Insecticidal Activity

Chapter VII
Entomology, the study of insects is highly fascinating biological science. Insects are the most abundant form of animal life on the earth. They are found nearly everywhere in the world except in the open seas and some parts of the polar regions. Whether they are considered helpful, harmful or neutral to man depends largely on whether man cooperating or competing or indifferent to their presence.

Insecticides are agents of chemical or biological origin that control insects. Control may result from killing the insect or otherwise preventing it from engaging in behaviors deemed destructive. Insecticides may be natural or man made and are applied to target pests in a myriad of formulations and delivery systems (sprays, baits, slow-release diffusion, etc.). The science of biotechnology has, in recent years, even incorporated bacterial genes coding for insecticidal proteins into various crop plants that deal death to unsuspecting pests that feed on them.¹⁻⁴

Though by no means exhaustive, we will touch on major classes and technologies whether decades old or recently revealed. Some 10,000 species of more than 1 million species of insects are crop-eating, and of these, approximately 700 species worldwide cause most of the insect damage to man’s crops, in the field and in storage.

Humanoids have been on earth for more than 3 million years, while insects have existed for at least 250 million years. We can guess that among the first approaches used by our primitive ancestors to reduce insect annoyance was hugging smoky fires or spreading mud and dust over their skin to repel biting and tickling insects, a practice resembling the habits of elephants, swine, and water buffalo. Today,
such approaches would be classed as *repellents*, a category of *insecticides*.\(^5\,^6\)

Historians have traced the use of pesticides to the time of Homer around 1000 B.C., but the earliest records of insecticides pertain to the burning of "brimstone" (sulfur) as a fumigant. Pliny the Elder (A.D. 23-79) recorded most of the earlier insecticide uses in his *Natural History*. Included among these were the use of gel from a green lizard to protect apples from worms and rot. Later, we find a variety of materials used with questionable results: extracts of pepper and tobacco, soapy water, whitewash, vinegar, turpentine, fish oil, brine, lye among many others.

At the beginning of World War II (1940), our insecticide selection was limited to several arsenicals, petroleum oils, nicotine, pyrethrum, rotenone, sulfur, hydrogen cyanide gas, and cryolite. It was World War II that opened the *Modern Era of Chemical control* with the introduction of a new concept of insect control -- synthetic organic *insecticides*, the first of which was DDT.\(^7\,^8\)

*Insects*\(^9\) are members of phylum *Arthropoda* having a well defined body structure. Insects may be helpful to man by producing directly or indirectly material of economic value, such as silk, honey beewax, shellac, etc. by aiding in the production of fruits, vegetables, flowers, and seeds, through pollination activity, by acting as scavengers-attacking and destroying dead plants and animals, by destroying noxious plants, by their medicinal value particularly honey bee venom for treating arthritis.

Insect may be harmful\(^9\) to men and cause great economical loss by damaging or destroying agricultural crop and other valuable
plants by aiding in the spread and development of bacteria, fungi, viruses that produce disease in plants.

Insects are highly injurious\textsuperscript{11} to human and animal health and comfort. Some insects notably mosquitoes and flies annoy men and other animals by their bites and stings. Others such as lice, have become adapted to more or less continuous life upon animals and cause much discomfort and loss of vitality. Not only do they live externally on animals, but also internally in the skin tissue, and in a few cases they live within the flesh and in the alimentary tract, besides direct loss due to their presence, insects transmit disease organisms from one person or animal to another. Some important insect born disease organisms are responsible for malaria, bubonic plague, typhoid, and yellow fever, cases of allergy (hay fever; asthma) are frequently caused by exposure of susceptible person to dried insect scales and hairs. Not only is the loss of life because of insect borne disease a serious, but the total loss of productive labour through illness is tremendous.

Insects destroy at least 5\% of the world production of all cereal grains after they are harvested and while they are in storage on the form in elevators or warehouses.

It is difficult to make an accurate estimate of the monetary loss suffered from insects directly detrimental to man, but time lost from work, loss in business at resort and vacation areas. Cost of screening homes and buildings, lowered efficiency and medical expense, would amount to a considerable sum.

The damage caused by insects to agriculture crop and human health is enormous. This damage is particularly great in tropical countries like India and other Asian countries, where the conditions of
temperature and humidity are quite favourable for their growth. Though several methods are available for their control, the chemical method of using insecticides has been playing a vital role. Artificial controls are applied by man. They are employed to reduce the population of insects.

The ultimate goal of any control programme is to shift on adverse “balance of nature” to favour man. These include physical control (use of electromagnetic energies light, and colour trap etc.): prophylactic control by creating physical and sensory barriers like repellents (oil of citronella, repels mosquito, dimethyl phthalate, indolone), attractants (pheromones, methyl eugenol), antifeedants (like flavonoids, carbamates), cultural control is accomplished by farming practices like crop rotation; legislative control includes quarantine measures, rules for inspection and testing of seeds, seedling and insecticides; biological control measures are usually expensive and tedious like genetic control and introduction of parasites (ex, introduction of lady beetle from Australia to California to control scale in 1988-1989 to control citrus black fly in Cuba and Mexico). Mechanical control is useful in small forms. This includes hand picking of easily located and detectable pest and their destruction ex. egg batches of hairy caterpillars. Destruction of infected parts of plants can also be done.

Chemical control involves the use of inorganic natural, and synthetic organic insecticides. Natural control of insects does not depend on man and it affects the distribution and welfare of insects. They depend on environmental conditions and also known as environmental resistance. These include climatic factors temperature extremes, humidity, high winds etc., biotic factors (predators,
parasites, natural resistance of plants) and topographical factors (oceans, deserts, mountain ranges, which act as natural barriers to their free migration).

The word insecticides means insect killer. Insecticides are employed for the protection of man, domestic crops and agricultural products from insect depredations. To kill an insect with an insecticides, the poisonous chemical, usually most penetrate to vital organs and tissue of the insect. Certain insecticides penetrate rapidly through the body wall of some insect species. Other insects with the body wall thick, waxy, or, other size wall protected are likely to be resistant to direct penetration. In these it may be desirable for the insecticides to be taken into the digestive tract along with food or water.

Insecticides were in use from very early times and as early as 200 B.C. boiling mixture of bitumen (mineral pitch or asphalt) and blowing the fumes through grape leaves were advocated to keep away the insects.

**Classification of insecticides**

<table>
<thead>
<tr>
<th>Based on mode of entry&lt;sup&gt;10&lt;/sup&gt;</th>
<th>Based on chemical nature</th>
</tr>
</thead>
<tbody>
<tr>
<td>a- Stomach poisons</td>
<td>Natural insecticides</td>
</tr>
<tr>
<td>b- Contract poisons</td>
<td>Inorganic insecticides</td>
</tr>
<tr>
<td>c- Fumigants</td>
<td>Organic Insecticides</td>
</tr>
<tr>
<td>d- Systemic insecticides</td>
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</tr>
</tbody>
</table>

Based on the chemical nature of insecticides they are classified as natural, inorganic and organic.
Chapter VII: Insecticidal activity

1. Natural Insecticides control\(^{[11]}\):

   Natural control can be defined as any condition of the environment that checks insect population and can not be altered. Some factors (i) climate as temperature, humidity, and air movement (ii) topography, land and water barriers, soil texture and composition and (iii) parasites and predators are responsible for natural control.

1.1 Biological control\(^{[12-26]}\):

   Biological control may be defined as the artificial manipulation of natural biological phenomenon for the purpose of reducing or checking destructive population of insects, other animals or plants.

2. Inorganic insecticides:

   Industrial revolution has started with synthetic insecticides. In 1867 Paris green (copper acetoxarsenate) was used as dust or spray. Leadarsenate, white arsenate and calcium arsenate comes under arsenicals. Lime sulphur and HCN were used for controlling scale insect. Chromates, thallium compounds and mercury compounds (cabbage maggot) were also tried. Fluorine compounds were useful in cockroach and ant control. They have been known since 1842 (NaF, Na\(_3\)SiF\(_5\); Na\(_3\)AlF\(_6\) and Borax). Although they are cheap and most effective, their continuous use involved considerable health hazards. They have been replaced by D.D.T. for lead arsenate, toxaphene and aldrine for calcium arsenate in cotton pest control.

3. Organic insecticides:

   Made their appearance in mordern era of insecticides with thiocyanates in 1930's. All alkyl thiocyanates are insecticidal (R-S-C≡N). They act as contact insecticides when R is dodecyl and as fumigants when R is lower alkyl group. In 1936, lethane was
introduced in U.S.A. Its development was ceased due to DDT's success. Thanite is the only compound used commercially.

These are the most important type of insecticides, whose action is very fast. Almost maximum percentages of insecticides used today are synthetic organic insecticides.

The synthetic organic insecticides are classified into:

a. Organophosphorus insecticides\(^{(27)}\).

b. Carbamate insecticides\(^{(28)}\).

c. Pyrethroid insecticides\(^{(29)}\).

d. Chlorinate hydrocarbons\(^{(30)}\).

e. Organotin compounds.

f. Acylurea compounds\(^{(31)}\).

g. Formamidines\(^{(32)}\).

h. Phosphine

i. Ovicides of the clofentezine/hexythiazox type\(^{(33)}\).

Heterocyclic ring plays a major role in the synthesis of insecticides\(^{(34)}\). Here are some of the commonly used insecticides, which have a heterocyclic ring in them.

i. **Carbosulfan\(^{(35)}\):**

Group – Carbamate

\[
\text{IUPAC Name} - 2,3\text{-dihydro-2,2-dimethyl benzofuran-7-yl (dibutylaminothio) methyl carbamate.}
\]
Mode of action – Cholinesterase inhibitor

Use – It controls millipedes, springtails, symphyllids, wireworm’s pygmy, mongold, bettles, fruitflies, white grube, coloradobutles, codling moth etc.

ii. Chlorfluazuron

Group – Benzoyl urea

IUPAC Name – 1-[3',5'-dichloro-4'-(3''-chloro-5'' tri fluoromethyl-2''-pyridyloxy) -3-[2'', 6'' difluoro benzoyl] urea.

Mode of action - Insect growth regulator which acts as an anti moulding agent.

Use – Its control includes Heliothis, Spodoptera, Bemisia tobbaci and other chewing insects on cotton.

iii. Diazinone

Group – Organophosphorus

IUPAC Name – o,o-diethyl o-2-isopropyl-6-methyl pyrimidin-4-yl phosphorothioate.

Mode of action – Non-systemic insecticides and acaricide. It is a cholinesterase inhibitor.
Use – Controls sucking and chewing of insects and mites. It is also used as a veterinary ectoparasiticides.

iv. Fipronil\(^{(38)}\):

Group – Phenyl Pyrazole

![Fipronil Structure](image)

IUPAC Name – \((\pm)\) 5-amino-1-(2', 6'-dichloro-α, α, α-tri-fluoro-p-tolyl) - 4-trifluoro methyl sulfinyl pyrazole-3- carbonitrile.

Mode of action – Insecticides, which acts as a potent blocker of the GABA, regulated chloride channel.

Use – Control of many soil and foliar insects.

v. Imidaclopride\(^{(39)}\):

Group – Pyridyl imidazole

![Imidaclopride Structure](image)

IUPAC Name – 1-(6'-chloro-3'-pyridyl methyl) N-nitroimidazolidin-2-yl ideneamine.

Mode of action – Acts on the CNS, causing irreversible blockage of past synaptic nictotinergic acetylcholine receptors.

Use – It controls sucking insects, rice hoppers, aphids, thrips and white flies.
vi. Quinalphos\(^{(40)}\):

**Group** - Organophosphorus

![Quinalphos Structure](image)

**IUPAC Name** - o,o-diethyl o-quinoxalin-2-yl phosphorothioate.

**Mode of action** - Insecticide and acaricide with contact and stomach action.

**Use** - Control of many insect pests of the orders Lepidoptera, Coleoptera, Diptera, Hemiptera etc.

vii. Triazamate:

**Group** - Carbamate

![Triazamate Structure](image)

**IUPAC Name** - Ethyl (3-tert-butyl-1-dimethyl carba-moyl-1H-1,2,4-triazol-5yl thio) acetate.

**Mode of action**: Fast acting non-fumigant selective aphicide with contact and systemic action.

**Use** - It controls aphids including those resistant to carbamate and organo phosphorus insecticides.

viii. Phoslone\(^{(41)}\):

**Group** - Organophosphorus
IUPAC Name – S-6-chloro-2,3-dihydro-2-oxo benzoxazol-3-yl methyl o,o-diethyl phosphorodithioate.

Mode of action: None systemic insecticides and acaricide showing localized penetration of plant cuticle, with contact and stomach action.

Use – Control of many insect pests of the orders lepidoptera etc.

ix. Hydromethylnone:

Group – Organtoin

IUPAC Name – 5,5-dimethyl per hydro pyrimidine-2-one 4-tri fluoro methyl-α-(4-tri fluoro methyl styryl) cinnamylidenehydrazone.

Mode of action – Non-systematic insecticides with stomach action.

Use – Selective control of agricultural and household formicides.

x. Fiproles (or Phenylpyrazoles)

Fipronil is the only insecticide in this new class, introduced in 1990 and registered in the U.S. in 1996. It is a systemic material with contact and stomach activity. Fipronil is used for the control of many soil and foliar insects, (e.g., corn rootworm, Colorado potato beetle,
and rice water weevil) on a variety of crops, primarily corn, turf, and for public health insect control. It is also used for seed treatment and formulated as baits for cockroaches, ants and termites. Fipronil is effective against insects resistant or tolerant to pyrethroid, organophosphate and carbamate insecticides.

Mode of action—Fipronil blocks the (γ-aminobutyric acid- (GABA) regulated chloride channel in neurons, thus antagonizing the "calming" effects of GABA, similar to the action of the Cyclodienes.

xi. Pyroles

Chlorfenapyr is the first and only member of this unique chemical group, both as a contact and stomach insecticide-miticide. It is used on cotton and experimentally on corn, soybeans, vegetables, tree and vine crops, and ornamentals to control whitefly, thrips, caterpillars, mites, leafminers, aphids, and Colorado potato beetle. It has ovicidal activity on some species. EPA took the unusual step of refusing to register chlorfenapyr in 2000 for cotton insect control because of potential hazards to birds. However, labels for greenhouse ornamentals were granted in 2001.
Mode of action - Chlorfenapyr is an "uncoupler" or inhibitor of oxidative phosphorylation, preventing the formation of the crucial energy molecule adenosine triphosphate (ATP).

xii. Pyrazoles

The original pyrazoles were tebufenpyrad and fenpyroximate (not illustrated). These were designed primarily as non-systemic contact and stomach miticides, but do have limited effectiveness on psylla, aphids, whitefly, and thrips. Tebufenpyrad, registered by EPA in 2002, is used on cotton, soybeans, vegetables, pome fruits, grapes and citrus. Fenpyroximate controls all stages of mites, gives fast knockdown, inhibits molting of immature stages of mites, and has long residual activity. Newer members of this class include ethiprole which is active on a broad spectrum of chewing and sucking insects, and tolfenpyrad (OMI-88) which is reputed to active on pests infesting cole and cucurbit crops.

Mode of action - Their mode of action is that of inhibiting mitochondrial electron transport at the NADH-CoQ reductase site, leading to the disruption of adenosine triphosphate (ATP) formation, the crucial energy molecule.
An evolution of safety

Research over time has led to the continuing discovery of new pest control products that offer both improved environmental profiles and improved safety to consumers, homeowners and applicators. Research in the latter half of the twentieth and into the twenty-first century in particular has focussed on the discovery and commercialization of products that provide a much higher level of safety to both users and the environment. These products are much more specific and less broad-spectrum in nature, targeting specific pests of pest families and using greatly reduced use rates.

<table>
<thead>
<tr>
<th>Insecticides</th>
<th>Oral LD$_{50}$ (mg ai/kg)$^*$ (Mammalian)</th>
<th>Discovery/Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine</td>
<td>50-60</td>
<td>1690</td>
</tr>
<tr>
<td>Rotenone</td>
<td>130-1500</td>
<td>1840’s</td>
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<tr>
<td>Paris Green</td>
<td>22</td>
<td>1880’s</td>
</tr>
<tr>
<td>Lead arsonate</td>
<td>150</td>
<td>1890’s</td>
</tr>
<tr>
<td>DDT</td>
<td>113</td>
<td>1930’s</td>
</tr>
<tr>
<td>Carbaryl (Sevin)</td>
<td>246-283</td>
<td>1950’s</td>
</tr>
<tr>
<td>Chlorpyrifos (Dursban)</td>
<td>96-270</td>
<td>1970’s</td>
</tr>
<tr>
<td>Cypermethrin (Cymbush)</td>
<td>250</td>
<td>1970’s</td>
</tr>
<tr>
<td>Imadacloprid (Admire/Merit)</td>
<td>450</td>
<td>1990’s</td>
</tr>
<tr>
<td>Indoxacarb (Avaunt)</td>
<td>687-1867</td>
<td>2000</td>
</tr>
</tbody>
</table>
MATERIALS AND METHODS:

Cockroaches were selected for the present investigation 2% (w/v) and 4% (w/v) solution of synthesized compounds of pyrazoline, 4-thiazolidinone, azetidinone and isoxazole derivatives have been prepared in acetone. 4% 1-2 millimoles of solution of synthesized compounds was injected into the abdominal region of cockroach with the help of microsyringe. The time of death was noted as KD value (Knock down values). At the time of death, the antennae become motionless the appendages shrunk and folded towards the ventral side and cockroach lay dorsally. For each sample four replications were performed and average KD value noted.

Standard: Cypermethrin\(^{42}\) 25% E.C. is used as a control. Its 4% (w/v) solution has been prepared in acetone. It belongs to pyrethroid group.

\[
\begin{align*}
\text{Cypermethrin} & \\
\text{Mode of action:} & \text{Non-systemic insecticides with contact and stomach action also exhibits antifeeding action.} \\
\text{Use:} & \text{Control of wide range of insects, especially lepidoptera, coleoptera, diptera and hemiptera. Control of flies and other insects in animal houses and mosquitoes, cockroaches, houseflies and other insect in public health. It is also used as animal ectoparasiticide.}
\end{align*}
\]

The KD value for the control Cypermethrin was 8 minutes. The KD value of synthesized compounds was compared with control drug. Data represented in bar graph and line graphs\(^{43}\).
Chapter VII: Insecticidal activity

Insecticidal activity of 5-arylidene 4-thiazolidinone derivatives

<table>
<thead>
<tr>
<th>Compound Code</th>
<th>K.D. Value (Min)</th>
</tr>
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<tbody>
<tr>
<td>GCR26</td>
<td>20</td>
</tr>
<tr>
<td>GCR27</td>
<td>22.5</td>
</tr>
<tr>
<td>GCR28</td>
<td>18.5</td>
</tr>
<tr>
<td>GCR29</td>
<td>25</td>
</tr>
<tr>
<td>GCR30</td>
<td>24</td>
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<td>GCR31</td>
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<tr>
<td>GCR38</td>
<td>26.5</td>
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<td>Standard</td>
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</table>

Insecticidal activity of 2-azetidinone derivatives

<table>
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<th>Compound Code</th>
<th>K.D. Value (Min)</th>
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<tbody>
<tr>
<td>GCR49</td>
<td>19.3</td>
</tr>
<tr>
<td>GCR50</td>
<td>20.4</td>
</tr>
<tr>
<td>GCR51</td>
<td>22</td>
</tr>
<tr>
<td>GCR52</td>
<td>30</td>
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<td>GCR60</td>
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<td>GCR61</td>
<td>26</td>
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<tr>
<td>Standard</td>
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</tbody>
</table>
Chapter VII: Insecticidal activity

Insecticidal activity of isoxazole derivatives

![Graph showing insecticidal activity of isoxazole derivatives with K.D. Value (Min) on the y-axis and Compound Code on the x-axis.]

Insecticidal activity of pyrazoline, 4-thiazolidinone, 5-arylidene 4-thiazolidinone, 2-azetidinone, isoxazole derivatives

![Graph showing insecticidal activity of pyrazoline derivatives with K.D. Value (min) on the y-axis and Compound Code on the x-axis.]

Chemical and Biological Activity Studies of Some Synthesized Heterocyclic Compounds 206
RESULT AND DISCUSSION:

In the pyrazoline group the chlorophenyl, nitrophenyl and 3-methoxy-4-hydroxy derivative has more activity than the rest. In the 4-thiazolidinone, their 5-arylidene derivatives showed more activity. In the azetidinone group the nitrophenyl, chlorophenyl and methoxy phenyl exhibited high activity. The isoxazole group compounds showed less activity.

SUMMARY:

4% (w/v) solutions of synthesized compounds have been prepared in acetone. Similarly 4% (w/v) solution of cypermethrin as standard drug was also prepared in acetone. The test sample solutions were injected into the abdominal region of the cockroach. The time of death is noted on an average. The time of death is known as KD value (knock down value).

The chloro- and nitro- derivatives have exhibited good activity than the rest of the compounds.

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