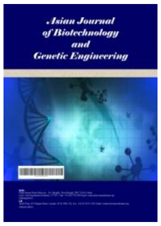

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Natural Pesticides (Biopesticides) and Uses in Pest Management- A Critical Review

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Authors' contributions

This work was carried out in collaboration among all authors. Author OCE designed the study, performed the statistical analysis and wrote the protocol. Author OCO wrote the first draft of the manuscript. Authors UCS and OU managed the analyses of the study. Authors JPS and AEU managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

This paper focuses on new types of biopesticides, examine the specificity to harmful pests, and the selectivity to beneficial animals. Many of the modern pesticides used today, persist in soil for years and compound the store of toxins in the soil, air and water. The toxic build-up of these chemicals has been shown to cause damage in animals, plants, human health and are not easily degradable in the environment. Study has shown that some plants contain components that are toxic to insects and pest called biopesticides or natural pesticides. Natural pesticides are pesticides made by organisms usually for their own defense, or are derived from a natural source such as plant, animal, bacteria, and certain mineral, use to control pest naturally with less effect or no effect. Examples of these natural pesticides are Rotenone (*Derris sp.*), carboxin, fluroacetate, nicotine, neem (*Azadiracta*

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indica), microbial pesticide *Bacillus thuringiensis*, and pyrethrins. Natural pesticides usually target specific sites in the insect such as nervous system, resulting in knock-down, lack of coordination, paralysis and death. Rotenone inhibits the transfer of electron from NADH to ubiquinone, it disrupts energy metabolism by inhibition of the electron transport system (ETS) and blockage of ATP synthesis in the mitochondria. Nicotine inhibits and compete with neurotransmitter by binding to acetylcholine receptors at the nerve synapses and causing uncontrolled nerve discharge. Fluoroacetate and carboxin inhibits the citric acid cycle by binding to aconitase and succinate dehydrogenase respectively. Pyrethrin exerts their toxic effect by disrupting the sodium and potassium ion exchange process, which interrupt the normal transmission of nerve impulses. Most botanical pesticides shows their effect through contact, respiratory, or stomach poisons to the target organism. Botanical pesticides are generally highly bio-degradable, and they become inactive within hours or a few days and can easily be broken down by stomach acids in mammals, so toxicity to humans and animals is very low to non-target organisms and are ecofriendly. Since they are also very effective, natural pesticides should be the first choice for pest management, which in turn reduces the bioavailability of metal and noxious effect in the environment. This review explains the major natural pesticides, mechanism, mode of action and origin.

Keywords: Biopesticides; low-risk pesticide; mechanisms; pest management; selectivity.

ABBREVIATIONS

ETS : Electron Transport System;
ATP : Adenosine triphosphate;
Bt : Bacillus thuringiensis;
IRM : Intergrated resistance management;
IPM : Integrated Pest management;
DDT : Dichloro-diphenyl-trichloroethane;
PBO : Piperonyl butpxide.

1. INTRODUCTION

During the past three decades, efforts have been made to reduce the exposure and human risk of pesticides, especially insecticides. There is great demand for selective and safe insecticides that spare natural enemies and non-target organisms. Some conventional pesticides have been replaced by newer bio-rational (Biopesticides) or "low risk" pesticides. Natural pesticides are pesticides that are made by other organisms usually for their own defense, or are derived from a natural source such as plant, animal, bacteria, and certain mineral [1]. About 80% of pesticides applied enters various environmental resources as a result of run-off, exposing animals, and farmers as well as consumers of the agricultural produce to severe health problem. Natural pesticides or “reduced risk” pesticides are natural compounds that effectively control insect pests, with low toxicity to nontarget organisms such as humans, animals and natural enemies and the environment. Most of natural pesticides break down very quickly in sunlight so they should be stored in darkness for effectiveness. Both highly alkaline and highly acid conditions speed up degradation or break down these type of pesticides [2]. The common natural pesticides use are Neem, *Bacillus thuringiensis* (Bt), Nicotine, Rotenone, Pyrethrins, Sabadilla, Fluoroacetate, carboxin, and Ryania.

Plants and some microorganism produce many natural chemicals that they use for their own defense against insects and disease organisms. Natural pesticides for plants also are considered to be those chemical made from natural ingredients. People believe that natural pesticides are always safe and more eco-friendly than man-made or synthetic pesticides and while this is mostly true but it is not always so for example, nicotine as a natural pesticide in tobacco leaves, and the highly addictive component of cigarette smoke, but it is much more toxic than most modern synthetic or man-made pesticides. While some natural pesticides are also toxic many are actually much safe and more eco-friendly than synthetic pesticides. Since natural pesticides are also very effective, it should be the first choice for most home and farm pest control needs [3]. Chemicals assault or enters the body at almost every hour of the day. They may come through air, food, products use on the body, and in drinking water. Toxic buildup of these chemicals has been shown to cause several damage in the body and minimize health. Many modern pesticides (synthetic) used persist in soil for years and compound the store of toxins such as heavy metals in the soil, air and water [4,1].

Natural pesticides are not products of chemical engineering and are return to the environment with less impact and reduced danger. Pesticides for organic gardens must meet certain criteria set forth by the United States Department of Agriculture (USDA) and bear a logo stating they are certified for use. The benefits of using organic or natural pesticides for plants are their specific target range, a slow mode of action, shorter persistence, low residue levels and safe use than conventional or synthetic pesticides [5]. These attributes are a win-win for consumers and the earth alike, but strict attention to time and mode of application and the precautions have to be strictly followed. That doesn't mean they are free from chemicals, just that the chemicals are derived from botanical and mineral sources. They must still be used carefully, but the chemicals break down more quickly than commercial sources and are deemed less threatening [6].

The recognized categories of bio-rational pesticides may be synthetic or natural compounds of microbial, plant protectant and biochemical (pheromones, hormones, natural growth regulators and enzymes) origins. Most biopesticides are nerve poisons acting at specific target sites in the insect's nervous system. Some pesticides act similarly to the old nerve poisons that result in knock-down, rapid intoxication, lack of coordination, paralysis and death, and have higher affinity to insect receptors than to mammalian. The other pesticides affect specific systems, such as the molting processes, metamorphosis and the pest endocrinology system. Biopesticides are third-generation pesticides that are environmentally friendly and closely resemble or are identical to chemicals produced in nature. The examples of biopesticides are the microbial pesticide *Bacillus thuringiensis* (Kurstaki), Most of the biopesticides show effectiveness against different strains of resistant species, with no evidence of cross-resistance; hence these can play an important role in integrated resistance management (IRM) strategies [7].

Most of the newer biopesticides are preferable to the conventional pesticides because of their specificity to target pests, effectiveness at low rates, selectivity to beneficial insects and their non-persistent characteristics in the environment. However, they are an alternative to the use of conventional pesticides such as organophosphates, organochlorine, organosulphur, carbamates and pyrethroids [8]. However, insect control using integrated pest management (IPM) means by use of several techniques to reduce the favorable environmental factors that promote to the pests and their ability to thrive are ideal options [9]. While the term pesticide is now often associated with synthetic chemical compounds, it was not until relatively recently that synthetic pesticides came into use. Naturally occurring compounds or natural extracts have been used as pesticides since ancient times. The earliest pesticides were most likely salt, sulfurous rock, and extracts of tobacco, red pepper, and the like. The napoleonic army used crushed chrysanthemums to control lice, with limited effectiveness [10].

Natural insecticides can be chemical, mineral, extract or biological. The common goal of all these is to kill, repel, or otherwise interfere with the damaging behavior of insect pests. Because this purpose corresponds with the legal definition of a pesticide, all-natural insecticide products must comply with federal and state regulations for registration, sales, transport, use, storage, and disposal. Some natural insecticides are allowed for use in certified organic systems if additional organic federal standards are met [11]. However, it is advisable to read the label of each product for specific application instructions. Many of the products described may also be used in commercial crop production, but do not represent the entire list available to commercial growers. As with any pesticide, it is important to choose a natural insecticide that fits the situation in which you will use it. These products vary in their toxicity to non-target organisms such as fish and bees, as well as their effectiveness at controlling specific insect pests. If used improperly, organic insecticides can harm people and the environment, so do not make the mistake of thinking that products labelled as "natural" are non-toxic. There is a great effort to reduce the risk of human exposure to pesticides and special demand for safe and more selective pesticides for natural enemies and non-target organisms.

1.1 Definition of Terms

1.1.1 Pest

Pest is any harmful, destructive, or troublesome animal, plant or microorganism.

1.1.2 Pesticides

Pesticides are chemical substance use to kill or retard the growth of pests that damage or interfere with the growth of crops, shrubs, trees, timber and other vegetation desired by humans. Practically all chemical pesticides, however, are poisons and pose a long-term danger to the environment and humans through their persistence in nature or body tissue. Most of the pesticides are non-specific and may kill life forms that are harmless or useful [12]. Pesticides are classified in three ways generally: Based on chemical structures, According to their mode of action and According to their mode of entry i.e. ingestion, inhalation, contact absorption.

1.1.3 Natural pesticides

Natural pesticides are naturally occurring chemicals extracted from plants. Natural pesticide products are available as an alternative to synthetic chemical formulations but they are not necessarily less toxic to humans. Some deadly, fast-acting toxins and potent carcinogens occur naturally [13].

1.1.4 Pest management

Pest management is a means of reducing pest numbers to an acceptable or economical threshold. While IPM is a developed method or ways use to control pests without relying solely on pesticides. The IPM is a systematic plan which brings together different pest control tactics into one program. Management does not mean eradicating pest. It means finding tactics that are effective and economical, and that keep environmental damage to a minimum level.

1.1.5 Selectivity

Selectivity is the use of pesticides to kill pests but not affecting their natural enemies. Or are a type of pesticide that target a specific pest species.

1.1.6 Mode of action

The mode of action or mechanism of action of pesticide is how the pesticide works. In other words, it is how the specific systems in the pest are affected by the pesticide. Mode of action refers to the specific biochemical interaction through which a pesticide produces its effect on the pest. Usually, the mode of action includes the specific enzyme, protein, or biological step affected. While most other classifications are the pests controlled, physical characteristics, or chemical composition, mode of action specifically refers to which biological process the pesticide interrupts [14]. Knowing the mode of action is integral for scientists to improve the quality and sustainability of a product. 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 know similarities and differences between humans and the pests we try to control. It is also very important to understand the modes of action of the pesticides we use is to prevent the development of pesticide resistance in the target pest(s). Using pesticides with same mode 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 [15].

2. SCOPE OF BIOPESTICIDES

Efforts is been made to find biopesticides with novel mechanism of action and have no cross-resistance with the old pesticides. Biopesticides are a distinct group of pesticides which is different from conventional pesticides. They are comprised of two major categories, which are the biochemical pest control agents (e.g., pheromones, hormones, natural plant growth regulators and enzymes) and the microbial pest control agents (e.g., microorganisms). Pesticides to be included in these categories must be naturally occurring, or if man synthesizes the chemical, and then it must be structurally safe and identical to a naturally occurring chemical. Minor differences between the stereochemical isomer ratios (found in the naturally occurring compound compared to the synthetic compound) will normally not rule out a chemical being classified as a biopesticides unless an isomer is found to have significantly different toxicological properties from those of another isomer. Thus, the application of active toxic biopesticides agents as an alternative control strategy results in an urge to look for environment-friendly, biodegradable and easily available at affordable prices products for pests control.

2.1 Uses of Biopesticides

Biopesticides give better control than conventional pesticides such as organochlorine, biopessticides are usually a narrow spectrum of activity; are cheaper, less toxic to workers or consumers; usually true to type, safer for the environment and for beneficial insects; and required for certified organic production surroundings. Biopesticides may be applied shortly before harvest without leaving excessive residues, are less persistence in the environment and have reduced risks to non-target organisms. They act very quickly in insect to stop feeding, they may not cause death for hours or days, but they often cause immediate paralysis or cessation of pests feeding. Most biopesticides insecticides may have low to moderate mammalian toxicity. In the field, their rapid degradation and action as stomach poisons make them more selective in some instances for plant-feeding pest insects and less harmful to beneficial insects. Many biopesticide are not toxic to plants, however, it is always best to test a new product on few plants first before applying on a large scale [16,17].

2.2 Various Types of Natural Pesticides

The major categories of biopesticides include botanicals, microbials, essential oil and minerals based, many of these come from plants themselves, insects, or naturally occurring minerals. Some of the more commonly used and effective natural pesticides are insect and mite growth regulators, *Bacillus thuringiensis* (Kurstaki), horticultural oils, insecticidal soaps, entomopathogenic nematodes and neem products. The advantage of using biological products is because they have less negative impact non-target organisms, including humans [18].

- **Microbial**

  This category include Fungi, bacteria, protozoans, algae, viruses, etc. which can be used to cause disease in an insect population. Several microbial have been genetically engineered to kill target insects more rapidly. These either introduce a disease to a certain insect population, produce a toxin or limit reproduction of insects. Milky spore is an example of this type of natural pesticide e.g. *Bacillus thuringiensis.*

- **Mineral**

  Mineral based controls include sulfur and lime-sulfur. Both combination are sprayed as part of the control of common insect pests.

- **Botanical**

  Botanical pesticides are gotten from plants. Nicotine, Neem, Rotenone, anabasine, azadirachtin, ryania, essential oil, Sabadilla and Pyrethrins are all derived from other plants. Pyrethrins for instance, is from the chrysanthemum plant and are effective on flying insects and to flush out larvae and grubs. Chemicals extracted or derived from plants may be present and subsequently extracted from the plant material (a constitutive chemical). It may be activated in the plant as a response to insect activity (inducible chemicals). Some are chemically modified after extraction to enhance their insecticidal properties.

- **Essential oil**

  Some plants also produce essential oils in specialized gland cells. Peppermint oil control of household pests such as cockroaches and ants. Clove oil inhibits soil-born fungal disease. Citrus oil control of flea, aphid and mites. Lavender oil insect repellent. Thyme oil, Rosemary oil and Cedar oil.

3. LIST OF NATURAL PESTICIDES (BIOPESTICIDES)

Natural pesticides are naturally occurring chemicals extracted from plants use to kill or retard the growth of pests that damage or interfere with the growth of crops, shrubs, trees, timber and other vegetation desired by humans. These natural pesticides include: Rotenone, Nicotine, Neem, Ryania, Pyrethrins, Sabadilla, Fluoroacetate, Carboxin and *Bacillus thuringiensis*.

3.1 Rotenone

Rotenone insecticides have been in use for centuries. Products containing rotenone are typically prepared from plant species of the genus Derris plant or Lonchocarpus (Leguminosae) with the majority from Cubé resin, a root extract of *Lonchocarpus utilis* and *Lonchocarpus urucu* [19]. Although rotenone is the major constituent in Cubé resin and hence in rotenone products, the active ingredients deguelin, rotenone, and tephrosin are also present [20]. Rotenone based products are approved for use as organic insecticides under many trade names and most are sold as blends containing both rotenone and pyrethrum extracts. Rotenone has been in use as a fish poison for more than 150 years [21]. It is also highly toxic to fish and is often used to eradicate unwanted fish populations, for instance, minnows in lakes before introducing trout, or to eradicate salmon in rivers in order to get rid of *Gyrodactilus salaries*, an obligate fish parasite that is a big threat to the salmon population [12].

Rotenone are derived from the roots of over 68 plant species and is very toxic to fish, pigs, and cool blooded animals. It is used to control leaf-eating caterpillars and beetles. Direct contact may cause skin and mucous membranes irritation. Rotenone is one of several isoflavonoids produced in the roots. Extraction of the root with organic solvents yields resins containing as much as 45% total rotenoids; studies indicate that the major constituents are rotenone (44%), and deguelin (22%) [22]. Rotenone is commonly sold as dust containing 1 to 6% active ingredients for home and garden use, but liquid formulations used in organic agriculture can contain as much as 9% rotenone and 16% total rotenoids.

Rotenone is a mitochondrial poison, which blocks the electron transport chain and prevents energy production. As a pesticide, it is considered a stomach poison because it must be ingested to be effective. Pure rotenone is comparable to Dichloro-diphenyl-trichloroethane (DDT) and other synthetic pesticides in terms of its acute toxicity to mammals (rat oral LD50 is 132 mg kg^{-1}), although it is much less toxic at the levels seen in formulated products. Safety of rotenone has recently been called into question because of: Controversial reports that acute exposure in rats produces brain lesions consistent with those observed in humans and animals with Parkinson's disease [23]. And the persistence of rotenone on food crops after treatment. A study of rotenone residues on olives conducted in Italy determined that the half-life of rotenone is 4 days, and at harvest residue levels were above the tolerance limit [24]. Moreover, residues were concentrated in oil obtained from the olives. As an Agricultural pesticide, use of rotenone is limited to organic food production.

3.1.1 Rotenone mode of action

Rotenone is an important insecticide extracted from various leguminous plants. It inhibits the transfer of electrons from nicotine amide-adenine (NADH) to ubiquinone. Rotenone is a powerful inhibitor of cellular respiration, the process that converts nutrient compounds into energy at the cellular level (Fig. 1). In insects rotenone exerts its toxic effects primarily on nerve and muscle cells, causing rapid cessation of feeding. Death occurs several hours to a few days after exposure. Rotenone is extremely toxic to fish, and is often used as a fish poison (piscicide) in water management programs.

Compound that disrupts energy metabolism has been identified from both natural and synthetic sources. Complex I is inhibited by rotenone which is derived from cube or derris root. Disruption of energy metabolism occurs in the mitochondria and usually takes the form of either an inhibition of the ETS, blockage of ATP synthesis. The ETS (complexes i-iv are macromolecular complexes that use high energy electrons to pump out hydrogen into the intermembrane space and to store this energy as a proton gradient, which is harnessed to synthesize ATP. Inhibition of ETS blocks indirectly the production of ATP and cause a decrease in oxygen consumption by the mitochondria. Rotenone inhibit complex I in the ETS and blockage at this site can reduce energy production and induce whole animal toxicity. The disruption energy metabolism and the subsequent loss of ATP results in a slowly developing toxicity, and the effects of all these compounds include inactivity, paralysis, and death [25] shown in Fig. 1.

3.2 Nicotine

Nicotine is an alkaloid obtained from the foliage of tobacco plants (*Nicotiana tabacum*) and related species, has a long history as an insecticide. Nicotine (Fig. 2) and two closely related alkaloids, nornicotine and anabasine, are synaptic poisons that mimic the neurotransmitter acetylcholine. As such, they cause symptoms of poisoning similar to those seen with organophosphate and carbamate insecticides [13]. Owing to the extreme toxicity of pure nicotine to mammals (rat oral LD50 is 50 mg kg^{-1}) and its rapid dermal absorption in humans, nicotine has seen declining use, primarily as a fumigant in greenhouses against soft-bodied pests. However, there remains some interest in preparing stable nicotine fatty acid soaps, presumably with reduced bioavailability and toxicity to humans [26]. Nicotine is a Pale yellow to dark brown liquid which is highly toxic to warm-blooded animals. Nicotine is a fast-acting contact killer for soft bodies but does not kill most chewing insects. Nicotine is highly lipophilic and can pass through dermal tissues as well as the blood brain barrier.

3.2.1 Nicotine mode of action

In both insects and mammals, nicotine is an extremely fast-acting nerve toxin. It competes with acetylcholine, the major neurotransmitter, by bonding to acetylcholine receptors at nerve synapses and causing uncontrolled nerve firing. This disruption of normal nerve impulse activity results in rapid failure of those body systems that depend on nervous input for proper functioning. In insects, the action of nicotine is fairly selective, and only certain types of insects are affected [27] shown in Fig. 2.

3.3 Sabadilla

Sabadilla is a botanical pesticide obtained from the seeds of the South American lily *Schoenocaulon officinale*. In purity, the active principles, celandine-type alkaloids, are extremely toxic to mammals (rat oral LD50 is ca. 13 mg kg−1), but commercial preparations typically contain less than 1% active ingredient, providing a margin of safety. These alkaloids are remarkably similar to that of the pyrethrins, despite their lack of structural similarity. Sabadilla is used primarily by organic growers; in California about 100 kg is used annually, primarily on citrus crops and avocado [19].

3.3.1 Sabadilla mode of action

In insects, sabadilla's toxic alkaloids affect nerve cell membrane action, causing loss of nerve cell membrane action, causing loss of nerve function, paralysis and death. Sabadilla kills insects of some species immediately, while others may survive in a state of paralysis for several days before dying.

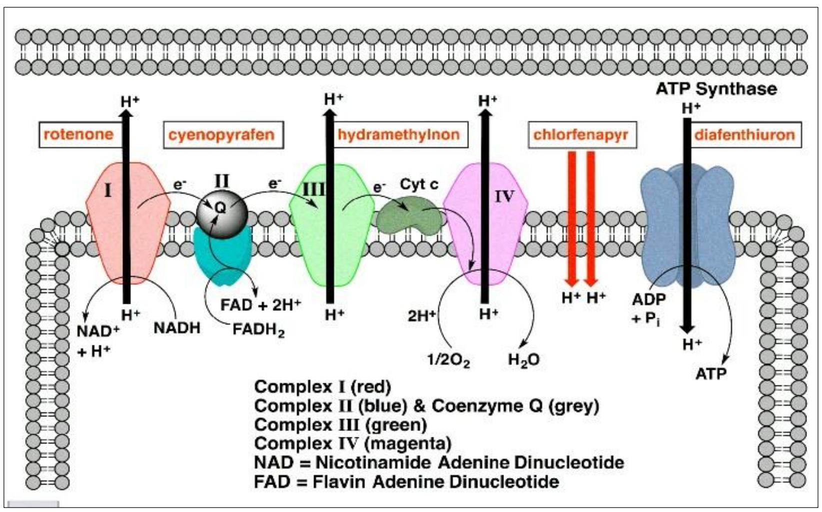


Fig. 1. Mode of action of rotenone in energy metabolism

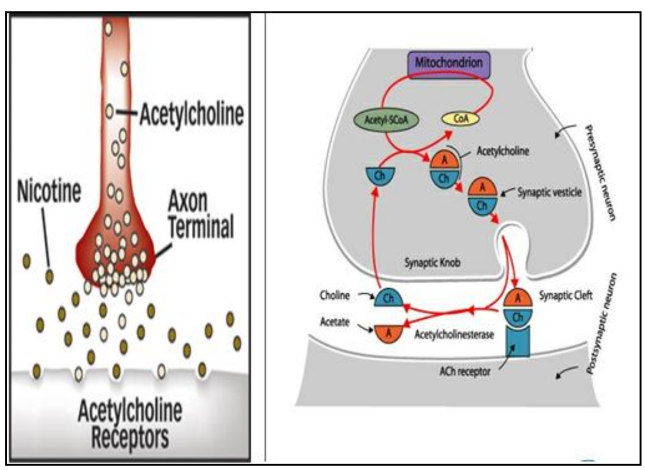


Fig. 2. Mechanism of nicotine in the nerve synapse

3.4 Ryania

Ryania Botanical insecticides are made from grounded stem of *Ryana speciosa*. Is highly toxic to the fruit moths, and citrus thrips. Another botanical in declining use is ryania, obtained by grinding the wood of the Caribbean shrub *Ryania speciosa* (Flacourtiaceae). The powdered wood contains < 1 % ryanodine, an alkaloid that interferes with calcium release in muscle tissue (National Research Council). It is used to a limited extent by organic apple growers for control of the codling moth, *Cydia pomonella*. More information on sabadilla and ryania can be found in the two reviews [19].

3.4.1 Ryania mode of action

Ryania is a slow-acting stomach poison. Although it does not produce rapid knockdown paralysis, it does cause insects to stop feeding soon after ingesting it. Little has been published concerning its exact mode of action in insect systems. Ryania is effectively synergized piperonyl butoxide (PBO) and is reported to be most effective in hot weather [28].

3.5 Pyrethrum

Pyrethrum, also known as pyrethrins, is extracted from the seed of *Chrysanthemum cineraria* folium and has been used as an insecticide for over 100 years. Today these plants are grown primarily in Kenya. Pyrethrum is effective against a wide range of soft-bodied garden pests such as scales, whitefly, mealybugs, and thrips, but will not control mites. Pyrethrins are neurotoxins that attack an insect's nervous system and cause repeated and extended nerve firings. They may also have a repellant effect. Pyrethrins are easily broken down by stomach acids in mammals, so toxicity to humans and pets is very low. However, toxicity can occur when significantly more product is applied than specified on the label. Do not spray pyrethrins around ponds or other bodies of water, as they can kill fish. Pyrethrum is a broad-spectrum insecticide that is toxic to beneficial insects. Pyrethrum can paralyze susceptible insects upon exposure, but also degrades in sunlight within hours Pyrethrum is a daisy-like Chrysanthemum. In the tropics, pyrethrum is grown in mountain areas because it needs cool temperatures to develop its flowers [29]. Pyrethrins is Very toxic to cool blooded animals, some peoples and cats. Very effective on most insects. It rapidly breaks down in sunlight, air and water.

Pyrethrins are insecticidal chemicals extracted from the dried pyrethrum flower. The flower heads are processed into a powder to make a dust. This dust can be used directly or infused into water to make a spray. Most of the world's pyrethrum crop is grown in Kenya. The term "pyrethrum" is the name for the crude flower dust itself, and the term "pyrethrins" refers to the six related insecticidal compounds that occur naturally in the crude material, the pyrethrum flowers. The flowers are ground to a powder and then extracted with hexane or a similar nonpolar solvent; removal of the solvent yields an orange-colored liquid that contains the active principles. These are three esters of chrysanthemic acid and three esters of pyrethric acid. Among the six esters, those incorporating the alcohol pyrethrolone, namely pyrethrins I and II, are the most abundant and account for most of the pesticidal activity. Technical grade pyrethrum, the resin used in formulating commercial pesticides, typically contains from 20 to 25% pyrethrins [19].

The insecticidal action of the pyrethrins is characterized by a rapid knockdown effect, particularly in flying insects, and hyperactivity and convulsions in most insects. These symptoms are a result of the neurotoxic action of the pyrethrins, which block voltage-gated sodium channels in nerve axons. As such, the mechanism of action of pyrethrins is qualitatively similar to that of DDT and many synthetic organochlorine pesticides. In purity, pyrethrins are moderately toxic to mammals (rat oral acute LD50 values range from 350 to 500 mg kg^{-1}), but technical grade pyrethrum is considerably less toxic (ca. 1,500 mg kg^{-1}) [30]. Pyrethrins are especially labile in the presence of the UV component of sunlight, a fact that has greatly limited their use outdoors. A recent study indicated that the half-lives of pyrethrins on field-grown tomato and bell pepper fruits were 2 h or less [31]. This problem created the impetus for the development of synthetic derivatives ("pyrethroids") that are more stable in sunlight.

The modern pyrethroids, developed in the 1970s and 1980s, have been highly successful and represent one of the rare examples of synthetic pesticide chemistry based on a natural product model. However, note that the modern pyrethroids bear little structural resemblance to the natural pyrethrins, and their molecular mechanism of action differs as well. *Pyrethrum* use data from California [32] in 2003 clearly demonstrate the dominance of this material among botanicals: Pyrethrum accounted for 74% of all botanicals used that year, but only 27% of that amount was used in agriculture (ca. 800 kg). Major uses of pyrethrum in California are for structural pest control, in public health, and for treatment of animal premises. *Pyrethrum* is the predominant botanical in use, perhaps accounting for 80 % of the global botanical insecticide market [19]. The organic solvent extract of the flowers was tenned pyrethrum, and it possessed many favorable properties. Its safety for mammals and rapid photodegradation led to many situations that required low mammalian toxicity and no residue problems (dairies, vegetables). This combination of desirable characteristics fueled numerous attempts to develop synthetic analogues that would be more widely available and perhaps more potent; the synthetic pyrethroids will be presented in the second-generation products of the botanical pesticides.

Pyrethrins break down very quickly in sunlight so they should be stored in darkness. Both highly alkaline and highly acid conditions speed up degradation so pyrethrins should not be mixed with lime or soap solutions. Liquid formulations are stable in storage but powders may lose up to 20 percent of their effectiveness in one year. To get adequate management of some pests, repeated applications are needed. *Pyrethrum* products frequently contain a low hazard activator or synergist such as piperonyl butoxide or piperonyl cyclonene that substantially increases the effectiveness of the pyrethrum and reduces its cost. Depending on the way these synergists have been manufactured, some pyrethrum products containing synergists may be allowed for use in organic agriculture.

3.5.1 Pyrethrin mode of action

Pyrethrins cause immediate paralysis to most insects. Low doses do not kill but have a knockdown effect stronger does kill. Pyrethrins are not poisonous for humans and warm-blooded animals. However, human allergic reactions are common. It can cause rash, and breathing the dust can cause headaches and sickness. Pyrethrins exert their toxic effects by disrupting the sodium and potassium ion exchange process in insect nerve fibers and interrupting the normal transmission of nerve impulses. Pyrethrins insecticides are extremely fast-acting and cause an immediate “knockdown” paralysis in insects. Despite their rapid toxic action, however, many insects are able to metabolize (break down) pyrethrins quickly. After a brief period of paralysis, these insects may recover rather than die. To prevent insects from metabolizing pyrethrins and recovering from poisoning, most products containing pyrethrins also contain the synergist, piperonyl butoxide (PBO) [33].

3.6 Neem Products (Azadirachtin)

Neem is derived from the neem tree (*Azadiracta indica*) of arid tropical regions, contains several insecticidal compounds. Neem (*Azadirachta indica*) belonging to the Meliaceae family has emerged as a highly potent biopesticide. The main active ingredients is azadiractin, which both deters and kills many species of caterpillars, thrips and whitefly. Both seeds and leaves can be used to prepare the neem solution. Neem seeds contain a higher amount of neem oil. The leaves of neem are available all year compared to the seed. A neem solution loses its effectiveness within about 8 hours after preparation, and when exposed to direct sunlight. It is most effective to apply neem in the evening, directly after preparation, under humid conditions or when the plants and insects are damp. High neem concentration can cause burning of plant leaves. Also, natural enemies can be affected by neem applications [34].

Seeds from neem tree comprises 40% of oil with azadirachtin as the major active ingredient responsible for the insecticidal activity of neem [35]. Neem oil contains more than a dozen azadirachtin analogs, but the major contributor to the insecticidal activity is azadirachtin. Further, the seed cake obtained during the processing of neem oil is a vital natural fertilizer used in common agricultural practices. Neem leaves have been employed for centuries against the stored grain pests due to its repellent properties. Collectively, all parts of neem plant are known to exhibit by-products that inherently impart an internal chemical defense making neem free from the pest attack, which can also be exploited to develop an efficient pest control strategy. Further, the functional ingredients of neem, exhibit, therapeutic significance as neem oil, bark, leaves and their purified biochemicals are documented to have anticancer [36] and antimicrobial [37] properties. Neem leaf extract possesses anti-inflammatory properties [38], while the neem oil acts as an antifertility agent [39]. This unique attribute of neem makes it an ideal bio-pesticide agent, as it does not cause non-specific toxicity to mammals.

Neem oil, obtained by cold-pressing seeds, can be effective against soft-bodied insects and mites but is also useful in the management of phytopathogens. Apart from the physical effects of neem oil on pests and fungi, disulfides in the oil likely contribute to the bioactivity of this material [4,40]. More highly valued than neem oil are medium- polarity extracts of the seed residue after removal of the oil, as these extracts contain the complex triterpene azadirachtin. Neem seeds actually contain more than a dozen azadirachtin analogues, but the major form is azadirachtin and the remaining minor analogues likely contribute little to overall efficacy of the extract. Seed extracts include considerable quantities of other triterpenoids, notably salannin, nimbin, and derivatives thereof. The role of these other natural substances has been controversial, but most evidence points to azadirachtin as the most important active principle. Neem seeds typically contain 0.2–0.6% azadirachtin by weight, so solvent partitions or other chemical processes are required to concentrate this active ingredient to level 10–50% seen in the technical grade material used to produce their products [41].

Azadirachtin has two profound effects on insects. At the physiological level, azadirachtin blocks the synthesis and release of molting hormones (ecdysteroids) from the prothoracic gland, leading to incomplete ecdysis in immature insects [11]. In adult female insects, a similar mechanism of action leads to sterility. In addition, azadirachtin is a potent antifeedant to many insects. The discovery of neem by western science is attributed to Schmutterer [42], who observed that swarming desert locusts in Sudan defoliated almost all local flora except for some introduced neem trees.

Indeed, azadirachtin was first isolated based on its exceptional antifeedant activity in the desert locust, and this substance remains the most potent locust antifeedant discovered to date. Unlike pyrethrins, azadirachtin has defied total synthesis to this point. In USA, Neem rapidly became the modern paradigm for the development of botanical pesticides. Enthusiasm for neem was fostered by several international conferences in the 1980s and 1990s, and several volumes dedicated to neem and neem insecticides have been published [43,34]. Unfortunately, neem's commercial success has fallen well short of the initial hype fueled by the explosive scientific literature surrounding it. In part this is due to the relatively high cost of the refined product [44] and the relatively slow action on pest insects. Nonetheless, several azadirachtin based pesticides are sold in the United States and at least two such products in the European Union. In California, azadirachtin-based insecticides constituted about one third of the botanicals used in agriculture in 2003 (ca. 600 kg). In practice, reliable efficacy is linked to the physiological action of azadirachtin as an insect growth regulator; the antifeedant effect, which is spectacular in the desert locust, is highly variable among pest species, and even those species initially deterred are often capable of rapid desensitization to azadirachtin (Bomford and Isman 1996). What is clear is that azadirachtin is considered nontoxic to mammals (rat oral acute LD50 is > 5,000 mg kg−1), fish [45], and pollinators [46]. The influence of azadirachtin on natural enemies is highly variable. Like the pyrethrins, azadirachtin is rapidly degraded by sunlight. For example, on olives growing in Italy, azadirachtin has a half-life of approximately 20 h [47]. Azadirachtin has systemic effect in certain crop plants, greatly enhancing its efficacy and field persistence [34]. On the other hand, [48] mentioned further that NeemAzal-T/S had reduced the parasitism rates, to 40, 55.4, 77.8 and 81.3% (at 2, 1, 0.5, 0.25% cons.), respectively, compared to 93.3% on control plants.

The seed has the highest content of azadirachtin of all plant parts, and most products are based on oil extractions from the seed kernel. Comparatively lower bioactivity occurs in leaves owing to lower concentrations of the bioactive compounds. However, many African farmers use the leaves in the preparation of crude pest control products, despite low efficacy as the leaves are easier to use: also, in some cooler climates neem trees do not flower so do not produce seed. Clearly practices need modifying and end-users need information to ensure time and resources are not wasted using ineffective materials. Neem seed oil has been formulated into hundreds of different products such as soaps, medicines and pesticides. A number of Neem pesticidal products are being produced and traded internationally, especially from China and India, whereas in Africa neem has enjoyed far less success [49].

Neem insecticides are effective against many caterpillars, flies, whitefly, and scales, and are somewhat effective against aphids. Neem may not show signs of efficacy for 3–8 days, and it can degrade within 3–5 days. Multiple applications are generally needed to obtain good management of the targeted pests. Neem is regarded as nontoxic to vertebrate animals and has been shown to minimally affect many beneficial insects such as bees, spiders, and ladybugs. Well known as a potent insect antifeedant, azadiractin. A appears to work by blocking the synthesis and release of molting hormones (ecdysteroids) from the prothoracic gland. Many neem/azadirachtin based products are approved for use as organic insecticides. An added advantage of neem oil-based products is their ability to control fungal infections as well as a wide variety of both insect and mite pathogens [50].

The seeds from the Indian neem tree, *Azadirachta indica*, are the source of two types of neem-derived botanical insecticides; neem oil and medium polarity extracts. Neem seeds contain more numerous azadirachtin analogues, but the major form is azadirachtin A (Fig. 3) and the remaining minor analogues likely contribute little to overall efficacy of the extracts [19].

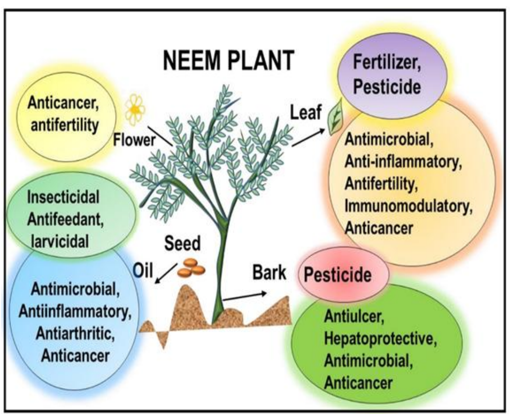


Fig. 3. Schematic representation of the agro-medicinal tree [51]

3.6.1 Azadirachtin mode of action

Neem products are complex mixtures of biologically active materials, and they are difficult to pinpoint the exact modes of action of various extracts or preparations. In insects, neem is most active as a feeding deterrent, but in various forms it also serves as a repellent, growth regulator, oviposition (egg deposition) suppressant, sterilant, or toxin. As a repellent, neem prevents insects from initiating feeding. As a feeding deterrent, it causes insects to stop feeding. As a feeding, either immediately after the first "taste" (due to the presence of deterrent taste factors), or at some point soon after ingesting the food (due to secondary hormonal or physiological effects of the deterrent substance). As a growth regulator, neem is thought to disrupt normal development interfering with chitin synthesis. Susceptibility to the various effects of neem differs by species.

3.6.2 Neem seed kernel extract: The recipe

Pound 30 g neem kernels (the seed of which the seed coat has been removed) and mix it in 1 litre of water. Leave that overnight. The next morning, filter the solution through a fine cloth and use it immediately for spraying. It should not be further diluted.

3.7 Bacillus thuringiensis (B.t.)

This is probably the most common microbial 'active ingredient'. This organism is incorporated into several products, most of which are used to control caterpillar pests. Specific strains of B.T. have been selected for their ability to control mosquitos, black flies and other organisms. For example, B. t. strains 'kurstaki', 'berliner' and 'aizawai' are used for controlling larvae of many Lepidoptera pests, while *B.T*. 'tenebrionis' is used against larvae of Colorado potato beetle, and B.T. 'israelensis' is used to control mosquito larvae. Be sure that the product chosen is labelled to control the pest the growers are targeting. Additionally, while some crops have been modified to express the insecticidal protein produced by *B. thuringiensis* these genetically altered plants are not considered.

3.8 Fluoroacetate

Fluoroacetate is produced by many plants in Australia and South Africa and has an important function as a natural pesticide for the plants. It is highly toxic to rodents and other mammals. In certain parts of Australia, where such plants are abundant, opossums have become resistant to fluoroacetic acid.

3.8.1 Mode of action of fluoroacetate

The mode of action of fluoroacetate is well understood: it is converted to fluoroacetyl-CoA, which is thereafter converted to fluorocitric acid. This structure analogue to citric acid inhibits the enzyme that converts citric acid to cis-aconitic acid, and the energy production in the citric acid stops. Citric acid, which accumulates, sequesters calcium. A-Ketoglutaric acid and therefore glutamic acid are depleted. These changes are, of course, detrimental to the organism. The nervous system is sensitive to these changes because glutamic acid is an important transmitter substance in the so-called glutaminergic synapses, and calcium is a very important mediator of the impulses. Furthermore, the halt of aerobic energy production is very harmful.

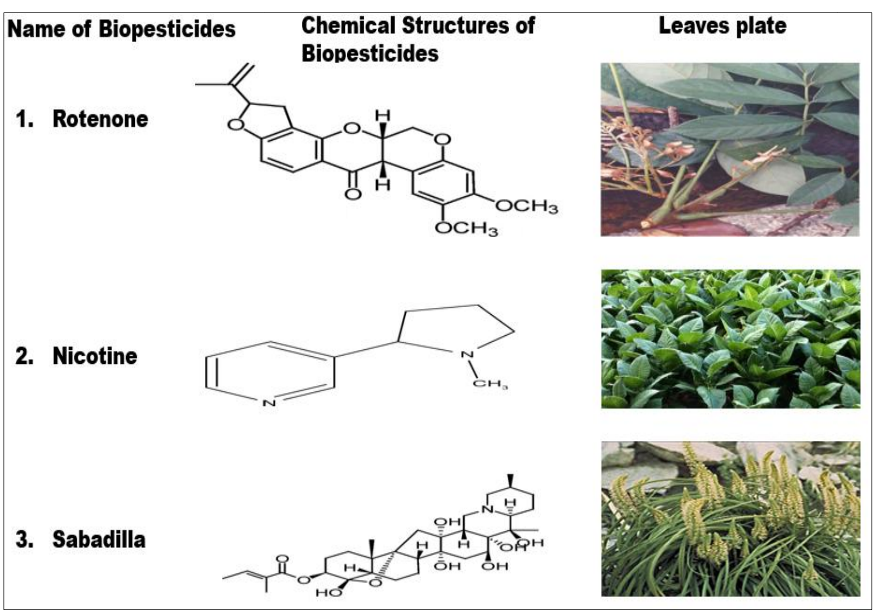
3.9 Carboxin

Carboxin is a systemic pesticide is taken up by the organism it protects and may kill sucking aphids or the growing fungal hyphae. The older fungicides are active only as a coating on the surface of the plants and do not fight back growing mycelia inside the plant tissue.

3.9.1 Carboxin mode of action

Carboxin inhibit the dehydrogenation of succinic acid to fumaric acid, an important step in the tricarboxylic acid cycle. The toxicity to animals and plants is low in spite of this very fundamental mode of action. The fungicides in this group are anilides of unsaturated or aromatic carboxylic acids.

Fig. 4. Steps in preparation of neem seed solution



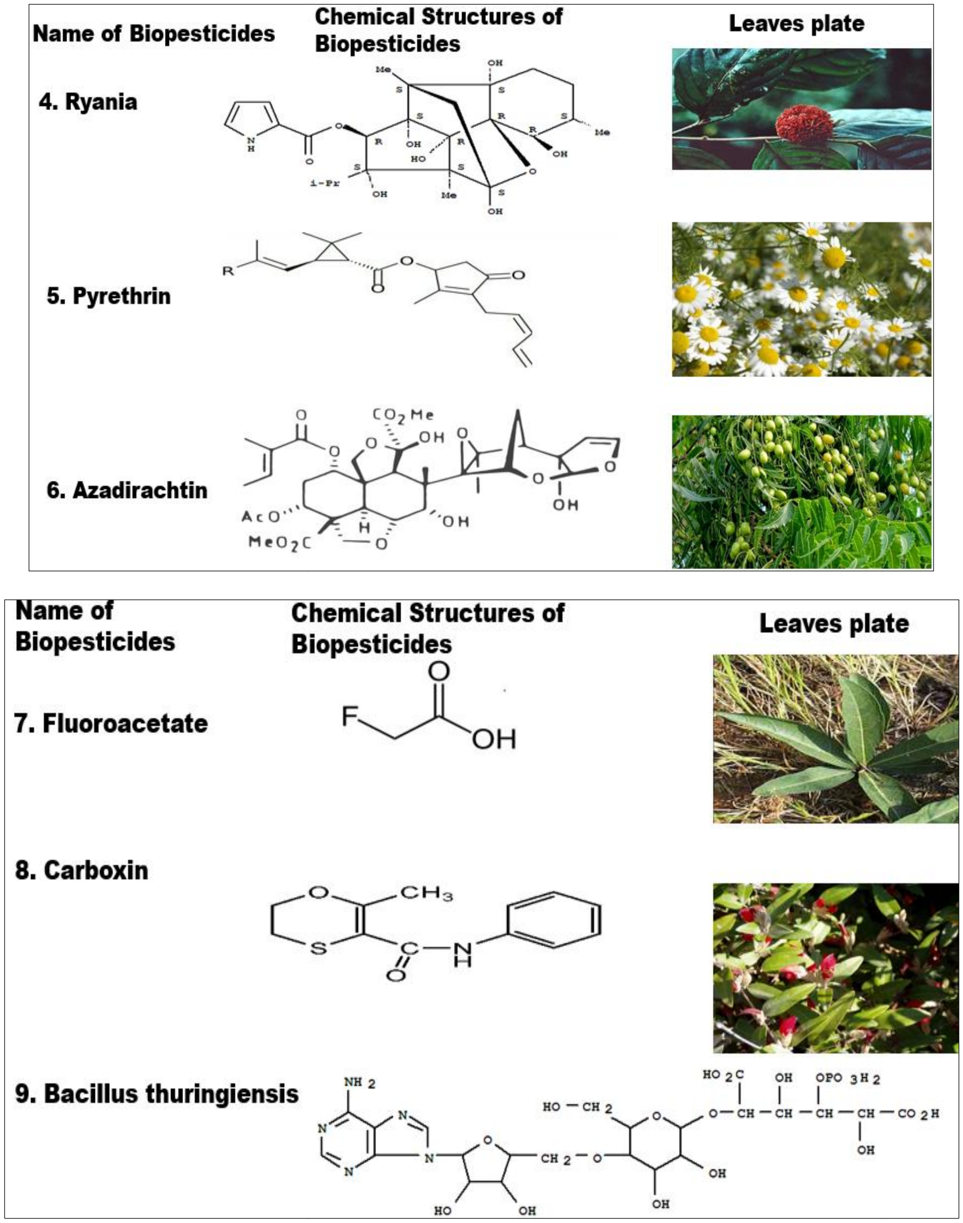


Fig. 5. Names, structure and leaves of biopesticides

4. GENERAL MODE OF ACTION OF NATURAL PESTICIDES

Mode of action is the sum of anatomical, physiological and biochemical interactions and responses that result in p toxic action of a chemical, as well as the physical (location) and molecular (degradation) fate of the chemical in the organism. These compounds have achieved several currently desired goals of pest managers and the greater public demands. These are very selective, targeting just the pest, usually do not persist in the environment, much safer to handle and apply when compared to most chemical pesticides, and tend to preserve beneficial organisms. The most of the bio-rational insecticides have diverse modes of action, show effectiveness against different strains of resistant species, with no evidence of cross-resistance, has assisted in managing resistance to insect pests and they can play an important role in IRM strategies. Most bio-rational pesticides are nerve poisons acting at specific target sites in the insect's nervous system. Some insecticides act similarly to the old nerve poisons that result from knocking-down, rapid intoxication, lack of coordination, paralysis and death, and have higher affinity to insect receptors than to mammalian. The other insecticides affect specific systems, such as the molting processes, metamorphosis and the insect endocrinology system. All the bio-rational or low-risk insecticides have relatively low detrimental effect on the environment and its inhabitants, and have little or no adverse consequence for non-target organisms, thus rendering them among important components in IPM program [12].

4.1 Scope of Biopesticides

Efforts have been made to find bio-rational insecticides with novel modes of action and have no cross-resistance with the old insecticides. Biopesticides are a distinct group, inherently different from conventional pesticides. They are comprised of two major categories, the biochemical pest control agents (e.g., pheromones, hormones, natural plant growth regulators and enzymes) and the microbial pest control agents (e.g., microorganisms). Pesticides to be included in these categories must be naturally occurring, or if man synthesizes the chemical, and then it must be structurally identical to a naturally occurring chemical. Minor differences between the stereochemical isomer ratios (found in the naturally occurring compound compared to the synthetic compound) will normally not rule out a chemical being classified as a bio-rational unless an isomer is found to have significantly different toxicological properties from those of another isomer. Thus, application of active toxic bio-rational agents as an alternative control strategy results in an urge to look for environment-friendly, biodegradable and easily available at affordable prices products for pest's control.

4.2 Regulations of Bio-rational Pesticides

The philosophy and approach to the regulations of bio-rational pesticides shall require registrants to obtain clearance from the expert's committee prior to the registration of the products. In regulating bio-rational pesticides, it shall be recognized that these kinds of pesticides are inherently different from conventional pesticides and will take due consideration that many classes of biopesticide control agents might pose lower potential risks than conventional pesticides. The most important inherent difference

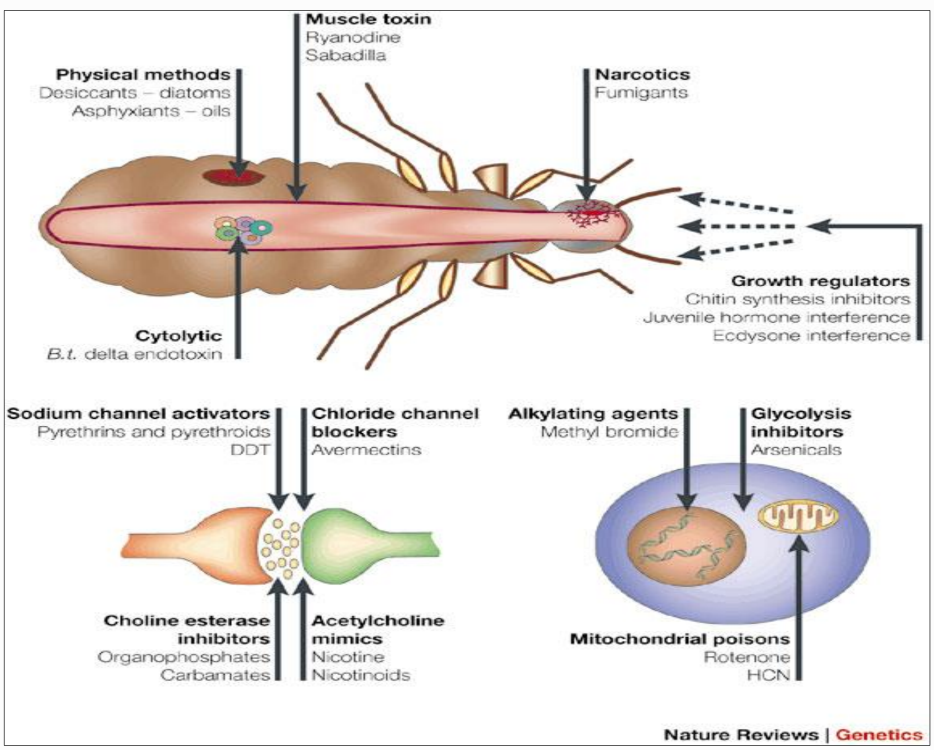


Fig. 6. Mode of action of natural pesticides

between biopesticides and conventional pesticides are target species specificity, generally non-toxic mode of action and natural occurrence of the bio-rational agents. These factors provide the basis for the expectation that many classes of bio-rational pest control agents pose a lower potential hazard than conventional pesticides and support the approach to testing needed for the registration of manufacturing product. Thus, the Environmental Protection Act in various states has framed a number of rules and regulations to check the application of chemical control agents in nature [52].

4.3 Advantages of Natural Pesticides

1. Plants producing the above-mentioned compounds are known by the farmer because most of the time they grow in the same general area.
2. Eco-friendly safer for user/applicator, and very effective when used correctly.
3. Often these plants also have other uses like household insect repellents or are plants with medicinal applications.
4. The rapid degradation of the active product may be convenient as it reduces the risk of residues on food.
5. Some of these products may be used shortly before harvesting.
6. Many of these products act very quickly inhibiting insect feeding even though long term they do (will?) not cause insect death.
7. Since most of these products have a stomach action and are rapidly decomposed they may be more selective to insect pests and less aggressive with natural enemies.
8. Most of these compounds are not phytotoxic.
9. Resistance to these compounds is not developed as quickly as with synthetic pesticides.

4.4 Disadvantages of Natural Pesticides

1. Most of these products are not truly pesticides since many are merely insect deterrents and their effect is slow.
2. They are rapidly degraded by UV light so that their residual action is short.
3. Not all plant pesticides are less toxic to other animals than synthetic ones.
4. They are not necessarily available season long.
5. Most of them have no established residue tolerances.
6. There are no legal registrations establishing their use.
7. Not all recommendations followed by growers have been scientifically verified.
8. Short residual activity (some users consider this to be an advantage), maybe more expensive than older conventional pesticides, and somewhat less pest-specific, especially when compared to newer synthetic pesticides.

4.5 Pest Management

Pest management is a way to keep pests below the levels where they can cause economic damage. Management does not mean eradicating pests. It means finding tactics that are effective and economical, and that keep environmental damage to a minimum. The IPM is the managing of crops using many tactics to keep pest levels below an economic threshold. The IPM has been developing as a way to control pests without relying solely on pesticide. Integrated pest management is a systematic plan which brings together different pest-control tactics into one program. It reduces the emphasis on pesticides by including cultural, biological, genetic, physical, regulatory, and mechanical controls. To carry out an IPM program, you need to scout and monitor your fields, recognize abnormal conditions and identify their causes, understand the different control methods available, and determine the economic costs and benefits. A good IPM program requires planning, monitory and evaluation. Pest management are very site-specific. Pest management is based on the identification of pests, accurate measurement of pest populations, assessment of damage levels, and knowledge of available pest management strategies or tactics that enable the specialist to make intelligent decisions about control. The IPM offers the possibility of improving the effectiveness of pest control programs while reducing some of the negative effects. Many successful IPM programs have reduced pesticide use and increased protection of the environment.

5. CONCLUSION

Soil pollution, Air pollution has occurred from the use of synthetic pesticides and it takes years and sometimes decades for some of these chemicals to break down. These pesticides are also harmful to the animal, microorganisms, plants as well as human health. Luckily there are many Natural pesticides (Biopesticides) that are also effective in pest control. People need to break the habit of using harmful pesticides and switch to biopesticides which break down quickly in sunlight and in the soil. The faster a chemical breaks down, the sooner the soil can return to a healthy state. Most biopesticides are also safe to use around people and pets. They can easily be washed from fruits and vegetables making them healthier for us and our family to eat.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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