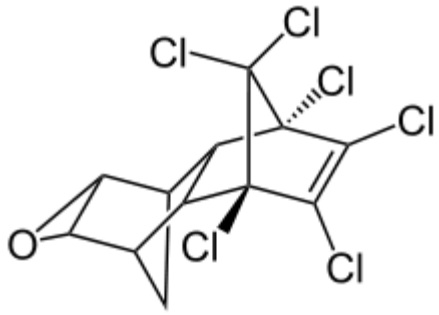
Kepone, also known as chlordecone, is an organochlorine compound and a colourless solid. This compound is an obsolete insecticide related to Mirex and DDT. Its use was so disastrous that it is now prohibited in the western world, but only after many millions of kilograms had been produced. Kepone is a known persistent organic pollutant (POP), classified among the "dirty dozen" and banned globally by the Stockholm Convention on Persistent Organic Pollutants as of 2011.

(4) DDT.



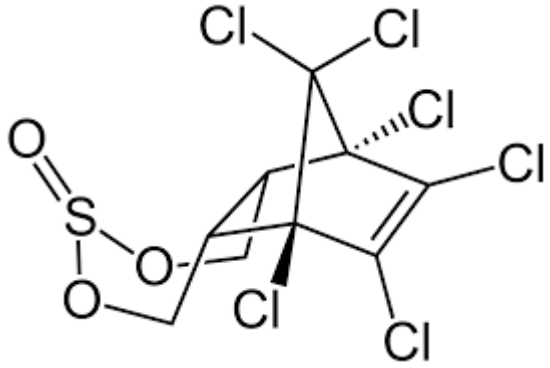
Dichlorodiphenyltrichloroethane, commonly known as DDT, is a colorless, tasteless, and almost odorless crystalline chemical compound, an organochlorine. Originally developed as an insecticide, it became infamous for its environmental impacts. DDT was first synthesized in 1874 by the Austrian chemist Othmar Zeidler.

(5)Dieldrin.



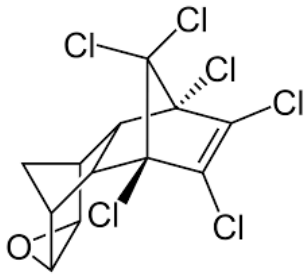
Dieldrin is an organochloride originally produced in 1948 by J. Hyman & Co, Denver, as an insecticide. Dieldrin is closely related to aldrin, which reacts further to form dieldrin. Aldrin is not toxic to insects; it is oxidized in the insect to form dieldrin which is the active compound.

(6)Endosulfan



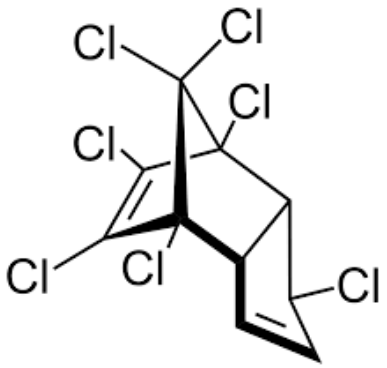
Endosulfan is an off-patent organochlorine insecticide and acaricide that is being phased out globally. The two isomers, endo and exo, are known popularly as I and II. Endosulfan sulfate is a product of oxidation containing one extra O atom attached to the S atom.

(7)Endrin.



Endrin is an organochloride with the chemical formula $C_{12}H_8Cl_6O$ that was first produced in 1950 by Shell and Velsicol Chemical Corporation. It was primarily used as an insecticide, as well as a rodenticide and piscicide. It is a colourless, odorless solid, although commercial samples are often off-white.

(8)Heptachlor



Heptachlor is an organochlorine compound that was used as an insecticide. Usually sold as a white or tan powder, heptachlor is one of the cyclodiene insecticides. In 1962, Rachel Carson's Silent Spring questioned the safety of heptachlor and other chlorinated insecticides.

Merits of Organochlorides (OC's)

(1)Fat soluble (2)Not dissolved in Water (3)Stomach Poison(Mode of Acton) (4)Contact Poisons(Mode of Entry) (5)Few have fumigant action (6)Non phyto-tocic except cucurbits

De-Merits of Organochlorides (OC's)

(1)Highly Persistent (2)Lipophilic (3)Residual effect (4)Highly mammalian toxicity (5)Carcinogenic (6)Mutagenic

►Pyrethroids

A **pyrethroid** is an organic compound similar to the natural pyrethrins, which are produced by the flowers of pyrethrums (*Chrysanthemum cinerariaefolium* and *C. coccineum*). Pyrethroids constitute the majority of

commercial household insecticides. In the concentrations used in such products, they may also have insect repellent properties and are generally harmless to humans.

Mode of action

Pyrethroids are axonic excitotoxins, the toxic effects of which are mediated through preventing the closure of the voltage-gated sodium channels in the axonal membranes. The sodium channel is a membrane protein with a hydrophilic interior. This interior is shaped precisely to allow sodium ions to pass through the membrane, enter the axon, and propagate an action potential. When the toxin keeps the channels in their open state, the nerves cannot repolarize, leaving the axonal membrane permanently depolarized, thereby paralyzing the organism.[2] Pyrethroids can be combined with the synergist piperonyl butoxide, a known inhibitor of key microsomal cytochrome P450 enzymes from metabolizing the pyrethroid, which increases its efficacy (lethality)

Types of Pyrethroids

- Allethrin, the first pyrethroid synthesized
- Bifenthrin, active ingredient of *Talstar*, *Capture*, *Ortho Home Defense Max*, and *Bifenthrine*
- Cyfluthrin, an active ingredient in Baygon, Temprid, Fumakilla Vape Aerosol, and many more, dichlorovinyl derivative of pyrethrin
- Cypermethrin, including the resolved isomer alpha-cypermethrin, dichlorovinyl derivative of pyrethrin
- Cyphenothrin, active ingredient of K2000 Insect spray sold in Israel and the Palestinian territories
- Deltamethrin, dibromovinyl derivative of pyrethrin
- Esfenvalerate
- Etofenprox
- Fenpropathrin
- Fenvalerate
- Flucythrinate
- Flumethrin
- Imiprothrin
- lambda-Cyhalothrin
- Metofluthrin

- Permethrin, dichlorovinyl derivative of pyrethrin and most widely used pyrethroid.
- Resmethrin, active ingredient of *Scourge*
- Silafluofen
- Sumithrin, active ingredient of Anvil
- tau-Fluvalinate
- Tefluthrin
- Tetramethrin
- Tralomethrin
- Transfluthrin, an active ingredient in Baygon

►Carbamates

A **carbamate** is a chemical compound that is formally derived from carbamic acid (NH_2COOH). The term includes organic compounds (e.g., the ester ethyl carbamate), formally obtained by replacing one or more of the hydrogen atoms by other organic functional groups; as well as salts with the carbamate anion H_2NCOO^- (e.g. ammonium carbamate).

Polymers whose units are joined by divalent carbamate groups –NH–(C=O)–O– are an important family of plastics, the polyurethanes.

Properties

While carbamic acids are unstable, many carbamates (covalent or ionic) are stable and well known.

Carbamate insecticides

The so-called carbamate insecticides feature the carbamate ester functional group. Included in this group are aldicarb (Temik), carbofuran (Furadan), carbaryl (Sevin), ethienocarb, fenobucarb, oxamyl, and methomyl. These insecticides kill insects by reversibly inactivating the enzyme acetylcholinesterase. The organophosphate pesticides also inhibit this enzyme, although irreversibly, and cause a more severe form of cholinergic poisoning. Fenoxycarb has a carbamate group but acts as a juvenile hormone mimic, rather than inactivating acetylcholinesterase.

The insect repellent icaridin is a substituted carbamate.

TABLE 2.2 MAMMALIAN TOXICITIES OF SOME INSECTICIDES

Name of insecticide	Acute oral LD_{50} for rat (mg/kg)	Acute dermal LD_{50} (mg/kg)	Toxicity class according to WHO
Organochlorines			
DDT	113-118	2510 (♀ rats)	II
dicofol/kelthane	595-578	>5000 (rabbits)	III
Endosulfan	70	395 (rabbits)	II
Gamma-HCH	88-270	900-1000 (rats)	II
Heptachlor	147-220	200-2000 (rabbits)	II
Methoxychlor	6000	2000 (rabbits)	III
Orgsnophosphates			
Acephate	1030-1477	>10000 (rabbits)	III
Azinphos-ethyl	12	500 (rabbits)	1b
Azinphos-mthyl	9	150-200 (rats)	1b
Chlorfenvinphos	10	31-108 (rats)	1b
Chlorpyrifos ethyl	135-163	>2000 (rats)	II
Chlorpyrifos methyl	>3000	3700 (rats)	III
Diazinon	1250	>2150 (rats)	II
Dichlorvos	56-108	75-108 (rats)	1b
Dicrotophos	17-22	111-136(rats)	1b
Dimethoate	387	>2000 (rats)	II
Disulfoton	2-12	3.6-15.9 (rats)	1a
Fenitrothion	1700-1720	810-840 (rats)	II
Fenthion	250	586-800 (rats)	II
Malathion	1375-2800	4100 (rabbits)	III
Methamidophos	13-15.6	69-122 (rabbits)	1b
Methidathion	25-54	297-1663 (rats)	1b
Mevinphos	3-12	4-90 (rats)	1a
Monocrotophos	14	336 (rats)	1b
Oxydemeton	50	130 (rats)	1b
Parathion ethyl	2	71-76 (rats)	1a
Parathion methyl	3	45 (rats)	1a
Phenthoate	249-270	>5000 (rats)	II
Phorate	1.6-3.7	2.5-2.6 (rats)	1a
Phosalone	120	1500 (rats)	II
Phosphamidon	17.4	374 (rats)	1a
Phosphamidon	17.9-30	374-530 (rabbits)	1a
Pirimiphos-methyl	1414	>2000 (rats)	III
Profenofos	358	3300 (rats)	II
Quinalphos	71	1750 (rats)	
Triazophos			

Butoxycarboxim	458	>2000 (rabbits)	
Bytocarboxim	153-215	360 (rabbits)	Ib
Carbaryl	500-850	>4000(rats)	Ib
Carbofuran	8	>2000 (rats)	II
Carbosulfan	185-250	>2000 (rats)	Ib
Cartap	325-345	>1000 (mice)	II
Fenobucarb	632-657	10250 (rabbits)	II
Furathiocarb	53	>2000 (rats)	II
Isoprocarb	450	>500 (rats)	Ib
Methomyl	30-34	>2000 (rabbits)	II
Pirimicarb	142	>2000 (rats)	Ib
Thiodicarb	66	>2000 (rabbits)	II
			II

Synthetic Pyrethroids

Allethrin	900-2150	2660-4390 (rabbits)	III
Alphamethrin	79-400	>2000 (rats)	II
Betacyfluthrin	500	>500 (rats)	Ib
Betacypermethrin	166-178	>5000 (rats)	II
Bifenthrin	54.5	>2000 (rabbits)	II
Cycloprothrim	>5000	>2000 (rats)	III
Cyfluthrin	500	>5000 (rats)	Ib
Cyhalothrin	114-166	1000-2500 (rats)	II
Cypermethrin	250-4150	>4920	II
Deltamethrin	135->5000	>2000(rats)	II
Esfenvalerate	75-88	>5000 (rats)	II
Fenpropathrin	66.7-70.6	>2000 (rabbits)	II
Fenvalerate	451	1000-3200 (rats)	II
Flucythrinate	67-81	>1000(rabbits)	Ib
Fluvalinate	261-282	>2000 (rabbits)	II
Lamda-cyhalothrin	56-79	632-692 (rats)	II
Permethrin	430-4000	>2500 (rats)	II
Resmethrin	>2500	>3000 (rats)	III
Theta-cypermethrin	3200-7700	>5000 (rats)	III
Tralomethrin	99-3000	>2000 (rabbits)	II
Zeta-cypermethrin	105.8	>2000 (rabbits)	Ib

NATURAL INSECTICIDES

Azadirachtin	>5000	>2000 (rabbits)	III
Nicotine	50-60	50 (rabbits)	Ib
Pyrethrins (Pyrethrum)	1030-2370	5000 (rabbits)	II
Rotenone	132-1500	>5000 (rabbits)	II
Sabadilla	4000	-	III

NEW CHEMISTRY INSECTICIDES

Abamectin			
	10		

Etofenprox	>42880	>2140(rats)	III
Fenoxycarb	>10000	>2000(rats)	III
Flufenoxuron	>3000	>2000(rats)	III
Gossyplure	>5	>2000(rats)	Ib
Hexaflumuron	>5000	>5000(rats)	III
Imidacloprid	450	>5000(rats)	II
Indoxacarb	268-1723	>5000(rabbits)	II
Lufenuron	>2000	>2000(rats)	III
Metdyfenozide	>5000	>5000(rats)	III
Novaluron	>5000	>2000(rats)	III
Pymetrozine	5820	>2000(rats)	III
Pyriproxyfen	>5000	>2000 (rats)	III
Spinosad	3783-75000	>2000 (rabbits)	III
Tebufenozide	>5000	>5000 (rats)	III
Teflubenzuron	>5000	>2000 (rats)	III
Thiomethoxam	1563	>2000 (rats)	III