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MINI-REVIEW

The modes of action of biopesticidal compounds in insect control

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Abstract
Botanical or plant-derived insecticides are compounds of plant origin with insecticidal properties. Several insecticidal compounds from plants, such as pyrethrins, nicotine, azadirachtin, rotenone, and many others, have been found in different species of plants. Each of the compounds has specific physiological targets, mechanisms of action, and efficacy. The rise in demand for plant-derived insecticidal compounds is due to their non-toxic activity on non-target organisms. Some of the plant-derived insecticides used in commercially produced insecticides are azadirachtin present in neem tree *Azadirachta indica* (Meliaceae) and pyrethrins present in *Chrysanthemum tanacetum cinerariifolium* (Asteraceae). Limonene, eugenol, cinnamaldehyde, spinosads, and rotenone which are plant sources have also been used for insecticidal purposes. Most of these insecticidal compounds have been reported to mediate neurotoxic effects by acting on ion channels, receptors, or enzymes found in the insect nervous system. Pyrethroids act on voltage-gated sodium channels. This study reviewed the insecticidal effects of some plant-derived insecticides and their mechanisms of action.

Keywords Plant-derived insecticides · Pyrethrin · Azadirachtin · Rotenone · Mechanism of action

Introduction

Insecticides are generally defined as toxic substances, but not necessarily toxins that are released deliberately into the environment to kill insects. Insecticides can be biological or chemical sources and can be used to control insects (Turchen et al. 2020). These substances can be from natural sources or are synthetically made and applied to insects via slow-release diffusion, spray cans, or bottles (Kovalkovičová et al. 2015). Insecticides are important tools for controlling insect-borne diseases and preserving crop health and for centuries, have been curated specifically for the management of insect populations in several areas, such as agriculture, forestry, and horticulture (Araújo et al. 2023). They are also applied to curb insect vectors such as mosquitoes and ticks that spread diseases of public health concern, such as malaria, Lyme disease, and many others (Gupta et al. 2019). During the earliest history of insecticides, sulfur burning (brimstone) as a fumigant was used to ward off insects, gall from green lizards was used to protect apples from rot-causing worms, and compounds such as turpentine, fish oil, vinegar, and a mixture of pepper and tobacco were used in different ways to protect plants and animals from insect vectors (Kovalkovičová et al. 2015). During World War II in the 1940s, insecticides were limited to petroleum oils, chlorophenols, naphthalene, nicotine, pyrethrum, sulfur, rotenone, azadirachtin, and nitrophenols, which were mostly botanically derived. The period of World War II marked the opening of the wave of synthetic organic insecticides with the introduction of dichlorophenyl trichloroethane (DDT) in 1939 (Kovalkovičová et al. 2015). Insecticides combine different classes of chemicals that are toxic to insects and several other organisms via different modes of action (Gupta et al. 2019). As a result of the distinct chemical properties of insecticidal compounds, they mediate their

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action by interacting with various target and non-target sites, such as enzymes, ion channels, several molecules, and receptors. Most of these insecticides are neurotoxicants that target the nervous system, but can target other systems and organs of the organism (Abubakar et al. 2020). Insecticides can be classified as synthetic or natural (plant-derived), depending on the source of their insecticidal compounds. Natural insecticides are derived from phytochemicals, such as alkaloids, phenolic compounds, and terpenes, which have been proven to possess insecticidal properties. They also include a variety of essential oils and plant extracts derived from plant leaves, stems, roots, flowers, or fruits. They generally have low toxicity levels in mammals and temporary environmental persistence. Synthetics are insecticides derived from inorganic compounds, including chlorine, organophosphates, and carbamates (Abubakar et al. 2020). Plant-derived insecticides have been generally accepted for a long time because they have some significant advantages as shown in Fig. 1 over synthetic insecticides (Oguh et al. 2019; Shivkumara et al. 2019). The selectivity and safety of natural insecticides are not guaranteed; some natural compounds can be toxic and may cause adverse effects in experimental animals. Furthermore, not all natural insecticides are inherently safe, and the label "natural" does not necessarily imply that these compounds are free from toxicity (Mossa et al. 2018). The advantages of plant-derived insecticides over synthetic insecticides include:

Plant-derived insecticides

Botanical insecticides are developed by plants as a defense mechanism against predators, which are usually insects (Grdiša and Gršić 2013). This served as a foundation for scientists to carry out tests using scientific methods. Based on these findings, several synthetic insecticides have been developed, but issues of environmental contamination and food safety have kept the demand for botanically derived insecticides. Plant-derived insecticides are the oldest known insecticides used to control the effects of insects on humans, crops, and domestic animals. Botanical or plant-derived insecticides are naturally occurring substances found in plants that possess insecticidal or pesticidal properties for plant protection (Grdiša and Gršić 2013). Over time, several insecticidal compounds, such as pyrethrins, nicotine, azadirachtin, rotenone, and many others have been discovered in different plant species, with each having a unique mechanism of action, physiological targets, and efficacy (Araújo et al. 2023). Plant-derived or natural insecticides are also called bioinsecticides or botanical insecticides and have been used for longer than any other, although they have not been scientifically proven to be effective. Among the 6,000 plant species screened, approximately 2,500 belonging to 235 families were found to have diverse resistant compounds against pests (Shivkumara and Manjesh 2019). Demand for naturally derived insecticides has increased over the years because of the toxic effects of synthetic insecticide on non-target organisms (Koul 2016). Some known plant-derived insecticides that have been used in commercial applications are azadirachtin and pyrethrin from the neem *Azadirachta indica* (Meliaceae) *and Chrysanthemum tanacetum cinerariifolium* (Asteraceae) respectively. Other plant-derived insecticides that have been discovered include limonene, eugenol, cinnamaldehyde, spinosads, and rotenone so many others (Ahmed et al. 2021). This study reviewed plant-derived insecticide and their mechanisms of action.

Fig. 1 Advantages of plant-derived insecticides over synthetic insecticides

Classification of plant-derived insecticides

The classification of botanical insecticides shown in Fig. 2 is based on their mode of penetration into the target, their toxicological mechanisms, and their chemistry. These insecticidal agents can be categorized as stomach poisons that are ingested, contact poisons that are absorbed through the body surface, or fumigants that are inhaled. Most insecticides affect the insect nervous system, energy production, endocrine system, integument (cuticle) development, or water balance (Rajashekar and Shivanandappa 2014).

Pyrethrum

Pyrethrum, also called pyrethrin, is an extract of *chrysanthemum* flowers that is usually grown in Ecuador and Kenya. As early as the 19th century, the flowers were dried, ground into powder, and used in Napoleonic wars to control body lice. It is one of the safest and oldest plant-derived insecticides used to date (Khater 2012). Pyrethrin, a potent insecticidal substance, is a mixture of six compounds obtained from the seeds and flowers of *Tanacetum cinerariifolium* (Jeran et al. 2021). The majority of pyrethrin is present in

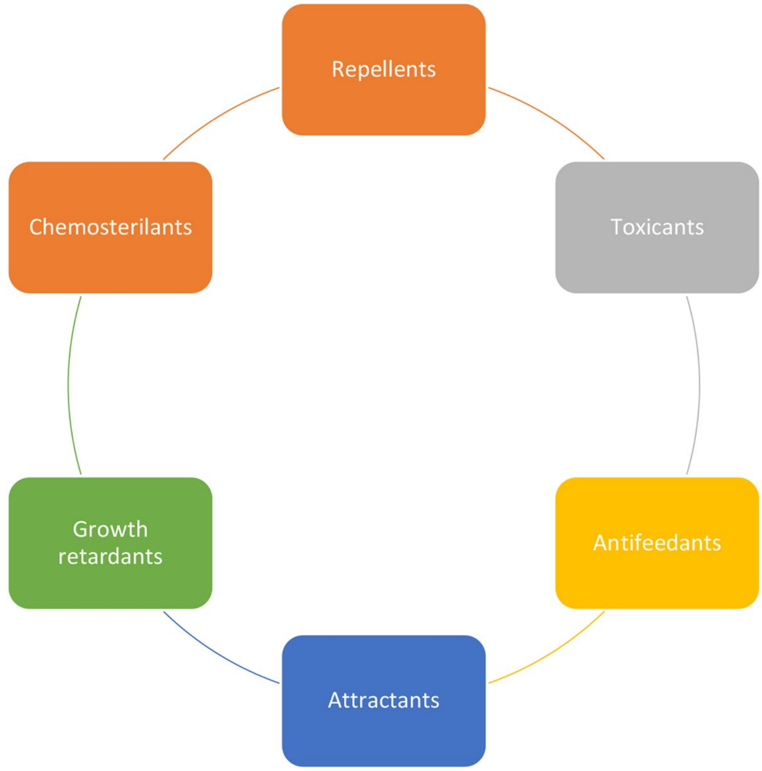


Fig. 2 Classifications of the insecticidal actions of botanical insecticides Shivkumara and Manjesh (2019)

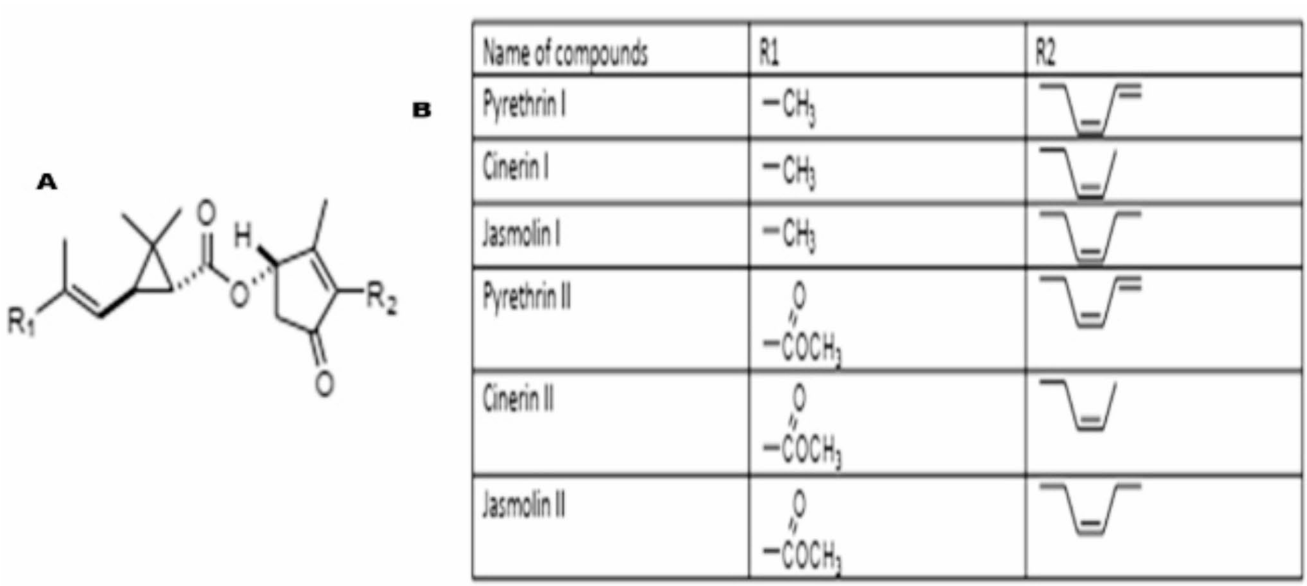
the flower, but minor quantities are found in other parts of the plant. Approximately 94% of pyrethrin accumulates in the secretory tissue of achenes of the flower, protecting them from light degradation (Grdiša and Gršić 2013). It carries out its effect by being a contact and stomach poison and paralyzing its target by interrupting the normal transmission of nerve impulses in the sodium-potassium ion exchange pump in the nerves of its target. Pyrethrin has a low toxicological effect on mammals with only a few cases of human poisoning reported but significantly toxic to fish and aquatic vertebrates (Rajashekar and Shivanandappa 2014). Pyrethrins and Pyrethroids (synthetic pyrethrins) are widely used worldwide in agriculture, animal health, residential settings, and public health. They are used to disinfect military uniforms and commercial aircraft. Pyrethrins are easily degraded by light, air, water, and high temperatures, and do not accumulate in groundwater, food chains, or the environment (Grdiša and Gršić 2013). They break down slowly in dark places and water, making them toxic to some aquatic organisms. Owing to their very high biodegradability, they are environmentally safe and perfect substitutes for synthetic insecticides, although their usage is limited due to instability. Pyrethrins are used in agriculture as a preharvest treatment for fruits, vegetables, plants, forage, and crops. They are effective against mosquitoes, caterpillars, aphids, beetles, and many other insects (Grdiša and Gršić 2013).

Chemistry of pyrethrins

Pyrethrins are lipophilic, naturally occurring compounds containing a group of six structurally related insecticide esters based on a common structure (Hansen and Khan 2013). They are rapidly metabolized and excreted via oral or dermal routes (Hansen and Khan 2013). Pyrethrins exert their insecticidal effects through a combination of six distinct compounds (Fig. 3): pyrethrin I, pyrethrin II, cinerin I, cinerin II, jasmolin I, and jasmolin II (Grdiša et al. 2020). Pyrethrin type I esters have a chyrsanthemoyl moiety, while type II esters have a pyrethroyl moiety with an additional ester linkage, a methoxycarbonyl group (Matsui et al. 2020). They are collectively called pyrethrins (Fig. 4), with pyrethrin I being the most potent of the six. Extracts of pyrethrin contain jasmolins, cinerins, and pyrethrins in a ratio of 1: 3:10 (Grdiša and Gršić 2013). They are structurally similar to esters of cyclopropane carboxylic acid (acid moiety) and cyclopentenolone alcohol (alcohol moiety) (Matsui et al. 2020). To achieve a more photostable compound while retaining insecticidal activity, pyrethroids were synthesized, which are synthetic derivatives of natural pyrethrins (Soderlund 2020).

Mode of action of pyrethrins

Pyrethrins exert their effect on insects by initiating an initial hyper-excitatory effect on their nervous system (Soderlund



Name of compounds	R1	R2
Pyrethrin I	$-CH_3$	
Cinerin I	$-CH_3$	
Jasmolin I	$-CH_3$	
Pyrethrin II	$-COCH_3$ (O)	
Cinerin II	$-COCH_3$ (O)	
Jasmolin II	$-COCH_3$ (O)	

Fig. 3 Q2 resolutioned image

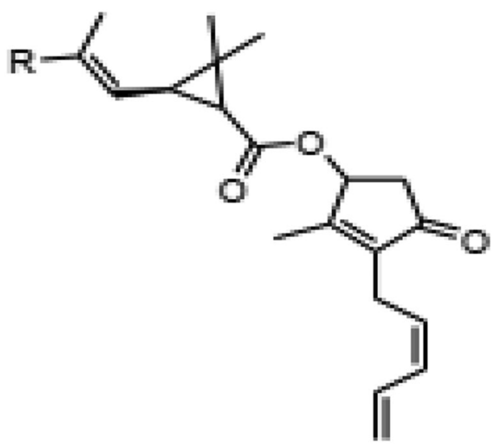
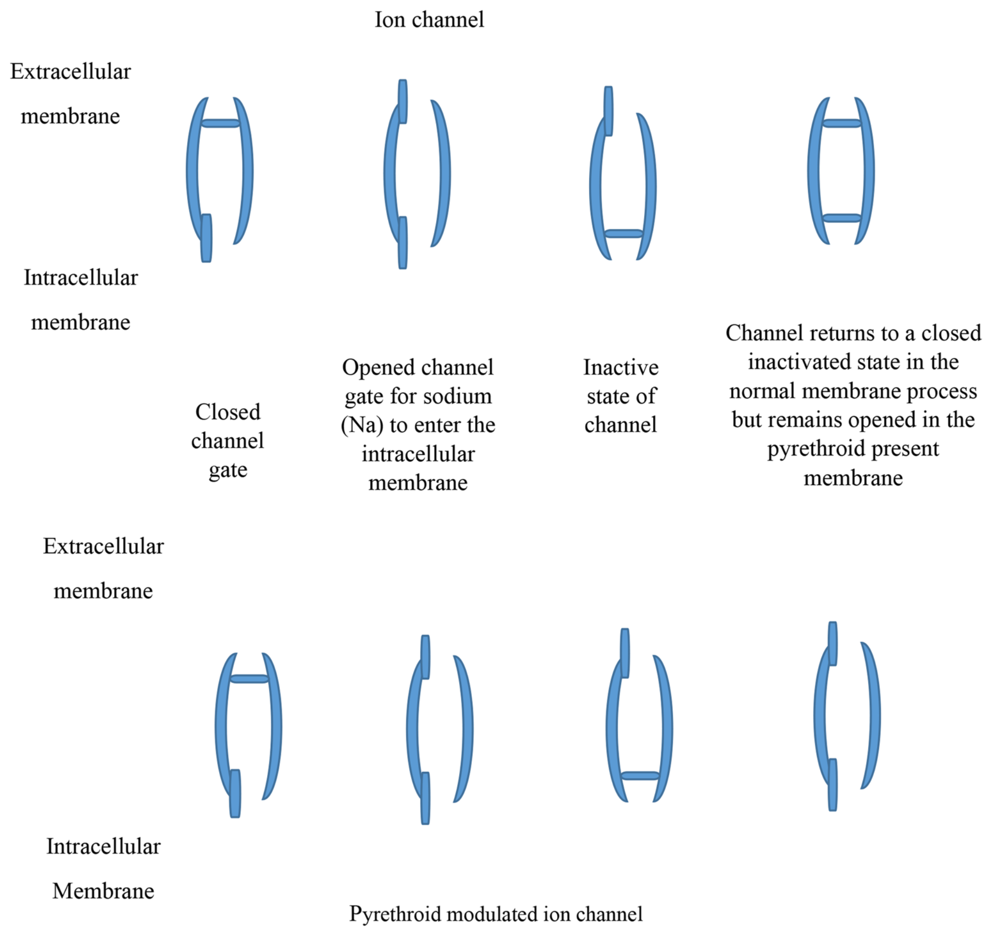


Fig. 4 Chemical structure of pyrethrins

2020). The principal effect of the pyrethroids is an axonic poison which means they affect the electrical transmission of impulses along the nerve axon (Mpumi et al. 2016). Pyrethrum causes its paralytic action by stimulating the nerve cells for the production of repetitive discharges in the sodium channel pump leading ultimately to paralysis and death. The sodium channel is a passage that allows for the flow of sodium ions into the axon causing excited charges (Khater 2012). Pyrethrins insecticides causes a delayed closing of the sodium channel, leading to an increase influx of sodium ion in the channel ultimately resulting to abnormal excitation of the neurons which causes loss of coordinated controlled movements, paralysis, and eventually death (Rajashekar and Shivanandappa 2014). Membrane depolarization involves the flow of sodium ions into the nerve axon through the sodium channels on the nerve fibers.

As the sodium ion inflow decreases, it inactivates the action potential. The potassium channel opens up at the apex of the action potential, releasing potassium out of the cell. This process allows the membrane to return to its original rest state through the mediation of the energy-dependent sodium and potassium pumps (Hansen and Khan 2013). However, exposure to pyrethrins causes a prolonged period of sodium inflow extending the length of depolarization of the action potential, invariably resulting in repetitions of nerve firing (Hansen and Khan 2013). Since pyrethrum is metabolized quickly, most insects recover quickly from its effect, a short period after which the insect recovers. The required dosage to kill an insect is very high and requires a longer time. However, to accelerate its potency, synergists such as piperonyl butoxide are mixed with it to prevent its metabolization (Oguh et al. 2019). Pyrethrins are observed to bind more strongly with the sodium channel at lower temperatures, causing them to bind more effectively in insects as they have an ambient temperature of 25^{0}C compared to 37^{o}C in mammals (Fig. 5). Sodium channels in insects are more sensitive to pyrethrins than sodium channels in mammals which recover more quickly from depolarization than insects (Ensley 2018). Pyrethrins exhibit a knockdown phenomenon in insects which is caused by inhibition of the cell but not leading to a lethal effect. This is due to the ability of the sodium channel to maintain most of its normal functions such as conductance and selectivity for sodium ions after exposure to pyrethrins. If the sodium concentration in the ion channel is within the capacity of the sodium pump to remove it, the cells continue to function normally. Depolarization and conduction block are seen only at high

Fig. 5 Modulation of the ion Na^+ channel by pyrethroid



concentrations of pyrethrin beyond the cell maintainable limits (Ensley 2018).

Azadirachta indica

Azadirachta indica (Neem) from the Meliaceae (mahogany) family, referred to as Indian lilac or margosa is a tree with multi-purpose uses. It grows in southern and southeastern Asia and recently in the tropical and subtropical areas of North and South America, Australia, and Africa (Grdiša and Gršić 2013). Neem has been known for its distinct insecticidal and health-beneficial properties (Dawkar et al. 2019). Its products have been one of the oldest used in insecticides, contraceptives, antipyretic, antiseptic, and anti-parasitic. It is also useful for shades and woods (Allan et al. 1999; Kader et al. 2022). The principal active agent in the neem tree with insecticidal properties is azadirachtin. It is the main component of the tree oil that is obtained from its fruits, which is used for detergents and soap production, while its other by-products are used in fertilizer production (Kader et al. 2022). The neem tree grows to about 30 m in height with its branches spreading across 10 m. It is a perennial and fast-growing tree and can survive in areas with high temperatures, degraded soils, and low annual rainfall (Fernandes et al. 2019). It houses various compounds and from studies, azadirachtin has been identified as the major bioactive compound (Fernandes et al. 2019). The fruits contain a seed that houses the azadirachtin and its other components. Its leaves and barks contain other active sulphur and limonoid compounds with, contraceptive, antiparasitic, antiseptic, repellent, and antipyretic abilities and also azadirachtin but in low quantities (Khalil 2013) while the highest quantity is found in the seeds (Grdiša and Gršić 2013). Neem-derived insecticides are mostly insect growth regulators and can also act as sterilants against a wide range of arthropods. This has been proven via the usage of crude neem seed extract at small, local farms over years in countries that grow neem trees indigenously and are considered safe for the environment and public health (Ashraf et al. 2018). The dosage of the botanical insecticide varies based on how the plant source is prepared. For example, a commonly recommended amount of neem leaf powder for protecting stored beans from insects is 25 g per kilogram of seeds (Boeke et al. 2001, 2004). In addition, *Helicoverpa armigera* (Hübner) (*Lepidoptera*: Noctuidae) fed on chickpea, *Cicer arietinum* (L.) was used to evaluate the efficiency of neem using a laboratory bioassay. Neem leaf extract, neem seed kernel extract, and neem oil were used alone and in combination at a concentration of 5% for each treatment. All the treatments were effective and showed significant *Helicoverpa armigera* (Hübner) (Lepidoptera). Similarly, the 2nd instar larvae were more susceptible to neem products, and after 72 h, the maximum mortality (50%) was observed in the neem leaf extract + neem seed kernel oil treatment. In addition, this treatment resulted in 40% mortality of the 4th instar larvae of *H. armigera* at the same exposure interval (Wakil et al. 2008).

Azadirachtin

Azadirachtin is an environmentally friendly bioactive compound, due to its high degradability in sunlight (Kilani-Morakchi et al. 2021; Su et al. 2023). It is useful in pest management programs and organic farming (Grdiša and Gršić 2013). It is the most abundant, relevant, and active compound of the Neem tree that is responsible for its toxic and anti-feeding effects on insects (Nisbet 2000). It can be found in many parts of the tree in smaller quantities but is most abundant in the seed. It is well used in various applications as therapeutic agents and biopesticides. An example of commercially available neem-derived insecticide is NeemAzal and it is available in several countries and used against various insects (George et al. 2014).

Chemistry of *Azadirachtin*

Azadirachtin is a complex tetranortriterpenoid in the class C-seco-limonoid (Kale et al. 2020). It is a molecule that has 8 rings, (5 of which have oxygen atoms), three quaternary carbon atoms, and 16 chiral centers. It has functional groups like enol ether, an epoxide, a hydroxyl group, two hemiacetals, acetal, and four carboxylic esters. Azadirachtin appears as a white microcrystalline solid and has an odour of garlic or sulfur. It has an empirical formula of $C_{35}H_{44}O_{16}$ and a molar mass of 720.71 g/mol. It melts at a temperature of 165°C. It is a hydrophilic compound, highly soluble in polar solvents, non-volatile, and photosensitive (Fernandes et al. 2019). The current chemical structure of azadirachtin (Fig. 6) was described first in 1976. It has an extremely complex structure and is a highly oxidized compound. It has intramolecular hydrogen bonds and many functional reactive groups in really close proximity giving its rigid conformation (Fernandes et al. 2019). Azadirachtin is a biodegradable compound making it a safe pesticide as it shows a reduced level of toxicity to mammals and other non-targeted organisms (Dawkar et al. 2019).

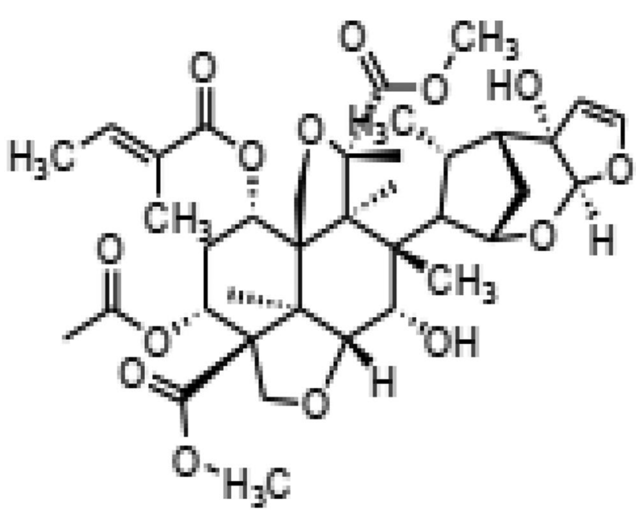


Fig. 6 Chemical structure of azadirachtin

Mode of action of azadirachtin

Azadirachtin has a broad mode of action as an insect growth regulator, feeding deterrent, sterilant, and repellent, and is also considered a contact poison. It may also inhibit oviposition (Rajashekar and Shivanandappa 2014). Qiao et al. (2014) gave report that azadirachtin also interferes with the central nervous system of an insect by blockage of the calcium channel and inhibiting the excitation of cholinergic transmission (Rajashekar and Shivanandappa 2014).

Azadirachtin as a repellant and antifeedant

As a repellent, azadirachtin prevents insects from feeding by deterring their taste factors after the first bite or by secondary hormonal or physiological effects of the deterrent substance (Rajashekar and Shivanandappa 2014). The ability of insects to feed normally depends on inputs from the chemical senses of the insect which are the mouthparts, taste receptors on tarsi, and oral cavity, and the central nervous integration of this sensory code (Manna 2021). The antifeedant effect observed in insects after being exposed to azadirachtin is traced to be related to a chemoreceptor sensory response on the mouthparts of the insects that causes a blockage of receptors that normally respond to phagostimulants. It stimulates the presence of cells that are deterrent in the chemoreceptors and prevents the release of sugar receptor cells that stimulate feeding. All of these inhibits feeding which causes the insect to starve and eventually die (Souto et al. 2021). Another antifeedant effect occurs in some insects and is referred to as secondary antifeedancy. This happens after ingestion and results in a reduction of continual food intake and digestion. This is a result of a bitter taste, disturbed hormonal activity, or other physiological systems which could be a result of inhibitory activities on the production of certain digestion enzymes, food passage through the guts, and many more (Oguh et al. 2019). An example of this secondary antifeedant effect was seen in an experiment carried out on locusts by Nasiruddin (1993), proving that Azadirachtin-injected locusts, showed a by-pass of taste receptors but reduced ingestion of food observed by fecal production.

Azadirachtin as a growth regulator

Certain compounds can interfere with the endocrine system of an insect and these compounds are said to be insect growth regulators (IGRs). They act as juvenile insect hormone inhibitors or mimics, as well as inhibitors of chitin synthesis. Under normal circumstances, keeping insects in their immature state is done by the juvenile hormones (Souto et al. 2021). In the state of adequate maturation level, the trigger for the production of growth hormones that activate molting to the adult stage stops. The application of IGRs keeps the insect in larvae stage preventing it from molting thereby serving as a mechanism of pest control (Souto et al. 2021). Azadirachtin also disrupts the normal development of insects by interfering with the synthesis of chitin (Rajashekar and Shivanandappa 2014). Substances that inhibit chitin synthesis usually referred to as Chitin synthesis inhibitors (CSI) are often categorized with insect growth regulators (IGRs). These compounds inhibit the production of chitin, a major component of the insect exoskeleton by inhibiting the synthesis of new cuticles thereby inhibiting successful molting to the next stage (Rajashekar and Shivanandappa 2014). Azadirachtin can perform its function as an IGR by interfering with the activity of ecdysone, which is an insect hormone, due to the similarity between the chemical structure of azadirachtin and that of the insect hormone (Fernandes et al. 2019). These IGR effects are caused by disruptions in the interaction between the molting hormone and the juvenile hormone at the molt. This disruption is caused by a blockage of the release of morphogenetic peptides from the brain, which controls the release of hormones from the endocrine glands. These peptide hormones are prothoracicotropic hormones (PTTH) and allatostatins (Souto et al. 2021).

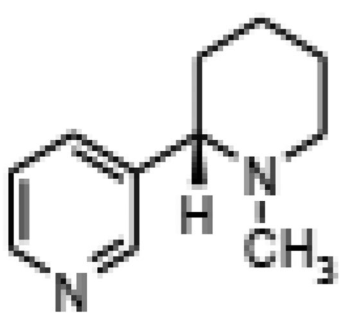


Fig. 7 Chemical structure of nicotine

Nicotine

Nicotine is an alkaloid (a chemical class of heterocyclic compound that contains a nitrogen atom) derived from *Nicotiana tabacum* a naturally occurring insecticide, which is most toxic to mammals among the other botanical insecticides (Rajashekar and Shivanandappa 2014). Nicotine was first isolated by Reimann and Posselt in 1828, and named after Jean Nicot, the person who introduced tobacco to the French court in 1560 (Alkam and Nabeshima 2019). Nicotine, an extract of tobacco was the first plant-derived insecticide reported in 1690 to have an insecticidal property and has been extensively used commercially since then (Wang et al. 2022). For hundreds of years, nicotine has been used as an insecticide and is presently used as a fumigant or foliar spray in controlling pests such as aphids. However, it is relatively toxic to several other organisms, mammals inclusive (Costas-Ferreira and Faro 2021). Additionally, the potent insecticidal properties were reported of the Australian plant, native tobacco *Nicotiana megalosiphon* against three major pests of brassicas: the diamondback moth (*Plutella xylostella*), cabbage aphid (*Brevicoryne brassicae*), and the green peach aphid (*Myzus persicae*). The 100% mortality exhibited by the aqueous extract (1%, 5%, and 10% w/v) of *N. megalosiphon* on *P. xylostella* was better than the recommended rate of tau-fluvalinate (asynthetic pyrethroid) or equivalent extracts of a second Australian native plant, *Mentha satureioides* (Amoabeng et al. 2018).

Chemistry of nicotine

Nicotine is present at a concentration of 2–6% in dried leaves of tobacco plants as a dinitrogen alkaloid (Alkam and Nabeshima 2019). This alkaloid is unusual because of the presence of two nitrogen-containing heterocycles, pyrrolidine, and a pyridine. Nicotine has an empirical formula of $C_{10}H_{14}N_2$, a molar mass of 162.23 g/mol, boils at a temperature of 247^{o}C, and melts at a temperature of -79^{o}C (Alkam and Nabeshima 2019). Its IUPAC name is 3–2 S-1-methylpyrrolidin-2-yl pyridine and it appears as a colorless to light yellow or brown liquid. It is combustible, producing toxic oxides of nitrogen during combustion. It is also highly toxic to the skin and by inhalation. When warm it gives off a fish-like odour and has an acrid, burning taste. In water below 60^{o}C, it is miscible while very soluble in liquids like chloroform, alcohol, oils, ether, petroleum ether, and kerosene. Nicotine gradually turns brown when exposed to air or light making it photosensitive and it is highly toxic to mammals. The structure of nicotine as shown in Fig. 7 was determined by Pinner in 1893.

Mode of action of nicotine

Nicotine carries out its insecticidal activity by disrupting the nicotinic acetylcholine receptor of the synapse which is located in the cholinergic system of the insects central nervous system. (Rajashekar and Shivanandappa 2014). Nicotine acts by mimicking acetylcholine at the nerve-muscle junction in the central nervous system (Fig. 8) and then interacts with the receptors at the synapse. Nicotine binds to the receptor of acetylcholine as an agonist causing an inflow of sodium ions and the buildup of action potentials. This interruption of the normal activity of the nerve impulse causes a failure of the systems that depend on nervous input for their function (Oguh et al. 2019). The enzyme acetylcholinesterase is responsible for the termination of the synaptic action of acetylcholine via hydrolysis. As acetylcholinesterase does not hydrolyze nicotine, hence the persistent activation of the cholinergic synapses results in hyperexcitation, convulsion, paralysis, and eventual death of the insect (Rajashekar and Shivanandappa 2014). Nicotinic Acetylcholine receptors (nAChRs) are found in both vertebrates and invertebrates as major excitatory neurotransmitter receptors and belong to the super-family of ligand-gated ion channels. They serve as the target site for many synthetic and naturally existing compounds with insecticidal activity in insects (Millar and Denholm 2007). Nicotinic receptors for a long time have been identified as potential insecticidal target sites and over the years, this has been explored by the development of highly selective and potent agent, synthetic neonicotinoids and the spinosyn (Millar and Denholm 2007).

Rotenone

Rotenone is a plant-derived insecticidal compound present in derris, lonchocarpus, tephrosia, and mundulea plant species obtained originally from South America, the East Indies, and Malaya (Rajashekar and Shivanandappa 2014). However, most of its commercial supplies are derived from the *Lonchocarpus*, and *derris* species. It is an insecticidal compound that is used around the world due to its wide range of insecticidal properties (Gupta et al. 2019). Rotenone, in its powdered form, is applied in medicine (veterinary) in the control of parasitic mites on fowls, lice, and ticks on horses, cats, and dogs especially. In agriculture, it is used in dust form to control beetles and aphids on vegetables, berries, flowers, and fruits (Gupta et al. 2019). It is also used as a fish poison for over 150 years to prevent unwanted fish from water bodies (Oguh et al. 2019). *Rhopalosiphum padi* (L.) decreases wheat yield by sucking plant nutrients, transmitting plant viruses, and producing mildew. *R. padi* develops resistance to pyrethroids and neonicotinoids. The control of *R. padi* was evaluated based on the activity of ten (10) botanical insecticides. This finding further demonstrated that rotenone and pyrethrins were more toxic to *R. padi* than commonly used chemical insecticides. At low lethal concentrations (LC_{10} and L_{30}) of rotenone or pyrethrins for 24 h, the lifespan and fecundity of adults in the F0 generation decreased significantly compared to the control. A negative effect was also observed in the F1 generation, including decreased average offspring, longevity of adults, and a prolonged nymph period. The population parameters of the F1 generation of *R. padi* were inhibited by exposure to low lethal concentrations of rotenone adults or pyrethrins. These population parameters inhibited include a decreased

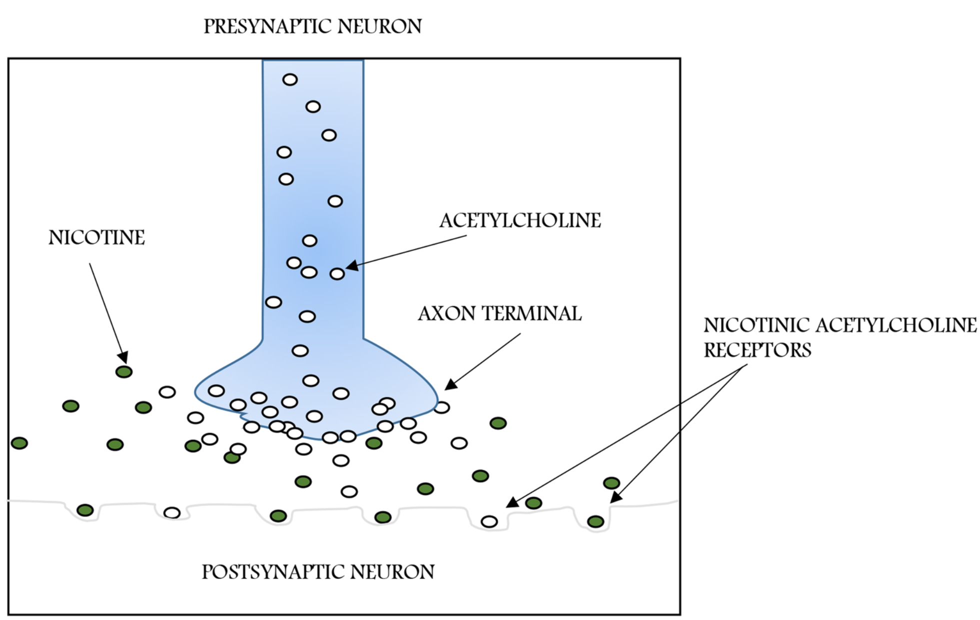


Fig. 8 Nicotine mimicks acetylcholine at the nerve–muscle junction in the central nervous system and interacts with the receptors at the synapse

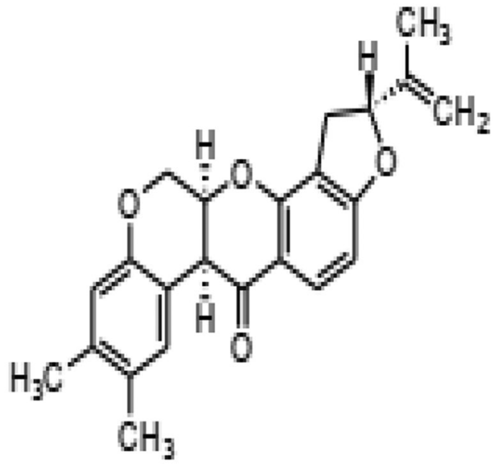


Fig. 9 Chemical structure of rotenone

net reproductive rate, intrinsic rate of natural increase, finite rate of population increase, and gross reproduction rate (Xu et al. 2024). Rotenone is considered safe when used cautiously, accounting for its popular use in and around homes. According to the World Health Organization (WHO), rotenone is a moderately hazardous class II insecticide as it can be toxic to mammals, and fish when used in higher doses (Gupta et al. 2019).

Chemistry of rotenone

Rotenone is classified as an isoflavonoid produced in the root of its plants (Fig. 9). It has a molecular weight of 394.42 g/mol and its molecular formula is $C_{23}H_{22}O_6$ (Gupta et al. 2019). It is a toxic compound with an LD_{50} of 350 mg/kg to mammals (Rajashekar and Shivanandappa 2014). Rotenone is easily degradable by air and sunlight and appears as a colorless to brownish crystal or a white to brownish-white crystalline powder. It is tasteless and colorless, with a boiling point of 215^0C and a melting point of 176^0C. Rotenone is soluble in acetone, ethanol, and benzene, very soluble in chloroform but slightly soluble in ether. When heated to decomposition, rotenone emits acrid smoke and irritating fumes.

Mode of action of rotenone

Rotenone acts both as a contact, stomach, and mitochondrial poison. It is referred to as a stomach poison because it has to be ingested to be effective (Oguh et al. 2019). It acts slower than other plant-derived insecticides in killing the insect as it takes several days (Rajashekar and Shivanandappa 2014). It acts as a metabolic inhibitor and as a neurotoxic poison. It blocks the nicotinamide adenine dinucleotide and thus inhibits the electron transport chain in the mitochondrial (NADH) dehydrogenase in complex 1 of the respiratory chain, which inhibits electrons flow from NADH to ubiquinone (coenzyme) resulting in the failure of respiratory functions (Fig. 10). This inhibition prevents the normal function of the electron transport chain which is a major channel for ATP production in the cell, inhibition by rotenone can reduce energy production in the form of ATP but still maintains ATP formation through flavin adenine dinucleotide ($FADH_2$) which results in a slowly developing toxicity which eventually leads to inactivity, paralysis and death. On exposure to rotenone, the muscle and nerve cells are affected, which leads to a cessation of feeding in insects followed by death occurring within several hours to a few days after exposure (Souto et al. 2021).

Conclusion

Considering the adverse effect of synthetic insecticides on human health, the ecosystem, and the environment, it is only a matter of time before plant-based insecticide becomes the

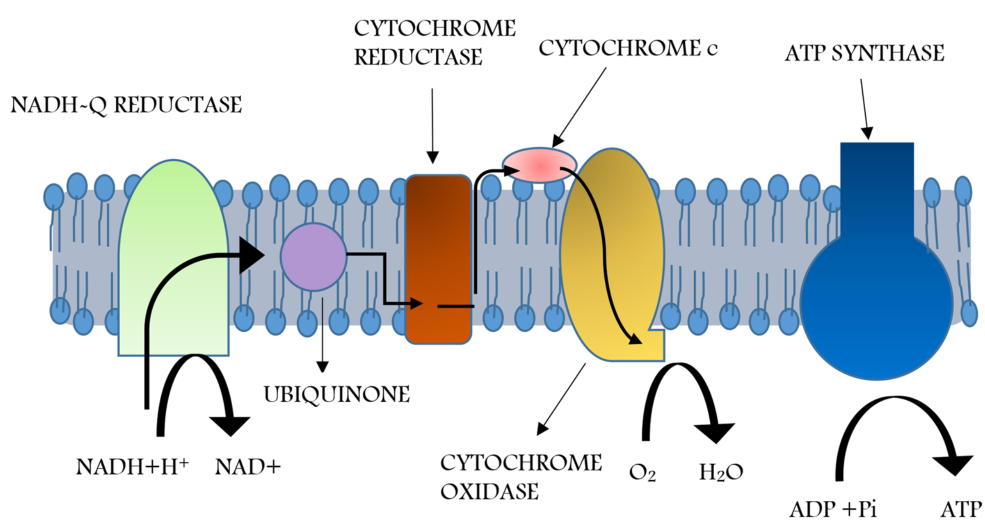


Fig. 10 The obstruction of energy metabolism via the inhibition of electron transport chain by rotenone insecticidal action

choice of use as many consumers are seeking organic products which are generally perceived as safer and less toxic to human health. More than 2000 plant species have been identified with insecticidal capabilities but only a few, such as nicotine, pyrethrum, and azadirachtin, have been discovered, and have made it to the commercial market for public use. These compounds exhibited various insecticidal modes of action, temporal environmental persistence and bioaccumulation, beneficial insect exclusion, and low toxicity to non-target organisms. Therefore, interest in plant-derived insecticides is still thriving as more scientists are searching for novel plants with insecticidal activity. As of 2019, a large number of plant-based insecticides derived from pyrethrum, neem, tobacco, and many others are used in insect pest management worldwide.

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Declarations

Conflict of interest The authors declared no conflict of interest.

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