# Chapter

# Botanical Insecticides for Crop Protection: Major Classes and Possible Mechanisms of Action

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#### **Abstract**

Botanical insecticides, derived from plant-based bioactive compounds with insecticidal activities, have been used to protect crops for more than a century. Synthetic insecticides have become essential in modern agricultural practices because they act quickly, are cost-effective, easy to use, and effective against a wide range of harmful species of insects and pests. Synthetic insecticides, once beneficial, have now become a threat to human health and the environment due to their toxic nature and environmental impact, and hence, botanical pesticides can be utilized as a substitute to synthetic chemical pesticides. Botanicals are easily available, biodegradable, have a broad spectrum of activity, are inexpensive, and have low toxicity to humans and non-target organisms. Various plants species including neem, pyrethrum, garlic, citrus, etc., contains various types of plant secondary metabolites including alkaloids, flavonoids, terpenes, essential oils, glycosides, esters, etc., were popular botanicals. These metabolites exhibited different physical/chemical characteristics and mechanisms of action and affect the insects in various ways such as insecticides, repellents, antifeedants, toxicants, growth retardants, herbicides, and attractants. This chapter describes the in-depth knowledge of various classes of bioinsecticides and their possible mode of actions.

**Keywords:** botanical insecticides, essential oils, neem, repellent, phototoxin, integrated pest management

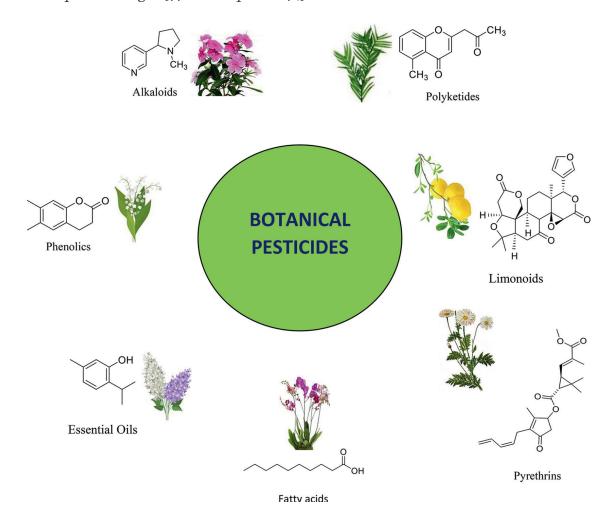
#### 1. Introduction

The global human population is increasing exponentially (about 75 million annually), and if this pattern persists, it is projected that the global population will exceed 10 billion by the end of the century [1, 2]. The rapidly growing population further put greater pressure on land, water, and resources, consequently requiring farmers in developing nations to significantly increase their agricultural output to sustain the growing individuals [3]. Pests and diseases considered as the major

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obstacles to achieving successful crop production. It is estimated that around 35–40% of global crop production is lost every year due to pests before harvest for all potential cereal, vegetable, and fiber crops [4]. Hence, it is crucial to implement cutting-edge, affordable agricultural methods to enhance food production, control pests, and manage diseases both before and after harvest in order to boost crop yields and promote sustainable farming. Over the past, conventional synthetic chemical insecticides have been effectively used to control pests and increase agricultural productivity. The major categories of chemical insecticides are belonged to chlorinated hydrocarbons, organophosphates, carbamates, and pyrethroids. While agrochemicals have increased agricultural production, their widespread and uncontrolled use has led to significant issues including environmental damage from water, air, and soil contamination, harm to non-target organisms, health risks from agrochemical residues in food, and decreased effectiveness due to pest resistance [5, 6]. Agrochemicals can enter the soil through direct use like applying them to control weeds and treating seeds and indirectly through spraying plant parts, the dropping of treated leaves or fruits, and movement of contaminated water on the surface and within the soil [7, 8]. When these chemical compounds accumulated in the soil, they can be transported by leaching and surface runoff and can decompose through chemical processes such as hydrolysis, photolysis, and chemical degradation. Additionally, they can interact with the soil's microbial community and break down naturally [9, 10]. The excessive use of agrochemicals leads to increased persistence in the soil, which can have a detrimental impact on soil microbial consortium. Different types of pesticides elicit varied responses from the microorganisms within the microbial consortium, potentially leading to increased or inhibited growth and metabolism [7, 11]. Previous studies found that extensive use of pesticides cause qualitative and quantitative changes in the soil microbial consortia [12, 13], alteration of nitrogen cycling [14], changes in soil enzymatic activity, and disruption of the symbiosis between mycorrhizae and root nodules in legumes. These factors collectively altered the soil fertility and, consequently, plant growth [15]. Therefore, in order to meet the increasing need for food, sustainable agriculture must effectively improve soil quality through methods like employing biopesticides and biofertilizers, crop diversification, crop rotation, and utilizing microbiota [16, 17]. The quest for better and environmentally friendly ways to manage pests has grown, with a focus on using natural enemies found in soil and plant-based products for biological control. Biopesticides provide a promising substitute for conventional chemicals in controlling the crop diseases for sustainable agriculture [18–20]. The use of biopesticides offers several advantages, including minimal persistence and residuality, which help prevent environmental pollution and minimize adverse effects on living organisms [21]. Additionally, biopesticides exhibit high specificity towards hosts, resulting in a delayed knockdown, and are less prone to encountering pest resistance because of their diverse chemical structures (Figure 1), which are attributed to the remarkable biosynthetic capabilities of plants.

Since ancient times, besides to manage animal pests, natural products have been utilized for the management of various plant diseases and to control weeds. Plants have served as the primary sources of natural pesticides for centuries. With the advancement of modern analytical methods, preparations standardized for the active ingredient(s) have become available in recent decades. This development has enabled the production of reliable products. Botanical insecticides, derived from plants and



**Figure 1.**Structural diversity of bioactive compounds in plant-based pesticides.

their extracts, are eco-friendly pest control solutions that are biodegradable and provide sustainable crop protection. These compounds have been used for centuries in various cultures for pest control, and their resurgence in modern agriculture reflects a growing demand for sustainable farming practices. These alternatives to synthetic insecticides have gained popularity due to advancements in pest control and the growing demand for Integrated Pest Management (IPM) strategies [22]. Among the botanical insecticides rotenone from *Derris elliptica*, nicotine from tobacco leaf, pyrethrins from pyrethrum flowers (Chrysanthemum cinerariaefolium), and azadirachtin from neem (Azadirachta indica) have attained commercial importance. Botanical insecticides are derived from plant sources and have insecticidal properties. These natural extracts are versatile, with low toxicity, high efficiency, and easy degradability. They leave behind no residual insecticide and do not contribute to insect resistance. Botanical insecticides are capable of effectively controlling various plant pests without causing harm to humans, animals, or the environment. Their composition, production methods, mechanism of action, and mode of operation differ from those of chemical insecticides. Some examples of botanical insecticides with their source plant, active ingredients, and manufacturing company are listed in **Table 1**. The present chapter describes an overview of different classes of botanical insecticides with their possible mode of actions for controlling the insect/pest for sustainable agricultural productivity.

Species (family)	Active compounds	Commercial product (company)
Allium sativum L. (Liliaceae)	Sulphur containing compounds e.g. diallyl trisulfide, diallyl disulfide, methyl allyl trisulfide	AjoNey (Invernaderos Hidroponicos Neisi, Mexico); EcoA-Z <sup>®</sup> , L'EcoMix <sup>®</sup> or CapsiAlil <sup>®</sup> (EcofloraAgro, Colombia)
Annona squamosa L. (Annonaceae)	Squamocin (annonin), debitterized annona oil	ANOSOM <sup>®</sup> (Agri Life, India)
Azadirachta indica uss. (Meleaceae)	Azadirachtin, salanin, nimbin	MARGOSOM <sup>®</sup> (Agri Life, India); Molt-X <sup>®</sup> (BioWorks, Inc., USA); NeemAzal T/S <sup>®</sup> (Trifolio-M, Germany); AZERA <sup>TM</sup> (MGK <sup>®</sup> , USA); Neemix 4.5 <sup>®</sup> (Certis, USA); Azatin XL <sup>®</sup> (OHP Inc., USA); Azamax <sup>®</sup> (UPL Ltd., Brazil); Fortune Aza 3%EC <sup>®</sup> (Fortune Biotech, USA)
Capsicum annum L. (Solanaceae)	Protoalkaloids e.g. capsaicin	Hot Pepper Wax (Rincon-Vitova Insectaries, USA); ChileNey (Invernaderos Hidroponicos Neisi, Mexico)
Celastrus angulatus Maxim. (Celastraceae)	Sesquiterpene pyridine alkaloids	CELAN-X SL (Marketing Arm International, Inc., USA)
Citrus sinensis (L.) Osbeck (Rutaceae)	Limonene and linalool	Demize EC (Paragon Professional Pest Control Products, U.SA); Prev-Am (Oro Agri SA (Pty) Ltd., South Africa)
Chrysanthemum cinerariaefolium (Trevir.) Vis. (Asteraceae)	Pyrethrins (cinerins; jamolins and pyerethrins)	Pruzit <sup>®</sup> (Neudorff, Germany); PyGanic <sup>®</sup> Crop Protection EC 5.0 or AZERA <sup>TM</sup> (MGK <sup>®</sup> , USA); 1.5% Aphkiller AS (Beijing Kingbo Biotech Co., Ltd, China)
Lonchocarpus spp., Derris spp. (Fabaceae)	Rotenone	5.% Rotenone ME (Beijing Kingbo Biotech Co., Ltd, China); Rotenone Dust (Bonide Products, Inc, USA)
Nictiana tabacum L. (Solanaceae)	Nicotine	Nico Dust or Nico Neem (Nico Orgo Manures, India); 10% Nicotine AS (Beijing Kingbo Biotech Co., Ltd., China)
Pongamia pinnata (L.) Pierre (Fabaceae)	Karanjin, debitterised karanjin oil	DERISOM® (Agri Life, India); RockEffect (Agro CS a.s. Czech Republic)
Schoenocaulon officinale A. Gray (Melanthiaceae)	Cevadine; veratridine	VERATRAN D <sup>®</sup> (MGK <sup>®</sup> , USA)
Thymus vulgaris L.	Phen(yl)ethyl propionate; Thyme oil	EcoVia WD <sup>®</sup> (Rockwell Labs Ltd., USA)
Origanum vulgare	Oregano oil	By-O-reg +® (By-O-reg +, USA)

**Table 1.**Most common commercially used botanical insecticides [23].

# 2. Classes of botanical insecticides

Plant-based botanicals exhibited various biological activities including, repellents, insecticides, herbicides, fungicides, nematicides, and bactericides with different modes of action [24]. Various botanical insecticides with their plant source, active ingredients, chemical structure, plant source, mode of action, and targets are listed in **Table 2**.

Plant species	Compound	Chemical structure	Class	Mode of action	Target insect/pest	References
Tanacetum cinerarifolium	Pyrethrin I, $R = CH_3$ Pyrethrin II, $R = CO_2CH_3$	R	Cyclopropylmono- terpene esters	Agonists of the voltage-gated Na+ channels of insects, causing their sensory nerve fibers and motor nerve cells to fire repeatedly, causing the insect excited, paralyzed and eventually dead.	Houseflies, beetles, fleas, spider mites	[25, 26]
Cedrus deodara	Himachalol	HOH	Sesquiterpene	Agonists of voltage-gated Na+ channels	Pulse beetle and Houseflies	[27]
Decalepis hamiltonii	Decaleside	HO OH OH OH OH	Trisaccharide	Inhibited the enzyme involving the ATP binding sites	Cockroaches, houseflies, stored grain pests	[28]
Schoenocaulon officinale	Cevadine R=(z)- CH <sub>3</sub> CH=C(CH <sub>3</sub> )CO Veratridine R= 3,4-(CH <sub>3</sub> O) <sub>2</sub> PhCO	ROHO OH OHOH	Sabadilla alkaloid or <i>Veratrum</i> alkaloid	Activate voltage-sensitive Na+ channels of nervous system	Leafhoppers, caterpillars, houseflies, stinks, thrips	[29–32]
Ryania speciosa	Ryanodine	NH HO O'MOH	Diterpene	Effects nervous system by binding to the intracellular Ca <sup>2+</sup> release channel proteins	Potato beetle, caterpillars, worms, lace bugs, aphids, squash bugs	[29, 33]
Lantana camara	(Coumaran)2,3- dihydrobenzofuran		Benzofuran	Inhibit Acetylcholin-esterase (AChE) enzyme activity	Stored grain pests, houseflies	[34]

Plant species	Compound	Chemical structure	Class	Mode of action	Target insect/pest	References
Eucalyptus globulus Labill.	1,8-Cineole (Eucalyptol)		Monoterpene	Inhibit Acetylcholin-esterase (AChE) enzyme activity	Head louse (Pediculus humanus capitis)	[35]
Chenopodium ambrosioides L.	δ-3-carene		Monoterpene	Inhibit Acetylcholin-esterase (AChE) enzyme activity	Tribolium confusum, Callosobruchus maculatus	[36]
Nicotiana tabacum, Stemona japonicum, Haloylon salicornicum	Nicotine	H CH <sub>3</sub>	Pyridine alkaloid	Interact with the nicotinic acetylcholine (nACh) receptors at neuron synapses, resulting unregulated nerve firing causing malfunctions of the neurons.	Leaf hoppers, aphids, thrips, mites, spider mites	[26]
Artemisia absinthium, Juniperus sp., Cedrus sp.	Thujone	0=	Monoterpene	Reversible modulator of $GABA_A$ receptor	Root worm larvae ( <i>Diabrotica</i> <i>virgifera</i> ), Fruit fly	[37]
Origanum vulgare	Carvacrol	НО	Monoterpene	Binds to nicotinic acetylcholine receptors	American cockroach (Periplaneta Americana)	[38]
Thymus vulgaris	Thymol	ОН	Monoterpene	Prevent octopamine receptors via tyramine receptor cascade.	American cockroach (Periplaneta Americana)	
Syzygium aromaticum	Eugenol	HO	Monoterpene	Inhibits octopamine receptor (OAR) system	Bug (Triatoma infestans), fruit fly, American cockroach	[39–41]

Plant species	Compound	Chemical structure	Class	Mode of action	Target insect/pest	References
Aniba rosaeodora	Linalool	НО	Monoterpene	Competitive and reversible inhibition of acetyl-cholinesterase activity	Fleas, houseflies, mosquitoes, spider mites	[42, 43]
Lonchocarpus Kunth, Derris Lour, Rhododendron L.	Rotenone	$H_3C$ $CH_3$ $H_3C$ $CH_3$	Isoflavonoid/ Rotenoid	Interact with NADH dehydrogenase resulting inhibit the oxidation of NADH to NAD	Caterpillars, lice, fleas, beetles, mosquitoes, fire ants	[26, 44]
Azadirachta indica	Azadirachtin	HO H	Tetranortriterpenoid limonoid	Acts as antifeedant, sterilant and repellent; disrupt insect growth by blocking the release of prothroracicotropic hormone (PTTH); distort phagostimulant disruptor by cholinergic transmission.	Stored grain pests, aphids, caterpillars, thrips, merely bugs	[30, 45–49]
Ageratum conyzoides	Precocene I (7-methoxy-2,2-dimethylchromene)	LoCo-	Chromene	Working as insect growth regulator	Grain beetle, Milkweed bug, Noctuid moth, Parasitic wasp	[50–53]
Catharanthus roseus	α-amyrin acetate		Steroid	Working as insect growth regulator	Helicoverpa armigera	[54]

Plant species	Compound	Chemical structure	Class	Mode of action	Target insect/pest	References
Xylopia aethiopica	(-) Kau-16-en-19-oic acid	H <sub>3</sub> C = CH <sub>2</sub> H <sub>3</sub> C = CH <sub>2</sub>	Kaurane diterpene	Antifeedant	Termites (Reticulitermes speratus)	[55]
Jatropha podagrica	15-epi-4E-jatrogrossi- dentadione	OH H HO	Diterpene	Antifeedant	Moth ( <i>Chilo</i> partellu)	[45]
Senecio palmensis	11-Acetoy-5- isobutyryloysilphinen-3- one	H H	Silphinene sesquiterpene	Antifeedant	Colorado potato beetle, Aphids	[56]
Lotus corniculatus; Trifolium repens	Linamarin	HO OH OH	Cyanogenic glycoside	Antifeedant	Snails, slugs, lemmings, aphids	[57]
Pterocarpus macrocarpus	(-)-homoptreocarpin	H <sub>3</sub> CO OCH <sub>3</sub>	Isoflavonoid/ Pterocarpan	Antifeedant	Common cutworm, subterranearn termite	[58]
Nepeta cataria	Nepetalactone	O H CH <sub>3</sub>	Monoterpene lactone	Repellent	Beetle, bees, flies, termites, lady beetle, mosquitoes	[59–61]
Tectona grandis	Tectoquinone		Anthraquinone	Repellent	Termites	[62–64]

Plant species	Compound	Chemical structure	Class	Mode of action	Target insect/pest	References
Alstonia boonei	Alstonine	CH <sub>3</sub>	Indoloquinolizidi ne alakaloid	Repellent, larvicidal	Mosquitoes	[65]
Pinus strobes	Limonene		Monoterpene	Attractant	White pine cone beetle	[66]
Zea mays	(E)-β-caryophyllene	H CH <sub>2</sub>	Sesquiterpene	Attractant	Nematodes (Heterorhabditis megidis), corn root worm (Diabrotica virgifera)	[67]
Juglans nigra	Juglone	OH O	Naphtoquinone	Working as herbicide, inhibiting certain enzymes needed for the photosynthesis.	Echinochloa crus- galli, Amaranthus retroflexus, Abutilon theopharasti	[68, 69]
Eupatorium adenophorum	5,6-dihydroxycadinan-3- ene-2,7-dione	CH <sub>3</sub>	Cadinane sesquiterpene	Working as herbicide	Arabidopsis thaliana	[70]

Plant species	Compound	<b>Chemical structure</b>	Class	Mode of action	Target insect/pest	References
Poaceae spp.	m-Tyrosine	HO OH NH <sub>2</sub>	Amino acid	Working as herbicide; inhibit root growth by direct interference with amino acid metabolism, inhibit cell wall synthesis, and alter the plant hormone signalling.	Weeds	[71]
Prosopis juliflora	Tryptophan	HN H <sub>2</sub> N OH	Amino acid	Working as herbicide	Barnyard grass (Echinochloa crus-galli)	[72]
Centaurea stoebe	(-)-Catechin	HO OH OH	Flavanol	Working as herbicide; inhibits seed germination and root growth by rapid Ca <sup>2+</sup> signalling cascade leading to cell death	Koeleria macrantha, and Festuca idahoensis	[73]
Cymbopogon citratus	Citronellol	но	Monoterpene	Herbicide; showed toxic effects on plant growth by reducing chlorophyll and protein contents.	Echinochloa crus- galli, Amaranthus tricolor	[74]

Table 2.
Botanical insecticides with their origin and insecticidal activity.

## 2.1 Botanical insecticides affecting the nervous system

Researches suggests that plant-based insecticides can exhibit various modes of action in insects and mammals, particularly targeting the nervous system. These insecticides can affect  $\gamma$ -aminoutyric acid (GABA) gated chloride channels, octapamine receptors, nicotinic acetyl-choline receptors (nAChR) and acetylcholinesterase enzyme (AChE), voltage-gated sodium channels, and voltage-gated calcium channels.

## 2.1.1 Inhibition of GABA (γ-aminoutyric acid)-gated chloride channels

GABA is an inhibitory neurotransmitter present in the nervous systems of nearly all insect species, and it is the primary targets for pesticides, including bioinsecticides [75]. On binding of GABA with its receptors, the chloride (Cl<sup>-</sup>) channels are activated, allowing chloride ions to flow into neurons, which leads to inhibition of the nervous system [76]. The active compounds present in various bio-insecticides can either inhibit or bind to the GABA receptors, resulting to the insect's death by hyperexcitation or by disturbance in neuronal activity [38].

The thujone found in *Artemesia absinthium* L. and the picrotoxin from *Anamirta cocculus* L. can block GABA-gated chloride channels, leading to reduced neuronal inhibition, hyper-excitation of the nervous system and potentially resulting in convulsions and death. Previous studies have indicated that thujone acts as a positive allosteric modulator of GABAA receptors and as a competitive inhibitor of [3H]Ethynylbicycloorthobenzoate ([3H]EBOB) binding [37]. Moreover, the GABA receptors may be inhibited by monoterpenoids carvacrol, pulegone, and thymol through [3H]EBOB binding [38]. Likewise, botanical compounds silphinene sesquiterpenes inhibit the aminobutyricacid (GABA) receptors by stabilizing nonconducting conformations of the chloride channels [26, 37]. GABA is considered as endogenous ligand that stimulates feeding and triggers taste cell responses in many plant-eating insects and suggests that compounds which inhibit GABA receptors could serve as antifeedants or deterrents, particularly affecting aphids, lepidopterans, and beetles [56, 77].

## 2.1.2 Inhibition of octopamine receptors

Octopamine play crucial role as endogenous amines [78] in the nervous system of arthropods, including insects [79]. They are derived from tyrosine [79] and function as neurotransmitters, neurohormones, and neuromodulators [39, 80]. The receptors are found throughout the nervous systems of insects, both in the central nervous system (CNS) and peripheral nervous system (PNS) areas. The octopaminergic system comprises different types of octopamine receptors that are associated with various second messenger systems, playing a pivotal role in controlling physiological functions and behaviours [81–83]. In honeybees (*Apis mellifera*), octopamine can influence memory and learning processes and modulate muscle performance, lipid metabolism, heart rate, and respiration in insects [79]. For instance, the octopamine1 receptor influences the rhythmic contraction of the locust extensor-tibiae muscle by altering the levels of calcium inside the cell. On the other hand, the effects of the octopamine2A and octopamine2B receptors are mediated by activating adenylate cyclase. Additionally, the octopamine3 receptors are responsible for regulating the levels of intracellular calcium and cAMP in the central nervous system of the locust [39]. The quick response of monoterpenes against certain insect/pest implies a

neurotoxic mechanism of action. Reynoso and colleagues [40] demonstrated that how eugenol can repel and kill the blood-sucking bug *Triatoma infestans* by activating the octopamine receptor.

According to previous researches, octopamine receptors have been found in a wide range of insects, such as fireflies, flies, nymphs, cockroaches, and lepidopterans [39–41]. Enan [41] research highlighted that eugenol's insecticidal effects are linked to the octopamine receptor system (OAR), emphasizing that phenolic compounds exhibit greater toxicity than other monoterpenoids. Furthermore, Enan pointed out that the positioning and spacing of a hydroxyl group (OH) on the benzene ring dictate the level of toxicity of the active compound found in essential oils through the OAR system. The monoterpenoids  $\alpha$ -terpineol and cinnamic alcohol inhibit octopamine receptors in the species *Camponotus pennsylvanicus*, *Periplaneta americana*, and *Blattella germanica* at an inhibitory concentration (IC<sub>50</sub>) of 9 nmol/mL [41].

Monoterpenoids can play another role in their interaction with OAR, such as menthol enhancing the toxic effects of carbamate, a synthetic pesticide, by activating OAR, thereby increasing the efficacy at a lower dosage than usual [84] and potentially reducing the negative environmental impact of synthetic pesticides. The octopamine receptors do not fit into the categories of receptors found in vertebrates. This means that octopamine receptor agonists could be a promising option for a commercial pesticide. It is crucial for the pesticides to be tailored to the specific target, have minimal impact on mammals, and employ a unique mode of action compared to other pesticides available.

## 2.1.3 Inhibition of voltage-gated sodium (Na<sup>+</sup>2) channels (VGSCs)

Voltage-gated Na<sup>+</sup>2 channels are vital transmembrane proteins that play a crucial role in transmitting electrical signals in various excitable cells, such as nerve, muscle, and neuroendocrine cell types, contributing to the establishment of resting potential as well as the initiation and spread of action potentials in neurons [85]. Pyrethrin, a secondary metabolite derived from the dried flowers of *Tanacetum cinerariifolium* (Asteraceae), contains two primary active components known as Pyrethrins I and II (cyclopropylmonoterpene esters) [24] that acts as a modulator of nerve membrane sodium current by prolonging the opening of VGSCs, resulting in over neuroexcitation, causing loss of coordinated movement control, paralysis, and death of insects. The same mode of action is followed by the other synthetic insecticides (synthetic pyrethroids derived from pyrethrins), but plant-based pyrethrins are more targetspecific than synthetic one [86]. When pyrethrins are applied, they cause an immediate knock-down effect and have low toxicity to mammals, as well as very short residual activity, which prevents accumulation in food chains and ground water. Pyrethrins break down rapidly when they come into contact with air, sunlight, water, and high temperatures, which means that you might need to apply them frequently [87]. Pyrethrins are used to manage various insects and mites, such as spider mites, flies, mosquitoes, fleas, and beetles [25, 26].

Decalesides I and II, derived from *Decalepis hamiltonii* root, have a similar mode of action and are considered trisaccharides. These plant-based products are toxic to a variety of insects upon contact exposure [28]. Sabadilla, extracted from the pulverized seed of the sabadilla lily (*Schoenocaulon officinale* Schltdl. and Cham.), has been used by native American Indians as insecticide against various pests for centuries. The alkaloids produced in sabadila are collectively known as veratrine which contains two main alkaloids, namely cevadine and veratridine exist in a ratio of 2:1. The alkaloids

have similar mechanism of action as pyrethrins have, however, the binding site seems to be different [30]. Sabadilla found least toxic plant-based insecticides effective either contact or ingestion and degrades rapidly when exposed to air and sunlight and has little residual toxicity. However, purified veratrine alkaloids are more toxic to mammals and effective against honeybees, caterpillars, leaf hoppers, thrips, stink bugs, and squash bugs [29, 31].

## 2.1.4 Inhibition of voltage-gated calcium (Ca<sup>+</sup>2) channels (VGSCs)

Ryanodine, an alkaloid derived from the roots and woody stems of *Ryania speciosa* Vahl (Salicaceae), a plant native to South America, exhibits insecticidal properties by disrupting the Ca<sup>+</sup>2 channels in skeletal muscle cells' sarcoplasmic reticulum. This interference leads to the release of excessive calcium ions into actin and myosin protein filaments, causing muscle contractions and eventual paralysis [88]. Ryanodine acts quickly as a poison, making it effective against insects through contact or ingestion. It has low toxicity for mammals and provides control for up to 2 weeks after the first application. When combined with piperonylbutoxide (PBO), Ryania crude extracts enhance their insecticidal activity against caterpillars, worms, potato beetles, lace bugs, aphids, and squash bugs [29, 33]. Ryania, a slow-acting stomach toxin, causes insects to cease consuming plants shortly after ingestion and exhibits greater residual activity than other plant-based insecticides, while posing less risk to humans.

# 2.1.5 Alteration the activity of acetylcholinesterases (AChEs) enzymes

The enzyme acetylcholinesterase (AChE) plays a crucial role in the nervous systems of most animals, including insects [89], by breaking down the neurotransmitter acetylcholine (ACh) into acetatic acid and choline [90], and enabling an activated cholinergic neuron to return to its resting state. It is important for regulating the nerve signals by preventing overstimulation of the postsynaptic neuron and also the target for most bioinsecticides and synthetic insecticides [91]. Germacrone, the primary bioactive compound derived from Rhododendron thymifolium L., inhibits the AchE activity by impeding cholinergic neurotransmission at synapses, leading to prolonged binding of the neurotransmitter to its postsynaptic receptor, resulting in heightened neuroexcitation, restlessness, hyper-excitability, paralysis, and ultimately death. It is found effective against post-harvest grain insects such as Lasioderma serricorne and Tribolium castaneum [92]. Similarly, coumaran, active compound extracted from Lantana camara L., exhibited AchE inhibition activity and found effective against houseflies and stored grain pests, in spite of its low toxicity to humans and short residual activity [93]. Recently, Li et al. [94], reported the AchE inhibition activity of new sequiterpenes; laggeranine extracted from Laggera pterodonta and proposed as new potential active compound for targeting AchE. The *in-vitro* evaluation of anti-AChE activity in many essential oils and their derived terpenes have been reported, but their contribution raises doubts about to insect mortality [93].

## 2.1.6 Activation of nicotinic acetylcholine receptors

The nicotinic acetylcholine receptors, located in the insect nervous system within the cell bodies of interneurons, motor neurons, and sensory neurons, have a crucial function in facilitating rapid excitatory neurotransmission in the central nervous system (CNS) of insects [95]. Nicotine, an alkaloid extracted from tobacco plants

(Nicotiana tabacum L), mostly contains phenolic compounds like nicotine and diterpene. Nicotine, nornicotine, and anabasine mimic the neurotransmitter acetylcholine and exert neurotoxic effect by binding nicotine acetyl-choline receptors (nAChRs), similar to organophosphate and carbamate insecticides [24]. Activation of nAChRs by nicotine results in a quick increase of sodium ions, leading to depolarization and ultimately generating an action potential. Generally, the synaptic action of acetylcholine is terminated by AChE; moreover, nicotine being resistant to hydrolysis by AChE leads to prolonged activation, resulting in excessive cholinergic transmission, which ultimately leads to convulsions, paralysis, and ultimately death [95]. Nicotine acts as a potent neurotoxin, specifically targeting insects and mites, making it the most toxic plant-derived compound, but also posing significant harm to humans [45]. Neonicotinoids, including imidacloprid, acetamiprid, and thiamethoxam, are a type of insecticide with a chemical structure resembling nicotine, featuring a heterocyclic ring structure with attached nitro and cyan groups. Similar to nicotine, neonicotinoids act as an activator of nicotinic acetylcholine receptors leading to over neuroexcitation and paralysis. Neonicotinoids showed to insect nAChRs and highly selectivity in toxicity, while being less harmful to non-target organisms like birds and mammals. The compounds are also easily dissolved in water, which enables them to be applied to soils and taken up by plants, ultimately enhancing their protective capabilities. These insecticides can act as contact or ingestion poisons, causing insects to stop feeding shortly after contact and leading to death, however, exhibited negative impact on pollinators like bees [96].

# 2.2 Inhibition of respiratory enzyme system

Cellular respiration is the conversion of nutrient compounds into cellular energy, i.e. adenosine triphosphate (ATP) at a molecular level, specifically carried out by the electron transport chain in the mitochondria, which includes important enzymes that could be targeted by insecticides. Rotenone, a type of isoflavonoid extracted from roots and stems of *Derris* (*Derris* elliptica, *D.* involute), *Lonchocarpus* (*Lonchocarpus* utilis, *L.* urucu), and *Tephrosia* virginiana [24], used as a botanical insecticide.

Rotenone works as both contact and ingestion toxin by inhibiting ubiquinone oxidoreductase (Complex I) of the electron transport chain in mitochondria. Rotenone inhibits the nicotinamide adenine dinucleotide (NADH) dehydrogenase activity and stops electrons flow from NADH to coenzyme Q, so prevents formation of ATP from NADH resulting ATP levels fall rapidly leads to cell death. By inhibiting Complex I, it also increases the levels of reactive oxygen species (ROS) and nitrogen oxide (NO), resulting in the production of free radicals and subsequent lipid peroxidation in cellular components, ultimately leading to programmed cell death (apoptosis). Rotenone has a slow effect and can be broken down by air and sunlight. It takes several days to kill insects by affecting their nerve and muscle cells, leading to them stopping feeding and eventually dying within hours to a few days of exposure. Furthermore, this plant-based insecticide has a broad spectrum activity and found effective against a wide range of insect species including caterpillars, aphids, suckers, trips, and other pests infecting fruits and vegetables [97], including the Colorado potato beetle (Leptinotarsa decemlineata), Plum curculio (Conotrachelus nenuphar), Diabrotica, and Acalymma species [98]. Rotenone is moderately harmful to mammals and extremely toxic to fish, exhibiting activity and persistence comparable to dichlorodiphenyltrichloroethane (DDT). Research conducted in the past has indicated a

potential association between rotenone exposure and Parkinson's disease (PD). The rapid exposure of rats led to brain damage similar to the lesions found in humans and animals affected by Parkinson's disease [99]. Rotenoids, despite their high toxicity, show potential as a source of new complex I inhibitors and could serve as a model for developing safer and more effective pesticide derivatives.

## 2.3 Alteration of the hormonal system

Insect growth regulators (IGRs) encompass chemical compounds that interfere with the endocrine system of insects, essentially mimicking or inhibiting their juvenile hormones and acting as chitin synthesis inhibitors (CSIs). Insects typically release juvenile hormones to sustain their immature state, and when they attain adequate growth, the production of hormones stops, causing them to move into the adult phase. Triterpenes such as  $\alpha$ -amyrin acetate and oleanolic acid extracted from *Catharanthus roseus* exhibited excellent growth regulator activity [54]. In addition, natural products like davanone, ipomearone, and the juvenile hormone produced by silkworm exhibit fascinating IGR activity due to their acyclic sesquiterpene composition. By consistently application of IGR to the crops, the insects will remain in their larvae state, preventing successful moulting and effectively controlling insects. The presence of Chromenes, Precocene I and II extracted from *Ageratum conyzoides* L. (Asteraceae) leads to the early transformation of the larvae and results in the production of sterile, moribund, and dwarfish adults upon exposure [100].

Azadirachtin, a complex tetranortriterpenoid limonoid, mainly extracted from the seeds of Azadirachta indica (Meliaceae) interacts with ecdysteroids present in insects bodies and reduces their population [101]. The neem tree, scientifically known as Azadirachta indica, is native to the arid regions of India and Myanmar but is now cultivated in arid, tropical, and subtropical areas across Southeast Asia, Africa, the Americas, and Australia [26, 30, 46]. Azadirachtin showed contact systemic activity which can be classified in two ways: either through direct impact on cells and tissues or indirect effects, which involve interference with the endocrine system. This compound is extremely active and functions as a deterrent for feeding and as a regulator of insect growth in a wide variety of insect groups, including Lepidoptera, Diptera, Hemiptera, Orthoptera, and Hymenoptera [46]. The growth regulatory effects of Azadirachtin involve impacting the neurosecretory system of insects and preventing the release of crucial metamorphosis hormones like prothoracicotropic hormone (PTTH) and allatostatins, which control the prothoracic glands and corpora allata. Consequently, any disruption in the functioning of these glands could result in molting defects or sterility. Azadirachtin directly affects somatic and reproductive tissues, as well as disrupts the endocrine processes, leading to impacts on feeding, developmental, and reproductive functions [46]. Neem oil, derived from cold-pressing of neem seeds and other neem-based products, are commonly utilized as noncommercial products to control insect, pest, and phytopathogens [102, 103]. Both azadirachtin and neem seed oil have been found to elevate aphid nymphal mortality rates by 80 and 77%, respectively, while also prolonging the development time of those that manage to survive to adulthood [104].

## 2.4 Alteration of the water balance

Certain oils derived from rice bran, cotton seed, and palm kernel, along with natural soaps (saponins), have the ability to interfere with the protective wax layer on insects, resulting in rapid water loss from the cuticle and ultimately leading to the insects' death from dehydration [105]. Furthermore, the crude oils can also disrupt insect respiration by clogging the openings known as spiracles, leading to death by suffocation, thus effectively managing various types of insects like whiteflies, mites, caterpillars, leafhoppers, and beetles [106].

## 2.5 Repellent

Some groups of pest control agents have unique biological properties and are closely associated with insecticidal substances, often being employed alongside insecticides in pest control tactics. They include insect repellents, deterrents, and attractants. Plant-based compounds can act as both an insecticide and repellent, depending on their concentration. The key distinction is that repellents do not eliminate insects; they instead keep them at bay by emitting strong odours or exhibiting mild toxic properties. Recent research on plants showing repellent properties has resulted in the isolation and identification of certain effective compounds. Terpenoids and sesquiterpenoid extracted from Cymbopogon nardus such as callicarpenal and intermedeol, respectively, significantly control the infestations by Amblyomma cajennense [107]. Nepetalactone (monoterpene lactone), an active compound found in catnip oil extracted from *Nepeta cataria* L. (Lamiaceae), showed repellent activity against Aedes aegypti L. (Culicidae) ten times more than DEET [59] and also reported as repellent against lady beetle, cockroaches, flies, termites, and mosquitoes [60, 61]. Monoterpens, the main constituent of many essential oils, showed powerful insect repellent activity. The essential oils extracted from lemongrass (Cymbopogon flexuosus (Poaceae)), eucalyptus (Eucalyptus globulus (Myrtaceae)), rosemary (Rosmarinus officinalis L. (Lamiaceae)), vetiver (Vetiveria zizanioides L. (Poaceae)), clove (Eugenia caryophyllus (Myrtaceae)), and thyme (Thymus vulgaris L. (Lamiaceae)) considered a highly effective repellent against a wide range of insects [108]. The anthraquinone tectoquinone showed repellent activity against termites [62, 63], and alstonine alkaloid has a repellent and larvicidal activity against *Anopheles gambiae* (Culicidae) [65]. Adegorite et al. [36] demonstrated that essential oil from Chenopodium ambrosioides L (Chenopodiaceae) can effectively repel cowpea adult insect Callasobruchus maculatus L. (Coleoptera: Bruchidae), leading to mortality rates that are dependent on the concentration and duration of contact. When test insects were placed in a sealed glass jar containing the leaf extracts, they experienced a 100% mortality rate due to prolonged exposure to high concentrations of the extracts.

#### 2.6 Attractants

Plants release attractants, which are semio-chemicals or communication compounds, to draw in insects or natural predators of the insects that feed on the plant [109]. These compound influence both taste and smell receptors. For controlling insects, attractants can be utilized in three ways: monitoring infestations, luring insects to traps or baits, and disrupting their mating and feeding behaviours. As they do not directly kill insects, they are environmentally friendly and can be used to mislead insects into laying infertile eggs or choosing unfavourable oviposition sites, reducing their numbers. In an experiment, Miller [66] applied (–) and (+) limonene from white pine (*Pinus strobus* L. (Pinaceae)) to attract the white pine cone beetle, *Conophthorus coniperda* Schwarz (Curculionidae), as well as the attraction of the predator beetle, *Enoclerus nigripes* say (Cleridae), through the release of

(–)- $\alpha$ -pinene, as well as the sesquiterpene caryophyllene [67]. However, they should only be used as part of a comprehensive pest management strategy and not as the sole control measure.

#### 2.7 Antifeedant

Antifeedant compounds take part in chemoreception mechanism that involves either blocking receptors that typically respond to phagostimulants or stimulating deterrent cells. These compounds discourage insects from feeding, and it is believed that plants with high levels of these compounds are less likely to be attacked by insects [110]. The antifeedant activity of azadirachtin and neem seed extracts against numerous pest is well established. Besides, numerous terpenes, terpenoids, phenolics, and flavonoids compounds also exhibited strong antifeedant activity [111, 112]. The research conducted earlier showed that phenolic compounds hinder cellular enzymes like proteases and other digestive hydrolases, as well as polyphenol oxidases (PPOs), which are involved in multiple metabolic processes [113], leading to a reduced digestibility of dietary proteins [114].

The multiple antifeedant activates of plant extract and fractions from Calceolaria integrifolia were attributed to inhibition of phenol oxidase, proteinase, or tyrosinase, resulting inhibition of cuticle synthesis and to molting sclerotization toxicity [115]. In a study, Qiao et al. [47] demonstrated that azadirachtin reduces the cholinergic transmission of neurons related to the suboesophageal ganglion (SOG) of Drosophyla melanogaster, which are strongly related to feeding behaviour. Furthermore, the ingestion of food may be reduced because of its poisonous impact following the initial consumption (secondary deterrent), encouraging astringency, unpleasant taste, or anti-digestive effect for herbivores [48, 55]. In an experiment, Chakraborty et al. [116] tested the extract from bitter gourd (Momordica charantia L.) against transgenic flies with impaired aversive taste sensitive neurons and demonstrated a decreased aversion when exposed to bitter gourd extract, indicating that the bitter-sensitive gustatory neurons depend on these compounds. Abdullah et al. [117] reported that 1,8-cineol, an active compound present in Galangal essential oil, showed good antifeedant and repellent activity, as well as toxicity effect against termites. Similarly, Jose and Sujatha [118] demonstrated that terpenoids, coumarin, and phenols, found in the methanol extracts of Gliricidium sepium, exhibited excellent antifeedant activity. The plantderived active compounds can either inhibit larval feeding by disrupting hormonal balance or making the food unpalatable, or they can directly affect the larvae's chemosensilla, resulting in feeding deterrence. Furthermore, despite the presence of many natural plant compounds that act as antifeedants, their commercial use in crop protection is limited due to insect habituation to feeding deterrents [119].

#### 2.8 Phototoxins

Photoactive compounds or phototoxins, a type of phytochemicals, maintain their effectiveness by being activated through two different mechanisms instead of being degraded by sunlight. In the less common mechanism, molecular oxygen from the phototoxin absorbs light energy, producing reactive oxygen species that ultimately harm essential cellular biomolecules [120]. The alternative action involves photogenotoxicity, in which plant compounds are activated by sunlight, causing DNA damage without needing oxygen. This process occurs when the

phototoxin absorbs sunlight energy in its ground state, becomes excited, and interacts with ground state O2 in the target tissue, producing reactive oxygen species and exhibiting insecticidal effects. This distinctive mechanism of phototoxins differs from conventional chemical pesticides and makes it unlikely for them to develop cross-resistance [121, 122].

Various classes of plant-derived active compounds such as quinones, furanocoumarins, and thiophenes exhibited phototoxic effect. Phototoxins, 3-methyl-3-phenyl-1,4-pentadiyne found in the essential oil extracted from *Artemisia monosperma* (Asteraceae), exhibited an activity similar to DDT against the housefly and cotton leaf worm larvae under sunlight exposure. Similarly, ponticaepoxide, an acetylenic epoxide derived from *Artemisia pontica* L. (Asteraceae), inhibited mosquito larvae growth at LC<sub>50</sub> of 1.47 ppm when subjected to UV light [123]. Thiophene also known as terthiophene or α-terthienyl, the main active compound found in the roots of *Tagetes minuta* L. (Asteraceae), showed high toxicity against various organisms including nematodes: red flower beetles, blood-feeding insects such as tobacco hornworm (Sphingidae) and mosquito larvae (dipteres): yellow fever mosquito (Culicidae), rockpool mosquito (Culicidae), when subjected to near-UV radiation [124]. However, till now no commercial product based on phototoxic activity has been formulated.

## 3. Conclusion

Sustainable agricultural development aims to enhance the quantity and quality of crop products while ensuring human health and reducing emission of toxic substances in the environment. The efficient utilization of plant-based products in plant protection is crucial to attain this goal. Standard crop protection practices lead to adverse effects, including issues related to environmental toxicity, disturbance of the natural equilibrium, and enhancing the development of resistance in insect. Therefore, botanical insecticides considered as the best alternative source of compounds having insecticidal activity and can help to protect crops from the insect and pests. Utilization of plant-based insecticides has several advantages, including insect selectivity, less toxic to humans, and no and non-bio-accumulative in the nature. Researchers and industry stakeholders are increasingly interested in exploring new bioinsecticides with different mechanisms of action and investigating the efficacy of these natural alternatives. Botanical insecticides are derived from various types of plant secondary metabolites including alkaloids, flavonoids, terpenes, essential oils, glycosides, esters, etc. These metabolites exhibited different physical/chemical characteristics and mechanisms of action and affect the insects in various ways such as insecticides, repellents, antifeedants, toxicants, growth retardants, herbicides, and attractants. Nevertheless, additional research is urgently required to investigate the impact on pest behaviour, the significance of applied methods, and the timing of application for these botanical biopesticide mixtures.

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