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Flavonoids as bio-insecticides: Harnessing plant metabolites as a biochemical shield against insects

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Abstract: The global decline in crop production poses a significant threat to food security, particularly in the context of a growing human population. Among various environmental constraints on agriculture, biotic stress, particularly that caused by insect pests, remains a major reason for yield losses. Traditionally, synthetic pesticides have been used to manage insect infestations; however, their excessive and non-targeted application has raised serious concerns regarding environmental pollution, adverse health effects, and the accelerated development of pesticide-resistant pest populations. In this context, plant-derived biocactive compounds, particularly flavonoids, have emerged as promising bioinsecticides due to their potent insecticidal properties. Flavonoids, a diverse group of secondary metabolites found abundantly in plants, exhibit strong insecticidal activity by disrupting insect digestion, interfering with nutrient absorption, and inhibiting growth and metamorphosis. These bioactive compounds act through multiple mechanisms, reducing the likelihood of resistance development while offering an eco-friendly alternative to conventional chemical pesticides. Additionally, flavonoids contribute to integrated pest management strategies by enhancing plant defence responses and synergising with other bioinsecticides. Despite their potential, research on flavonoid-based insect control remains limited, particularly in terms of their formulation, stability, and large-scale applicability. Further studies are needed to investigate their interactions with insect physiology, optimise delivery methods, and assess their environmental impact.

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Advancing flavonoid-based bioinsecticides can contribute significantly to sustainable pest management in modern agriculture, reducing dependence on synthetic pesticides while preserving ecosystem balance. This review examines the potential role of flavonoids as biopesticides in pest management, highlighting the existing research gaps and prospects.

Keywords: crop protection; plant defense; secondary metabolites; sustainable agriculture

Increasing agricultural crop production is crucial to ensure global food security and meet the demands of a growing population. It helps to address hunger, malnutrition, and poverty while promoting economic growth and development. However, agricultural crop production is threatened by various environmental stresses, including biotic and abiotic stresses, which can significantly impact crop yields and quality. Among the biotic stressors, insect pests have a significant impact on agricultural crop production, causing both direct and indirect damage, which reduces crop yields and affects crop quality. They transmit plant pathogens, consume nutrients, and destroy crops, resulting in significant economic losses (Pratap et al. 2020; Nikpay et al. 2023). Effective management strategies are crucial to minimise the impact of insect pests on agricultural crop production. Insect pest management can be achieved using several approaches, including chemical control, physical and mechanical control, host plant resistance, cultural control, and biological control (Stenberg et al. 2015; Tiwari 2024). Of all methods, the use of chemical (synthetic) pesticides to control pests is more effective in improving crop production, but excessive use of these pesticides raises environmental and health issues, causing ecological imbalances and harm to non-target species (Geier 1966; Mahmood et al. 2016; Sharma & Singhvi 2017; Kaur et al. 2024). Moreover, residue contamination in water and food poses risks to human health and biodiversity (Rani et al. 2021). The adverse effects of synthetic pesticides have intensified the search for safer alternatives in pest management. Plant-derived biopesticides have emerged as promising candidates, offering cost-effective, sustainable, and environmentally friendly solutions and can be used as natural alternatives to synthetic pesticides. (Ayilara et al. 2023).

Bioactive compounds derived from plants have insecticidal properties that can kill or repel insect pests (Gupta & Dikshit 2010). Notably, flavonoids have been identified as a promising class of bioactive compounds with insecticidal properties, exhibiting both anti-xenosis and antibiosis activities (Bentivenha et al. 2018). These activities effectively impede the growth and development of pests, providing resistance against insect damage (Treutter 2005). In plants, flavonoids function as signalling molecules that regulate growth and development (Wang et al. 2022a), as well as control phosphorylation of pathways, enzymes, and membrane fluidity (Peer & Murphy 2007). Accumulating evidence demonstrates that flavonoids are effective against a broad spectrum of pests, exhibiting a high degree of selectivity that harms target pests while sparing non-target organisms. Increasing the flavonoid concentration on an artificial diet fed by a rice brown plant hopper (Nilaparvata lugens) resulted in decreased survival rates, especially at 0.5 mg/mL, with no larvae surviving more than 24 h (Zhou et al. 2011). Total flavonoids exhibit high effectiveness comparable to chemical pesticides in controlling Spodoptera litura infestations in Gloriosa superba, as demonstrated by a field testing experiment (Suganthy & Sakthivel 2013).

In this review, we aim to explore the potential of flavonoids as eco-friendly pesticides, highlighting their benefits through an examination of their mechanism of action. We also identify areas that require further research and discuss prospects for increasing the commercialisation and acceptability of flavonoids as biopesticides in modern sustainable agriculture.

AN OVERVIEW OF PLANT FLAVONOIDS, THEIR INTERACTION WITH PHYTOHORMONES

Flavonoids are a type of phenolic compound that plays a vital role in plant defence mechanisms, serving as a biochemical barrier against insect her-

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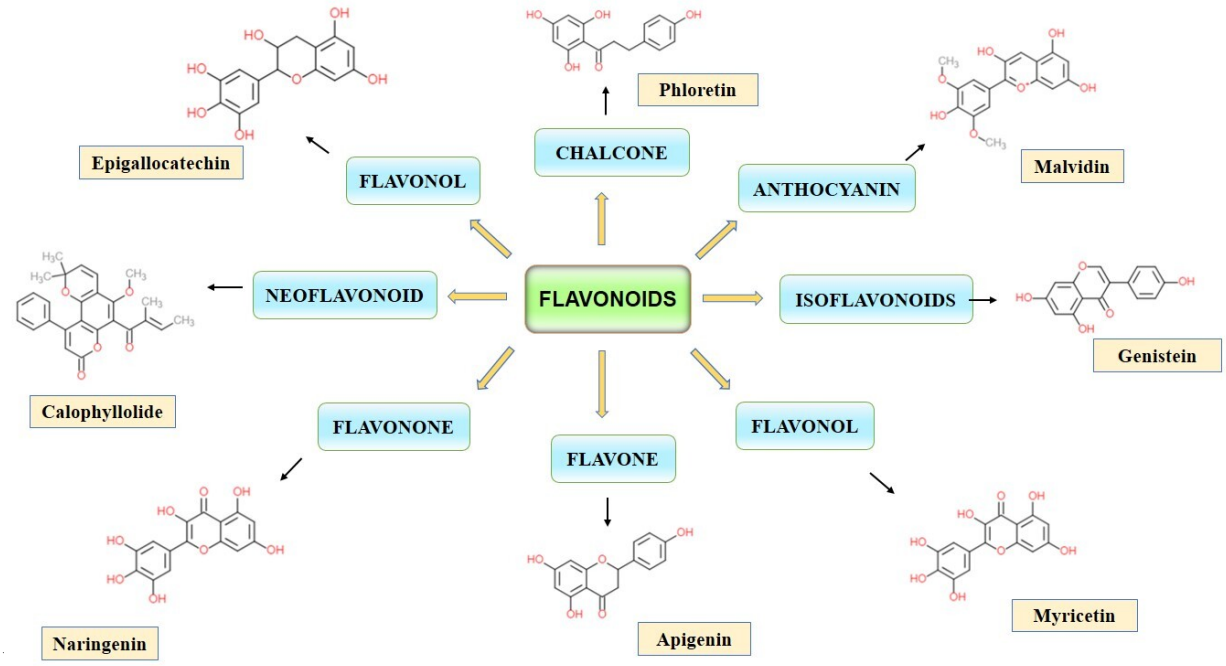
bivores (Ramaroson et al. 2022). Structurally, flavonoids are derived from 2-phenyl-benzyl-γ-pyrone and are characterised by a 15-carbon skeleton, comprising two benzene rings (A and B) linked by a 3-carbon linking chain [$C_{15}H_{10}O_X$] (x = 2 – 6) as C6-C3-C6 compounds. In many flavonoids, this central chain is further fused to a heterocyclic pyran or pyrone ring (ring C) (Corradini et al. 2011). Plant defence-related flavonoids are categorised into two main groups: preformed and induced compounds (Treutter 2006). Induced flavonoids are produced in response to physical injury, stress, or environmental stimuli, whereas preformed flavonoids are inherent compounds synthesised during regular plant development. Flavonoids are further classified into distinct subclasses based on structural differences and the oxidation degree of the central heterocycle, including: Flavonol, Flavones, Isoflavones, Anthocyanidins, Flavanone, Flavan-3-ols (Catechins), and Chalcones (Shen et al. 2022). The subclasses of flavonoids, along with their description and prominent sources, are detailed in Figure 1 and Table 1. A detailed summary of flavonoids present in crops and its resistance against various pest are given in the Table 2.

Flavonoids and phytohormones engage in intricate and dynamic interactions, significantly influencing plant growth, development, and defence mechanisms. Phytohormones, such as jasmonic acid (JA) and salicylic acid (SA), serve as key signalling molecules in plant defence, particularly in response to herbivory. For instance, upon attack by the tobacco hornworm (*Manduca sexta*), *Nicotiana attenuata* exhibits an upregulation of auxin biosynthetic YUCCA-like genes, leading to increased levels of indole-3-acetic acid (IAA). Elevated IAA levels contribute to enhanced developmental processes while simultaneously promoting JA signalling, which facilitates the accumulation of phenylamides in the stems, thereby strengthening the plant's defence response (Machado et al. 2016).

Flavonoids also influence plant-insect interactions. Quercetin and its glycosylated derivatives, quercetin 7'-O-glucoside and quercetin 3'-O-glucoside, extracted from *Gossypium hirsutum* L. (cotton) buds, act as feeding stimulants for the boll weevil (*Anthonomus grandis*), affecting insect behaviour and plant-insect dynamics (Hedin et al. 1968). Flavonoids play a crucial role in auxin transport and distribution by interacting with key membrane proteins, including PIN-FORMED (PIN) and multiple drug resistance (MDR) glycoproteins. Moreover, they modulate auxin signalling pathways by regulating the expression of auxin-responsive



This figure illustrates the subclasses of flavonoid compounds, namely flavanol, chalcone, anthocyanin, isoflavonoids, flavonol, flavone, flavonone and neoflavonoids, with an example for each class (the chemical structures were drawn using chemdoodle.com)

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Table 1. Detailed overview of the characteristics and source plants of the different classes of flavonoids

S. No.	Class	Description	Key Features	Flavonoids	Source plants	References
1	Flavonols	Building blocks of proanthocyanins	Have a ketone group with Hydroxyl group at position 3 of the C ring	Kaempferol, quercetin, myricetin, and fisetin	Onions, kale, lettuce, tomatoes, apples, grapes, berries, tea, and red wine	Ramesh et al. (2021)
2	Flavanones	Generally present in citrus fruits	Double bond between positions 2 and 3 is saturated	Hesperitin, naringenin, and eriodictyol	Oranges, lemons, and grapes	Ramesh et al. (2021)
3	Isoflavonoids	Limited distribution, predominantly found in soybeans and legumes	3-phenylchromen-4-one	Genistein and daidzein	Soybeans, and other leguminous plants	Brodowska (2017)
4	Neoflavonoids	Polyphenolic compounds with anti-inflammatory and antioxidation and are potential candidates for new drug development, cancer chemoprevention	4-phenylchromen backbone with no hydroxyl group substitution at position 2	Calophyllolide	*Calophyllum inophyllum* seeds, and *Mesua thwaitesii*	Chen et al. (2023)
5	Flavanols (Catechins)	Serve as potent antioxidants, playing a crucial role in contributing to plant defense mechanisms	3-hydroxy derivatives of flavanones with No double bond between positions 2,3	Epicatechin and Epigallocatechin	Bananas, apples, blueberries, peaches, pears	Daryanavard et al. (2023)
6	Anthocyanins	Pigments responsible for colors in plants and fruits	Responsible for red, blue, and purple colors	Cyanidin, delphinidin, malvidin, peonidin, and pelargonidin,	Cranberries, black currants, red grapes, raspberries, and strawberries	Brodowska (2017)
7	Chalcones	Ecological role as signalling molecules and precursors for many other flavonoid molecules	Subclass with open-chain flavonoid structure and lacks ring C of the basic flavonoid skeleton	Phloridzin, arbutin, phloretin, and chalconaringenin	Tomatoes, pears, strawberries, bearberries, and wheat products	Daryanavard et al. (2023)
8	Flavone	Yellow pigment and derivative of chromone with a phenyl substituent adjacent to the ether group	2-phenylchromen-4-one (2-phenyl-1-benzopyran-4-one) backbone	Apigenin, luteolin, baicalein, and chrysin	Parsley, thyme, celery, and hot peppers	Chen et al. (2023)

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Table 2. A detailed summary of flavonoids present in certain crops and their resistance against various pests

S. No.	Crops	Flavonoid compound(s)	Resistance to pests	Reference
1	Rice	Naringenin	Brown plant hopper	Dai et al. (2019)
2	Rice	Sakuranetin	Brown plant hopper	Liu et al. (2023)
3	Rice	Apigenin, naringenin, luteolin, apigenin-5-O-glucoside, neoschaftoside	Leaf folder	Zhao et al. (2023)
4	Rice	Flavanone 3-hydroxylase (*F3H*)*	White backed planthoppers	Kim et al. (2021)
5	Rice	Phenylalanine ammonia lyase*, Chalcone synthase*	Leaf roller	Cheah et al. (2020)
6	Maise	Maysin	Corn earworm	McMullen et al. (2009)
7	Maise	Apimaysin	Fall army worm and southwestern corn borer	Lattanzio et al. (2000)
8	Wheat	Total flavonoids	Wheat aphid	Zhang et al. (2022)
9	Wheat	Tricin	Aphid	Dreyer & Jones (1981)
10	Wheat	Epigallocatechin	Orange wheat blossom midge	Wang et al. (2022b)
11	Sorghum	3 - Deoxyanthocyanidins	Corn leaf aphid	Kariyat et al. (2019)
12	Sorghum, maize	3 - Deoxyfavonoids	Fall armyworm	Chatterjee et al. (2023)
13	Sorghum	Dihydroflavonol 4-reductase*, Flavanone 4-reductase*, Flavonoid 3-hydroxylase*	Sugarcane aphids	Puri et al. (2023)
14	Sorghum	Proanthocyanidins	Rice weevil	Ramputh (2002)
15	Pea	Pisatin	Pea aphid	Morkunas et al. (2016)
16	Cowpea	Quercetin, isorhamnetin	Aphids	Lattanzio et al. (2000)
17	Soybean	Daidzein, genistein, kaempferol	Cabbage looper	Hay et al. (2020)
18	Rice	Total flavonoids	Brown plant hopper	Hao et al. (2018)
19	Cotton	Rutin, quercetin, kaempferol	Cotton leaf worm/tobacco cutworm	Wang et al. (2024)
20	Spinach	Vitexin, Vitexin – 2" – O-arabinofuranoside	Tobacco cutworm	Aboshi et al. (2018)
21	Carrot	luteolin	Carrot root fly	Ramaroson et al. (2022)
22	Soybean	Daidzein, genistein	seed-sucking stink bug	da Graça et al. (2016)

*Enzymes involved in pest resistance

genes, ultimately influencing auxin levels in various plant tissues. In *Medicago* species, flavonoids contribute to nodule formation by maintaining a balanced cytokinin-to-auxin ratio (Dong & Song 2020). These compounds also induce the transcription of genes involved in *Nod* factor biosynthesis, which are essential for rhizobial signalling and symbiotic root infection. In many legumes, specific flavonoids exclusively activate *Nod* factor production in compatible rhizobia, playing a pivotal role in host range determination (Liu & Murray 2016). Additionally, plant growth-promoting rhizobacteria (PGPR) enhance plant resistance against insect herbivory by inducing systemic resistance, triggering the production of secondary metabolites such as terpenes and hydrogen cyanide. Some PGPR strains also exhibit direct insecticidal properties, contributing to effective pest suppression (Disi et al. 2019). Jasmonic acid plays a key role in flavonoid metabolism, promoting their accumulation in plant tissues, which may further enhance plant defence strategies (Woch et al. 2023).

Ethylene, another phytohormone, regulates plant branching and increases flavonoid accumulation in fruits and leaves. In the insect-resistant maise genotype *Mp708*, inhibition of ethylene synthesis increases susceptibility to caterpillar feeding, as demonstrated by the enhanced growth rates of fall armyworm (*Spodoptera frugiperda*) larvae in ethylene-inhibited plants. This suggests a crucial role for ethylene in plant defence against herbivory (Harfouche et al. 2006). Flavonoids also interact

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with abscisic acid (ABA) during stress responses. Ethylene increases the production of flavonols, which reduces the levels of reactive oxygen species (ROS) to trigger the stomatal closure. Since ABA relies on the ROS to trigger stomatal closure, the flavonols delay this process, which is evident that flavonols help control ROS levels and regulate how ABA affects stomatal movement (Watkins et al. 2014). Furthermore, ABA-deficient plants exhibit reduced resistance to the beet armyworm (*Spodoptera exigua*), underscoring the importance of ABA in plant defence (Thaler & Bostock 2004). The intricate interplay between flavonoids and phytohormones demonstrates a highly coordinated regulatory network that governs plant development and responses to biotic stressors. These interactions underscore the evolutionary adaptability of plants in regulating growth and defence processes through intricate chemical signalling pathways.

FLAVONOID BIOSYNTHESIS

The biosynthesis of flavonoids occurs within the cytosol, facilitated by a multienzyme complex known as the flavonoid metabolon, which is part of the general phenylpropanoid pathway (Stafford 1974). Flavonoids from varied groups of aromatic compounds originating from phenylalanine and malonyl-coenzyme A (CoA) through the fatty acid pathway (Winkel-Shirley 2001). The shikimic acid pathway in plants is vital, as it provides precursors to maintain redox balance and regulate plant growth and defence (Marchiosi et al. 2020**).** The shikimate pathway begins with glucose and produces shikimic acid. From there, the pathway branches out. One important branch leads to the production of aromatic amino acids L-Tryptophan, L-phenylalanine, and L-tyrosine. They are essential for protein synthesis and also act as precursors for various natural products, including pigments (anthocyanins, chalcones, aurones, and flavonols), alkaloids (capsaicin, colchicine, codeine, and caffeine), hormones (salicylic acid, jasmonic acid, brassinosteroids, ethylene, abscisic acid, auxin, cytokinin, and gibberellins) and cell wall components (cellulose, hemicellulose, and pectins). Another branch produces a vibrant array of secondary metabolites, including pigments (aurones and flavonols) and defence compounds (terpenoids and glycosides) (Maeda & Dudareva 2012). The products of shikimic acid pave the way for the dynamic regulation of overall plant growth and development (Santos-Sánchez et al. 2019).

The first three steps of the phenylpropanoid pathway are commonly referred to as the general phenylpropanoid pathway (Dong & Lin 2021). It begins with the enzyme phenylalanine ammonia-lyase (PAL), which specifically deaminates phenylalanine, producing trans-cinnamic acid as the first step in the phenylpropanoid pathway. The trans-cinnamic acid is hydroxylated using cinnamate 4-hydroxylase and converted to para-coumaric acid. The coumaroyl-CoA is produced from the amino acid phenylalanine through three enzymatic steps known as the general phenylpropanoid pathway (Petersen et al. 2010). The 4-coumaroyl CoA ligase (4CL) facilitates the transformation of p-coumaric acid to p-coumaroyl-CoA. The malonyl-CoA, on the other hand, is synthesised upon carboxylation of acetyl-CoA, a key intermediate in the Krebs tricarboxylic acid cycle (Jaganath & Crozier 2011).

Flavonoid synthesis initiates with the combination of one molecule of 4-coumaroyl-CoA and three molecules of malonyl-CoA, resulting in the formation of chalcone, facilitated by the chalcone synthase (CHS) (Williams et al. 2005). Subsequently, the chalcone undergoes isomerisation and intramolecular cyclisation through the action of chalcone flavanone isomerase (CHI) to yield a flavanone (Wohl & Petersen 2020). The flavanone further reacts with various enzymes, such as dihydroflavonol reductase (DFR), flavanone 3-hydroxylase (F3H), and isoflavone synthase (IFS), producing flavanol, dihydroflavonol, and isoflavonoids, respectively. The dihydroflavonol is further converted into flavonol under the activity of the enzyme flavonol synthase (FLS). The detailed biosynthesis of flavonoids is depicted in Figure 2.

MECHANISM OF ACTION OF FLAVONOIDS IN INSECT RESISTANCE

Plant flavonoids induce various changes in the insect body, disrupting its physiology and life cycle, which leads to the non-preference mechanism of resistance (Afroz et al. 2021). A few of the mechanisms include antifeedant activity, interference with growth and development, and disruption of digestive pathways. The biochemical con-

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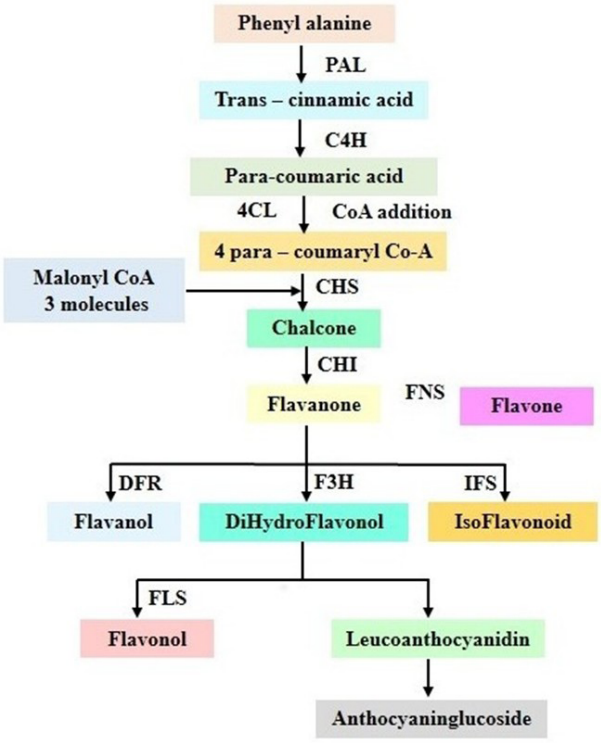

Figure 2. Biosynthesis pathway of flavonoids
This figure illustrates the pathway for the biosynthesis of flavonoids in plants, starting from their precursor, Phenyl alanine. Three molecules of malonyl Co-A on reacting with para-coumaryl co-A forms chalcone. PAL – phenylalanine ammonia lyase; C4H – cinnamate 4-hydroxyalse; 4CL – 4-coumaroyl CoA ligase; CHS – chalcone synthase; CHI – chalcone flavanone isomerase; FNS – flavone synthase; DFR – dihydro flavonol reductase; F3H – flavanone 3-hydroxylase; IFS – isoflavone synthase; FLS – flavonol synthase

stituents present in plant parts inhibit the juvenile hormones of insects, which are necessary for their development, resulting in premature metamorphosis (Maugh 1976). Some insects sequester plant flavonoids in their body cuticle for defence against predators or in their wings to attract mates (Simmonds 2003). Flavonoids can harm the feeding of insect pests that aren't adapted to them, thereby reducing their nutritional choices and acting as feeding deterrents, digestibility reducers, and toxins (Treutter 2005). Flavonoids exhibit chelating activity inside the insect body by binding to metal ions, potentially disrupting essential biological processes affecting the insect metabolism and leading to declined growth and development (Elliger et al. 1980; Harborne & Grayer 1994). The stability of flavonoids is enhanced through glycosylation, and it is proposed that the accumulation of higher quantities of stable flavonoid glycosides in plants could enhance their antioxidant properties (Mierziak et al. 2014). The detailed mechanism of action of flavonoids in the insect body is illustrated in Figure 3.

Antifeedant activity. Plant flavonoids exhibit antifeedant activity against insect pests by interfering with their feeding behaviour (Simmonds 2001). The taste-sensing system is crucial for recognising food in insects and animals. Additionally, some flavonoids may negatively impact insect feeding by inhibiting specific enzymes crucial for digestion (Vihakas 2014). These natural compounds serve as a defensive mechanism for plants, acting as chemical defences that discourage insect pests and contribute to the plant's overall resistance against herbivory (War et al. 2012). These compounds act as feeding deterrents by affecting the taste receptors and disrupting the digestive processes of the target organisms. Flavonoids can alter the palatability of plant tissues, making them less appealing to insects. The leaves of soybean plants exposed to both normal and elevated CO_2 levels, and affected by leaf skeletoniser herbivores such as Popillia japonica, exhibited a rise in the concentration of a single flavonoid – quercetin – under elevated CO_2 conditions, altering the palatability of the insect feeding on the soybean plants (O'Neill et al. 2010). Monophagous or oligophagous lepidopterans rely on gustatory receptors (Grs) to select host plants sensed by taste organs. The study on *Bombyx mori* gustatory receptor (BmGr) 16, BmGr18, and BmGr53 revealed that these Grs responded to various feeding deterrents, suggesting a broader role for Grs in host plant recognition. The coumarin present in plants prevented the feeding of the *Bombyx mori (*Kasubuchi et al. 2018*).* The Electropenetrography (EPG) analysis of the pea aphid *Acyrthosiphon pisum*'s feeding behaviour revealed that luteolin and genistein, when included in an artificial diet, clearly affected its feeding behaviour, thereby causing resistance in the plants (Goławska & Łukasik 2012). The antifeedant activity of certain flavonoids, such as catechinic acid and its derivatives, against the subterranean termite (*Coptotermes formosanus*) was observed (Ohmura et al. 2000). Many flavonoids have bitter tastes and unpleasant odors, acting as feeding-deterrents and reduces insect herbivory (Glas et al. 2012).

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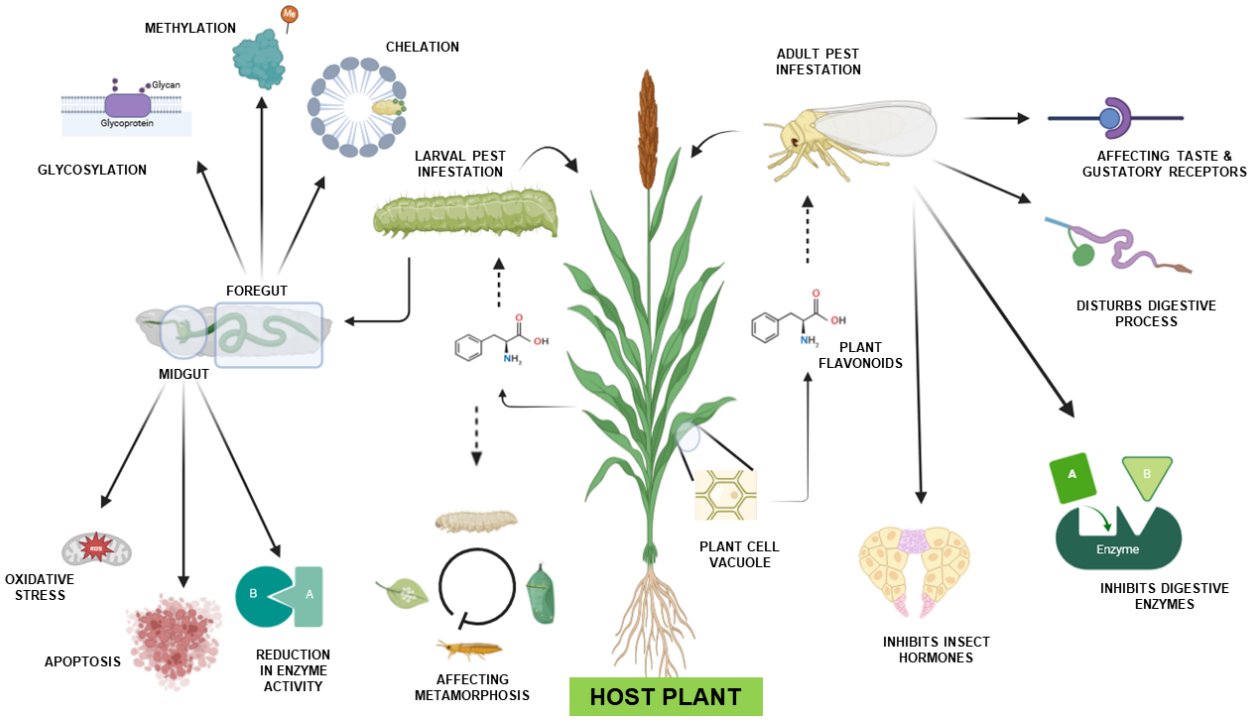

Figure 3. Schematic illustration of the mechanism of action of flavonoids in insect larvae and adults
The mode of action of flavonoids inside the insect adults and the larvae, and various reactions occurring inside their bodies as a resistance mechanism, and helping the host plant to protect itself (created with BioRender.com)

Disruption of digestion and nutrient absorption. Protease inhibitors (PIs) can interact with proteolytic enzymes, hindering their catalytic activity (Zhao et al. 2019). Found as secondary metabolites (e.g., tannins and flavonoids) or proteins, PIs disrupt digestion processes, resulting in reduced nutrient absorption and decreased amino acid bioavailability. This interference with digestive processes can have significant physiological effects on insects. Ingesting PIs may delay development, cause deformities, and decrease fertility in insects (Napoleão et al. 2019). Specifically, plant proteinase inhibitors have been shown to affect the growth and digestive physiology of larval insects, potentially hindering various enzymatic activities in the larval midgut and reducing the insect's growth (Lawrence & Koundal 2002). Additionally, lectins, proteins that interact with glycoconjugates, disrupt various midgut components and functions, including the peritrophic matrix, brush border, secretory cell layer, apoptosis, oxidative stress, interference with nutrient absorption, and harm to symbionts (Napoleão et al. 2019). Quercetin and other flavonoids undergo metabolic conversion primarily in the small intestine, predominantly through enzymatic processes such as glucuronidation and sulfation. After absorption from the intestinal lumen, these compounds are mainly transformed into conjugated metabolites before entering circulation. This conversion potentially helps the plant mitigate the harmful effects of pests, enabling it to maintain antioxidant activity and inhibit insect larval activity. The importance of dietary quercetin intake is linked to the conjugation reactions responsible for the physiological roles of antioxidative metabolites in insect resistance (Murota & Terao 2003). Flavonoids can inhibit key enzymes crucial for insect digestion and nutrient absorption, effectively starving them or reducing their ability to utilise food efficiently. For instance, quercetin significantly decreases lipase, protease, and α-amylase activities in the midgut of diamondback moth (*Plutella xylostella*) (Mikani 2019).

Interfere with insect growth and development: Flavonoids can mimic or interfere with essential insect hormones, such as ecdysone, which regulates moulting and metamorphosis (Vihakas 2014). Upon interference, vulnerable insects suffer developmental abnormalities, stunted growth, and even death at a premature stage. The flavonoids of the plant angico, *Piptadenia*

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rigida, include liquiritigenin, 7,3',4'-trihydroxyflavone, and 7,8,3',4'-tetrahydroxyflavanone, which inhibit the growth and alter the feeding behaviour of the larvae (Narciso et al. 2011). Incorporation of the flavonoid Rutin into sorghum and chickpea-based diets exerts a significant influence on the moulting process, which disrupts the functions of prothoracicotropic hormone and ecdysteroids, ultimately leading to the death of tobacco cutworm, *Spodoptera litura* (Jadhav et al. 2012). Flavonoids, such as rutin and quercetin, have shown ovicidal effects on bruchid eggs. When pulse beetle (*Callsobruchus chinesnsis)* was fed with the flavonoid extracts from *Calotropis procera,* both the number and weight of emerging adults were significantly reduced (Salunke et al. 2005). Application of rutin hydrate and quercetin dehydrate increased the nymph mortality of *Eriosoma lanigerum*, a woolly apple aphid (Ateyyat et al. 2012). Flavonoids possess strong antioxidant properties that allow them to neutralise free radicals within the insect cells, disrupting the normal cellular function. This oxidative imbalance can hinder insect growth and development, making the flavonoids effective plant defence compounds (Czerniewicz et al. 2017). At earlier stages, such as larvae, they are often more susceptible to the detrimental effects of flavonoids (Onyilagha et al. 2004). The mortality of first-instar Colorado potato beetle larvae was elevated by plant flavonoids taxifolin and quercetin through the detoxification process facilitated by glutathione S-transferases and esterase (Wang et al. 2016).

Flavonoids exhibit toxicity in various pests through mechanisms such as enzyme inhibition, disruption of hormonal balance, and interference with cell signalling pathways. Brown plant hopper (BPH) fed with methyl jasmonate, apigenin, kaempferol, gallic acid, and benzyl benzoate exhibited a slower rate of weight gain. It demonstrated inhibitory effects on the growth of newly emerged female adults (Deng et al. 2023). Additionally, 0.50% quercetin treatment significantly delayed the developmental period of *Hyphantria cunea* larvae and inhibited their growth (Gao et al. 2022). Apigenin, administered at 50 µg per primary reproductive pair, and Biochanin A were identified as the most toxic flavonoid and fecundity reducer. Oral feeding and topical application also showed a significant reduction in progeny numbers (Boué & Raina 2003).

RECENT ADVANCEMENTS IN FLAVONOIDS FOR INSECT RESISTANCE

Plant flavonoids can be formulated into a spray solution by dissolving them in a suitable carrier solution. This spray enhances plant defences, promoting growth and providing protection against stressors when applied correctly. In-silico molecular docking studies can confirm the practical application for biopesticides. *Ocimum basilicum* extract inhibited protease activities with IC50 values (*in vitro*) of 119.4, 91.0, 102.4, 76.4, and 52.4 µg/mL. *In silico* studies, including molecular docking, were conducted. The cell suspension technique is recommended for optimal *O. basilicum* extract production, yielding high levels of bio-insecticidal secondary metabolites (Darrag et al. 2022).

These plant-derived bioactive compounds have gained significant attention as eco-friendly alternatives to synthetic pesticides due to their potent insecticidal properties. Several phytochemicals have been identified for their strong larvicidal, adulticidal, and repellent effects against major agricultural pests, primarily targeting key enzymatic pathways in insect physiology. These compounds exhibited significant toxicity against both larvae and adults of *Rhynchophorus ferrugineus* (Red palm weevil), highlighting their potential as botanical insecticides. Further computational studies revealed that chicoric acid, another compound from

O. basilicum, demonstrated strong inhibitory activity against acetylcholinesterase (AChE), a critical enzyme in the insect nervous system (Darrag et al. 2024).

Similarly, ultra-performance liquid chromatography-mass spectrometry (UPLC-MS) analysis of *Solidago graminifolia* identified several flavanols, including quercetin, hyperoside, isoquercetin, kaempferol, and avicularin, which exhibited potent insecticidal activity with an LD_{50} value of 0.157 mg/mL. Docking studies further confirmed that quercetin displayed high binding affinity to AChE in *Spodoptera frugiperda*, leading to neural disruption and mortality (Herrera-Mayorga et al. 2022). In another study, essential oil constituents of *Rosmarinus officinalis*, particularly limonene (23.03%), cis-vaccenic acid (12.91%), and (2E,4E)-deca-2,4-dienal (11.67%), were found to have strong repellent activity against *Tribolium castaneum*, a significant stor-

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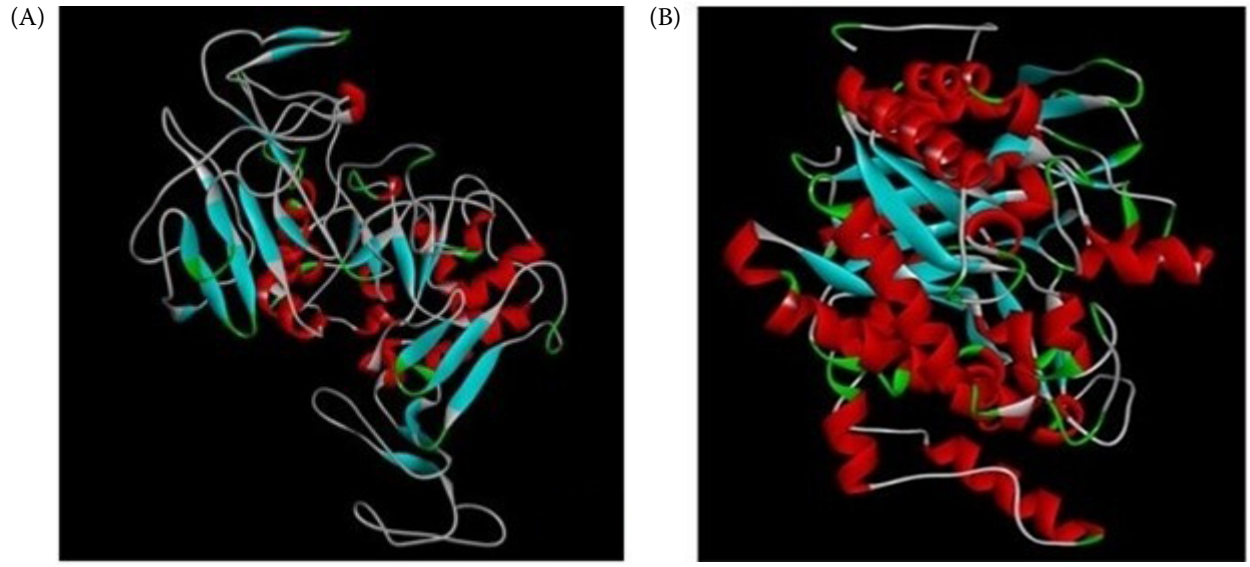

Figure 4. Structures of *Spodoptera frugiperda*
(A) Beta-glucosidase enzyme protein structure of *Spodoptera frugiperda* modelled in Modellor tool; (B) protein structure of beta-glycosidase receptor (A chain) in *Spodoptera frugiperda*

age pest. In-silico studies confirmed that limonene exhibited high binding affinity with insect detoxifying proteins, further reinforcing its potential as a natural insect repellent (Alhaithloul et al. 2023). The inhibitory effects of *Uncaria tomentosa*-derived compounds, including mitraphylline, chlorogenic acid, and llagate, were demonstrated through molecular docking studies targeting Farnesyl Diphosphate Synthase (FPPS), a crucial precursor in the juvenile hormone biosynthesis pathway of *Helicoverpa armigera*. These compounds exhibited strong inhibition, suggesting their role in disrupting insect growth and development (Alam et al. 2023). Extracts of *Ficus carica* containing psoralen and bergapten showed high insecticidal activity against *Euschistus heros*. Docking studies revealed that these compounds had a strong affinity towards AChE, indicating their neurotoxic effects on insects (Britto et al. 2021). Furthermore, nimbolide, a bioactive compound from *Azadirachta indica*, demonstrated a 66% reduction in larval populations of *Plutella xylostella*. Molecular docking studies confirmed its interaction with AChE, with a binding energy of −7.80 kcal/mol, further validating its role in pest control (Navinraj et al. 2023).

In addition, we have performed molecular docking studies to confirm the insecticidal properties of plant flavonoids by targeting the beta-glucosidase enzyme receptor, a key mode of action for insecticides against the polyphagous pest *Spodoptera frugiperda*. The protein structure of the beta-glucosidase enzyme receptor is computationally built using MODELLER and subsequently validated. The active site for the protein modelled was predicted using the CAASTp server. Molecular docking studies were performed using CB-DOCK software (Liu et al. 2020), and the interactions were visualised using LIGPLOT+. The results showed that flavonoids bound to the insect protein, similar to other chemical insecticides. The beta-glucosidase enzyme, used as an insect receptor for docking studies, is depicted in Figure 4A.

This study demonstrates that plant flavonoids, including rutin, quercetin, apimaysin, maysin, vitexin, pinocembrin, apigeninidin, kaempferol, and luteolinidin, have interacted with the beta-glucosidase receptor enzyme of Spodoptera frugiperda, resulting in mortality in this polyphagous pest, similar to chemical insecticides. Hence, formulations of plant flavonoids could be effective in controlling the insect pests. Figure 5 provides confirmation studies of the molecular docking of plant flavonoids to the modelled structure of beta-glucosidase enzyme, thereby proving a strong interaction and causing insecticidal effects on the pest. The interactions of the compounds, as indicated by the Vina score and coordinates, are mentioned in Table 3.

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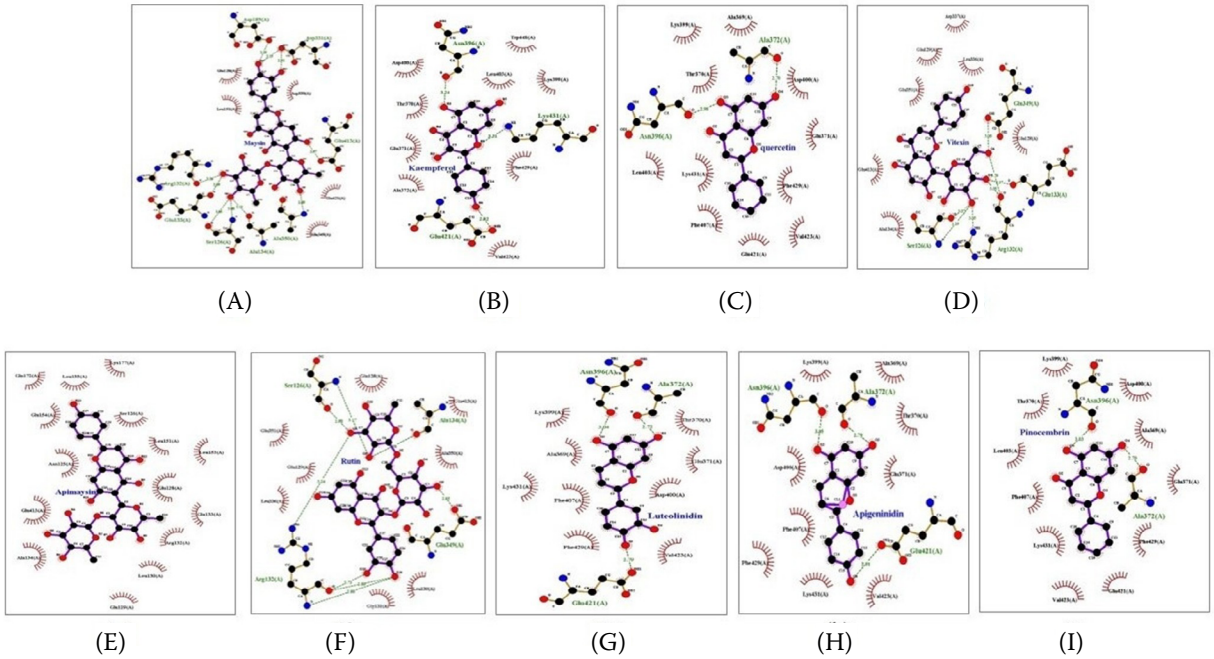

(A) (B) (C) (D)

(E) (F) (G) (H) (I)

Figure 5. Molecular docking of various plant flavonoids to the *Spodoptera frugiperda* beta-glucosidase enzyme and visualised through LIGPLOT+

The figure illustrates the interactions of the *Spodoptera frugiperda* beta–glucosidase enzyme with plant flavonoids, highlighting their role in pest resistance. (A) maysin; (B) kaempferol; (C) quercetin; (D) vitexin; (E) apimaysin; (F) rutin; (G) luteolininidin; (H) apigeninidin; (I) pinocembrin

Additionally, molecular docking studies have been performed on the insecticide binding receptor, beta-glycosidase. The insecticides bind to this receptor, repelling and killing the pest. The 3D structures of *Spodoptera frugiperda* beta glycosidase receptor (PDB ID: 5CG0, resolution: 2.09 Å) were acquired from the Protein Data Bank (PDB). The A chain of beta-glycosidase was processed by eliminating other chains, ligands, and water molecules (specifically water without hydrogen bonds) using the BIOVIA Discovery Studio software, as depicted in Figure 4B. Molecular docking studies were performed using the CB-DOCK software (Liu et al. 2020), and the interactions were visualised using LIGPLOT+. The results of this molecular docking showed that plant flavonoids bound to this target protein with a similar level of binding energy to that of chemical insecticides, and a few plant flavonoid compounds have higher levels of binding energy than chemical insecticides, as represented in Table 4, and the docking of the plant compounds was depicted in Figure 6. These findings collectively highlight the potential of plant-derived flavonoid compounds as natural insecticidal agents. Their ability to inter-

Table 3. Molecular docking analysis of the various plant flavonoids and beta–glucosidase enzyme

S. No.	Ligand name	Pub chem ID	Vina score	Cavity size	Coordinates of centre		
					x	*y*	*z*
1	Rutin	5280805	–9.7	817	–43	12	49
2	Quercetin	5280343	–8.8	7 560	–12	–2	23
3	Vitexin	5280441	–8.7	7 560	–12	–2	23
4	Kaempferol	5280863	–8.8	13 935	–14	2	22
5	Luteolinidin	441701	–9.0	13 935	–14	2	22
6	Apigeninidin	159360	–9.4	13 935	–14	2	22
7	Pinocembrin	68071	–8.8	13 935	–14	2	22
8	Maysin	70698181	–9.6	13 935	–14	2	22

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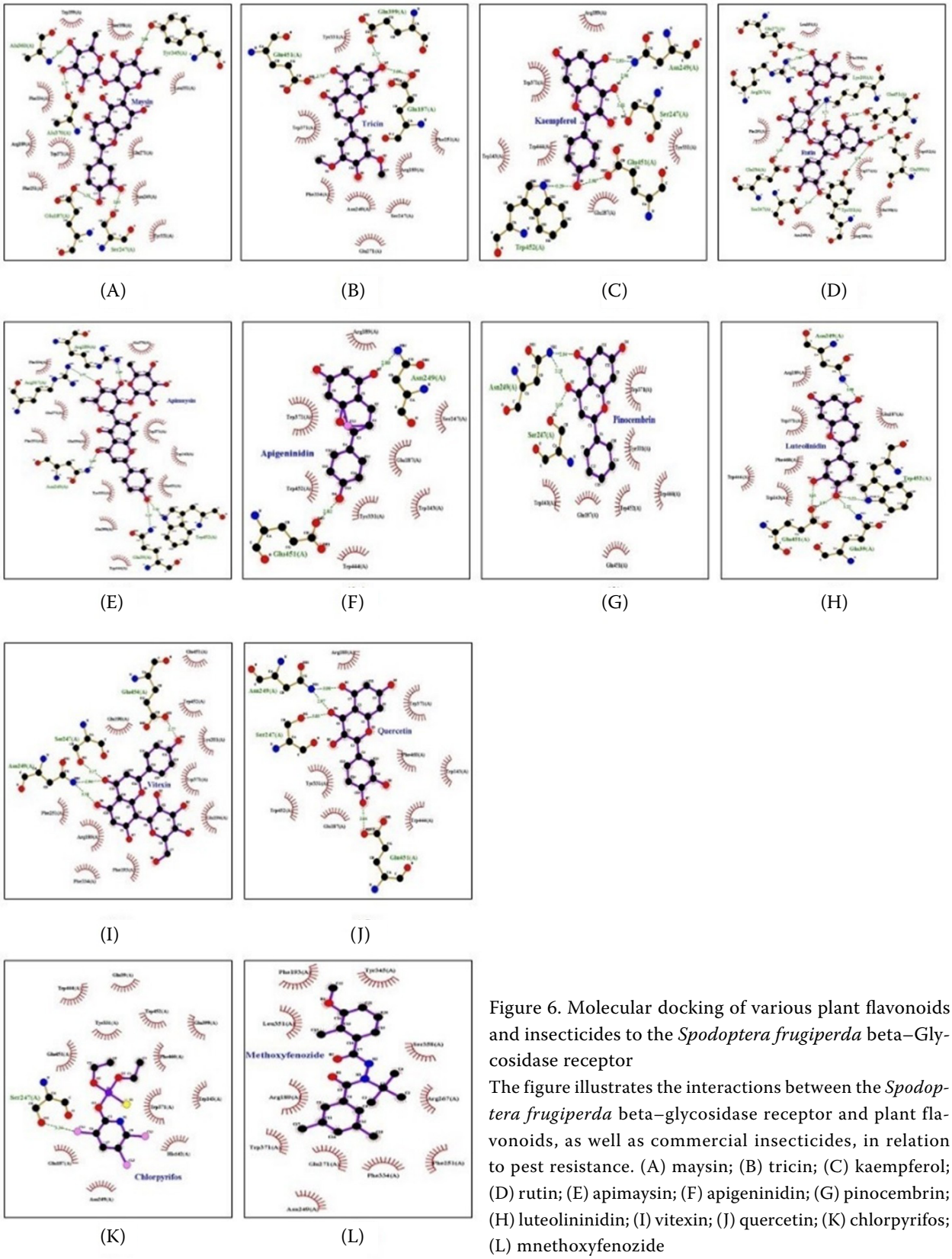
fere with key enzymatic and physiological pathways in insects underscores their viability as sustainable alternatives to synthetic pesticides, promoting eco-friendly pest management approaches.



(A) (B) (C) (D)

(E) (F) (G) (H)

(I) (J)

(K) (L)

Figure 6. Molecular docking of various plant flavonoids and insecticides to the *Spodoptera frugiperda* beta–Glycosidase receptor

The figure illustrates the interactions between the *Spodoptera frugiperda* beta–glycosidase receptor and plant flavonoids, as well as commercial insecticides, in relation to pest resistance. (A) maysin; (B) tricin; (C) kaempferol; (D) rutin; (E) apimaysin; (F) apigeninidin; (G) pinocembrin; (H) luteolininidin; (I) vitexin; (J) quercetin; (K) chlorpyrifos; (L) mnethoxyfenozide

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Table 4. Molecular docking analysis of the various plant flavonoids and beta-glycosidase receptor

S. No.	Ligand name	PubChem ID	Vina score	Cavity size	Coordinates of centre		
					x	*y*	*z*
1	Rutin	5280805	–9.6	816	–23	31	–69
2	Quercetin	5280343	–9.6	816	–23	31	–69
3	Vitexin	5280441	–10.1	816	–23	31	–69
4	Kaempferol	5280863	–10.6	816	–23	31	–69
5	Luteolinidin	441701	–7.6	816	–23	31	–69
6	Apigeninidin	159360	–6.4	816	–23	31	–69
7	Maysin	70698181	–8.7	816	–23	31	–69
8	Apimaysin	194566	–9.1	816	–23	31	–69
9	Pinocembrin	68071	–9.6	816	–23	31	–69
10	Tricin	5281702	–9.2	816	–23	31	–69
11	Chlorpyrifos	2730	–9.7	816	–23	31	–69
12	Methoxyferoxide	105010	–9.6	816	–23	31	–69

PROGRESS OF FLAVONOIDS AS BIOPESTICIDES

A study explored the interaction of soybean-exclusive flavonoids, daidzein, genistein, and kaempferol, with entomopathogenic baculovirus to enhance insect resistance against the cabbage looper (*Trichoplusia ni).* Combining these flavonoids at leaf-level concentrations synergistically enhanced baculovirus activity, with higher concentrations of genistein and kaempferol showing concentration-dependent improvements (Hay et al. 2020). Total flavonoids from fresh plant parts, such as roots, stems, and leaves, are extracted using solvents like ethanol, methanol, and acetone and then subjected to one of the chromatographic techniques for purification (Awouafack et al. 2017). These extracted flavonoid compounds can be used for direct applications or as insecticidal blends to enhance pest resistance in plants. Formulations of emulsifiable concentrate (EC) were prepared using seed oils derived from *Pongamia pinnata*, *Pachyrhizus erosus*, and *Annona squamosa,* which contain flavonoid compounds shown insecticidal effectiveness when assessed through *in-vitro* experiments targeting cabbage aphid (*Brevicoryne brassicae*) and *in-vivo* studies against eggplant aphid (*Aphis gossypii*) and whitefly (*Bemisia tabaci*). The botanical formulation of 40% EC derived from seed oils of *Annona squamosa* demonstrated comparatively higher insecticidal efficacy against the cabbage aphid than the synthetic insecticide dimethoate 30 EC (Aloke Purkait et al. 2019). The effect of myrrh extract from *Commiphora molmol*, along with sub-lethal treatments of profenofos/chlorofluazuron, fenvalerate, and pyriproxyfen, was studied on *Spodoptera littoralis* larvae, which displayed the highest activity, with a mortality rate of 44.4% of the pest (Shonouda et al. 2000). The use of biodegradable and non-toxic biochemical pesticides promotes environmentally safe and eco-friendly insect resistance strategies. The different biopesticidal activities of flavonoids against various pests are presented in Table 5.

CONCLUSION AND FUTURE PERSPECTIVES

Chemical pesticides have played a crucial role in the development of agriculture, contributing to improved crop yields and enhanced food production. However, excessive and inappropriate use can harm the environment and human health. Therefore, developing sustainable alternatives to replace traditional methods is essential. In this context, flavonoid-based pesticides are emerging as a highly effective solution for enhancing the efficacy of agricultural chemicals. To date, significant advancements have been made in researching the practical applications of flavonoids for insect resistance, but some gaps still need to be addressed. There is currently a lack of comprehensive understanding of the anti-feedant and anti-insecticidal activities of flavonoids. Therefore, the mechanisms underlying this activity need to be elucidated

Table 5. Different flavonoids' biopesticidal activity against various pests

S. No.	Source Plant	Extract of plant part	Name of the flavonoids	Insect pests	Effects in pest	Reference
1	Sweet wormwood	Leaf	Casticin, chryso-splenetin	African pod borer	Reduction in larval weight and growth	Anshul et al. (2013)
2	Soybean	Leaf	daidzein, glyceolin, sojagol, coumestrol	Cabbage semilooper	Anti-feedent activity	Sharma & Norris (1991)
3	Tarworts	Leaf	Pinocembrin	Ladybird beetle, Elm leaf beetle, Fall army worm	Antifeedant activity	Napal et al. (2009)
4	Cotton	Leaf	5-hydroxy-3,6,7,8,4' -pentamethoxyflavone	Common cutworm	Antifeedant activity	Morimoto et al. (2000)
5	Chrysanthemum	Leaf	Crude flavonoids	Cabbage looper	Insect growth-regulating activity	Beninger et al. (2004)
6	Sugar apple	Leaf	Quercetin	Grain pulse beetle	Block steroid hydroxylase involved in the moulting process	Kotkar et al. (2002)
7	Grapes	Leaf	Quercetin	Rice weevil	Free radical scavenging capacity	Zain et al. (2022)
8	Creat	Leaf	Total flavonoids	Red flour beetle	Mortality of the pest	Baliyarsingh et al. (2021)
9	Pepper	Leaf	Myrcene	Rice ear bug	Repellent activity	Nugroho et al. (2020)
10	Calotropis	Leaf	Quercitrin, rutin, fisetin, myricetin	Pulse beetle (storage pest)	Ovicidal effect on bruchid eggs	Salunke et al. (2005)
11	African locust bean tree	Pod husk	Total flavonoids	Flea beetle	Enhances the host plant yield by preventing pest infestation	Chacón-Fuentes et al. (2015)
12	Sage glory bower	Leaf	Pectolinaringenin	Spotted bollworm	Ovicidal and oviposition deterrent activity	Muthu et al. (2013)
13	Jack pine, Black Spurse	Cones	Taxifolin, quercetin	Colorado potato beetle	Mortality to the larvae and the enzyme inhibitor	Wang et al. (2016)
14	Balsam Fir, Tamarack	Bark				
15	Cowpea	Seed	Total flavonoids, anthocyanins	Thrips, pod sucking bug	Prevents infestation of pests	Makoi et al. (2010)

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through reliable results obtained by combining field and genomics advances. Moreover, it is crucial to understand the dynamic co-evolution between plants, pests, and their interactions with specific flavonoids to anticipate potential adaptations and ensure the long-term durability of resistance. The commercialisation of flavonoids as a biopesticide is still in its infancy. Several factors, including large-scale production, the unavailability of a standard extraction protocol/analytical approach, short shelf life, residual toxicity, environmental and human safety concerns, and the need for comprehensive field trials for host plants in multiple environments, are limiting the use and commercialisation of flavonoid-based pesticides. There is no doubt that flavonoids are promising natural pesticides for pest management; however, they still have a long way to go before being proposed as an alternative to chemical pesticides.

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REFERENCES

Aboshi T., Ishiguri S., Shiono Y., Murayama T. (2018): Flavonoid glycosides in Malabar spinach Basella alba inhibit the growth of *Spodoptera litura* larvae. Bioscience, Biotechnology, and Biochemistry, 82: 9–14.

Afroz M., Rahman M., Amin R. (2021): Insect plant interaction with reference to secondary metabolites: A review. Agricultural Reviews, 42: 427–433.

Alam M.S., Sharma M., Kumar R., Das J., Rode S., Kumar P., Prasad R., Sharma A.K. (2023): *In silico* identification of potential phytochemical inhibitors targeting farnesyl diphosphate synthase of cotton bollworm (*Helicoverpa armigera*). Journal of Biomolecular Structure and Dynamics, 41: 1978–1987.

Alhaithloul H.A., Alqahtani M.M., Abdein M.A., Ahmed M.A., Hesham A.E.-L., Aljameeli M.M., Al Mozini R.N., Gharsan F.N., et al. (2023): Rosemary and neem methanolic extract: antioxidant, cytotoxic, and larvicidal activities supported by chemical composition and molecular docking simulations. Frontiers in Plant Science, 14: 1155698.

Aloke Purkait A.P., Subrata Biswas S.B., Soumen Saha S.S., Hazra D., Kusal Roy K.R., Biswas P., Ghosh S., Kole R. (2019): Formulation of plant based insecticides, their bio-efficacy evaluation and chemical characterisation. Crop Protection, 125: 104907.

Anshul N., Bhakuni R.S., Gaur R., Singh D. (2013): Isomeric flavonoids of Artemisia annua (Asterales: Asteraceae) as insect growth inhibitors against *Helicoverpa armigera* (Lepidoptera: Noctuidae). Florida Entomologist, 96: 897–903.

Ateyyat M., Abu-Romman S., Abu-Darwish M., Ghabeish I. (2012): Impact of flavonoids against woolly apple aphid, *Eriosoma lanigerum* (Hausmann) and its sole parasitoid, *Aphelinus mali* (Hald.). Journal of Agricultural Science, 4: 227.

Awouafack M.D., Tane P., Morita H. (2017): Isolation and structure characterisation of flavonoids. In: Justino G.C. (ed.): Flavonoids-From Biosynthesis to Human Health. InTech: 46–58.

Ayilara M.S., Adeleke B.S., Akinola S.A., Fayose C.A., Adeyemi U.T., Gbadegesin L.A., Omole R.K., Johnson R.M., et al. (2023): Biopesticides as a promising alternative to synthetic pesticides: A case for microbial pesticides, phytopesticides, and nanobiopesticides. Frontiers in Microbiology, 14: 1040901.

Baliyarsingh B., Mishra A., Rath S. (2021): Evaluation of insecticidal and repellency activity of leaf extracts of *Andrographis paniculata* against *Tribolium castaneum* (red flour beetle). International Journal of Tropical Insect Science, 41: 765–773.

Beninger C.W., Abou-Zaid M.M., Kistner A.L., Hallett R.H., Iqbal M.J., Grodzinski B., Hall J.C. (2004): A flavanone and two phenolic acids from *Chrysanthemum morifolium* with phytotoxic and insect growth regulating activity. Journal of Chemical Ecology, 30: 589–606.

Bentivenha J.P., Canassa V.F., Baldin E.L., Borguini M.G., Lima G.P., Lourenção A.L. (2018): Role of the rutin and genistein flavonoids in soybean resistance to *Piezodorus guildinii* (Hemiptera: Pentatomidae). Arthropod-Plant Interactions, 12: 311–320.

Boué S.M., Raina A.K. (2003): Effects of plant flavonoids on fecundity, survival, and feeding of the Formosan subterranean termite. Journal of Chemical Ecology, 29: 2575–2584.

Britto I.O., Araújo S.H., Toledo P.F., Lima G.D., Salustiano I.V., Alves J.R., Mantilla-Afanador J.G., Kohlhoff M., et al. (2021): Potential of *Ficus carica* extracts against *Euschistus heros*: Toxicity of major active compounds and selectivity against beneficial insects. Pest Management Science, 77: 4638–4647.

Brodowska K.M. (2017): Natural flavonoids: classification, potential role, and application of flavonoid analogues. European Journal of Biological Research, 7: 108–123.

https://doi.org/10.17221/56/2025-PPS

Chacón-Fuentes M., Parra L., Rodriguez-Saona C., Seguel I., Ceballos R., Quiroz A. (2015): Domestication in murtilla (*Ugni molinae*) reduced defensive flavonol levels but increased resistance against a native herbivorous insect. Environmental Entomology, 44: 627–637.

Chatterjee D., Lesko T., Peiffer M., Elango D., Beuzelin J., Felton G.W., Chopra S. (2023): Sorghum and maise flavonoids are detrimental to growth and survival of fall armyworm *Spodoptera frugiperda*. Journal of Pest Science, 96: 1551–1567.

Cheah B.H., Lin H.-H., Chien H.-J., Liao C.-T., Liu L.-Y.D., Lai C.-C., Lin Y.-F., Chuang W.-P. (2020): SWATH-MS-based quantitative proteomics reveals a uniquely intricate defense response in *Cnaphalocrocis medinalis*-resistant rice. Scientific Reports, 10: 6597.

Chen S., Wang X., Cheng Y., Gao H., Chen X. (2023): A review of classification, biosynthesis, biological activities and potential applications of flavonoids. Molecules, 28: 4982.

Corradini E., Foglia P., Giansanti P., Gubbiotti R., Samperi R., Laganà A. (2011): Flavonoids: chemical properties and analytical methodologies of identification and quantitation in foods and plants. Natural Product Research, 25: 469–495.

Czerniewicz P., Sytykiewicz H., Durak R., Borowiak-Sobkowiak B., Chrzanowski G. (2017): Role of phenolic compounds during antioxidative responses of winter triticale to aphid and beetle attack. Plant Physiology and Biochemistry, 118: 529–540.

da Graça J.P., Ueda T.E., Janegitz T., Vieira S.S., Salvador M.C., de Oliveira M.C., Zingaretti S.M., Powers S.J., et al. (2016): The natural plant stress elicitor cis-jasmone causes cultivar-dependent reduction in growth of the stink bug, *Euschistus heros* and associated changes in flavonoid concentrations in soybean, Glycine max. Phytochemistry, 131: 84–91.

Dai Z., Tan J., Zhou C., Yang X., Yang F., Zhang S., Sun S., Miao X., et al. (2019): The OsmiR396–Os GRF 8–OsF3H-flavonoid pathway mediates resistance to the brown planthopper in rice (*Oryza sativa*). Plant Biotechnology Journal, 17: 1657–1669.

Darrag H.M., Almuhanna H.T., Hakami E.H. (2022): Secondary metabolites in basil, bio-insecticide, inhibition effect, and in silico molecular docking against proteolytic enzymes of the red palm weevil (*Rhynchophorus ferrugineus*). Plants, 11: 1087.

Darrag H.M., Ghazzawy H.S., Nasser Alzain M., Hakami E.H., Almuhanna H.T., Alqahtani N.K. (2024): Exploring *Ocimum basilicum*'s secondary metabolites: Inhibition and molecular docking against *Rhynchophorus ferrugineus* for optimal action. Plants, 13: 491.

Daryanavard H., Postiglione A.E., Mühlemann J.K., Muday G.K. (2023): Flavonols modulate plant development, signaling, and stress responses. Current Opinion in Plant Biology, 72: 102350.

Deng Z., Lai C., Zhang J., Sun F., Li D., Hao P., Shentu X., Pang K., et al (2023): Effects of secondary metabolites of rice on brown planthopper and its symbionts. International Journal of Molecular Sciences, 25: 386.

Disi J., Simmons J., Zebelo S. (2019): Plant growth-promoting rhizobacteria-induced defense against insect herbivores. In: Disi J., Simmons J., Zebelo S. (eds): Field Crops: Sustainable Management by PGPR. Springer: 385–410.

Dong N.Q., Lin H.X. (2021): Contribution of phenylpropanoid metabolism to plant development and plant–environment interactions. Journal of integrative plant biology, 63: 180–209.

Dong W., Song Y. (2020): The significance of flavonoids in the process of biological nitrogen fixation. International Journal of Molecular Sciences, 21: 5926.

Dreyer D.L., Jones K.C. (1981): Feeding deterrency of flavonoids and related phenolics towards *Schizaphis graminum* and *Myzus persicae*: aphid feeding deterrents in wheat. Phytochemistry, 20: 2489–2493.

Elliger C., Chan B., Waiss A. (1980): Flavonoids as larval growth inhibitors: structural factors governing toxicity. Naturwissenschaften, 67: 358–360.

Gao Y.L., Pan Z.Y., Meng X., Yuan Y.-F., Li H.-Y., Chen M. (2022): The effect of quercetin on the growth, development, nutrition utilisation, and detoxification enzymes in *Hyphantria cunea* Drury (Lepidoptera: Arctiidae). Forests, 13: 1945.

Geier P. (1966): Management of insect pests. Annual Review of Entomology, 11: 471–490.

Glas J.J., Schimmel B.C., Alba J.M., Escobar-Bravo R., Schuurink R.C., Kant M.R. (2012): Plant glandular trichomes as targets for breeding or engineering of resistance to herbivores. International Journal of Molecular Sciences, 13: 17077–17103.

Goławska S., Łukasik I. (2012): Antifeedant activity of luteolin and genistein against the pea aphid, *Acyrthosiphon pisum*. Journal of Pest Science, 85: 443–450.

Gupta S., Dikshit A. (2010): Biopesticides: An ecofriendly approach for pest control. Journal of Biopesticides, 3: 186.

Hao P.-Y., F. Y.-L., Zhou Y.-S., Song X.-.M, Li H.-L., Ma Y., Ye C.-L., Yu X.-P. (2018): Schaftoside Interacts with Nl-CDK1 protein: A mechanism of rice resistance to brown planthopper, *Nilaparvata lugens*. Frontiers in Plant Science, 9: 710.

Harborne J.B., Grayer R.J. (1994): Flavonoids and insects. In: Harborne J.B. (ed.): The Flavonoids Advances in Research Since 1986. Routledge, London: 589–618.

Harfouche A.L., Shivaji R., Stocker R., Williams P.W., Luthe D.S. (2006): Ethylene signaling mediates a maise defense response to insect herbivory. Molecular Plant-Microbe Interactions, 19: 189–199.

Hay W.T., Behle R.W., Berhow M.A., Miller A.C., Selling G.W. (2020): Biopesticide synergy when combining plant fla-

https://doi.org/10.17221/56/2025-PPS

vonoids and entomopathogenic baculovirus. Scientific Reports, 10: 6806.

Hedin P.A., Miles L., Thompson A., Minyard J. (1968): Constituents of cotton bud. Formulation of boll weevil feeding stimulant mixtures. Journal of Agricultural and Food Chemistry, 16: 505–513.

Herrera-Mayorga V., Guerrero-Sánchez J.A., Méndez-Álvarez D., Paredes-Sánchez F.A., Rodríguez-Duran L.V., Niño-García N., Paz-González A.D., Rivera G. (2022): Insecticidal activity of organic extracts of *Solidago graminifolia* and its main metabolites (quercetin and chlorogenic acid) against *Spodoptera frugiperda*: an *in vitro* and *in silico* approach. Molecules, 27: 3325.

Jadhav D.R., Mallikarjuna N., Rathore A., Pokle D. (2012): Effect of some flavonoids on survival and development of *Helicoverpa armigera* (Hübner) and *Spodoptera litura* (Fab) (Lepidoptera: Noctuidae). Asian Journal of Agricultural Sciences, 4: 298–307.

Jaganath I.B., Crozier A. (2011): Flavonoid biosynthesis. In: Ashihara H., Crozier A., Komamine A. (eds): Plant Metabolism and Biotechnology. John Wiley & Sons, Ltd., Chichester: 293–320.

Kariyat R.R., Gaffoor I., Sattar S., Dixon C.W., Frock N., Moen J., De Moraes C.M., Mescher M.C., et al. (2019): Sorghum 3-deoxyanthocyanidin flavonoids confer resistance against corn leaf aphid. Journal of Chemical Ecology, 45: 502–514.

Kasubuchi M., Shii F., Tsuneto K., Yamagishi T., Adegawa S., Endo H., Sato R. (2018): Insect taste receptors relevant to host identification by recognition of secondary metabolite patterns of non-host plants. Biochemical and Biophysical Research Communications, 499: 901–906.

Kaur R., Choudhary D., Bali S., Bandral S.S., Singh V., Ahmad M.A., Rani N., Singh T.G., et al. (2024): Pesticides: An alarming detrimental to health and environment. Science of the Total Environment, 915: 170113.

Kim E.-G., Yun S., Park J.-R., Kim K.-M. (2021): Identification of F3H, major secondary metabolite-related gene that confers resistance against whitebacked planthopper through QTL mapping in rice. Plants, 10: 81.

Kotkar H.M., Mendki P.S., Sadan S.V.G.S., Jha S.R., Upasani S.M., Maheshwari V.L. (2002): Antimicrobial and pesticidal activity of partially purified flavonoids of *Annona squamosa*. Pest Management Science: Formerly Pesticide Science, 58: 33–37.

Lattanzio V., Arpaia S., Cardinali A., Di Venere D., Linsalata V. (2000): Role of endogenous flavonoids in resistance mechanism of Vigna to aphids. Journal of Agricultural and Food Chemistry, 48: 5316–5320.

Lawrence P.K., Koundal K.R. (2002): Plant protease inhibitors in control of phytophagous insects. Electronic Journal of Biotechnology, 5: 5–6.

Liu C.W., Murray JD. (2016): The role of flavonoids in nodulation host-range specificity: an update. Plants, 5: 33.

Liu M., Hong G., Li H., Bing X., Chen Y., Jing X., Gershenzon J., Lou Y., et al. (2023): Sakuranetin protects rice from brown planthopper attack by depleting its beneficial endosymbionts. Proceedings of the National Academy of Sciences, 120: e2305007120.

Liu Y., Grimm M., Dai W.-T., Hou M.-C., Xiao Z.-X., Cao Y. (2020): CB-Dock: A web server for cavity detection-guided protein–ligand blind docking. Acta Pharmacologica Sinica, 41: 138–144.

Machado R.A., Robert C.A., Arce C.C., Ferrieri A.P., Xu S., Jimenez-Aleman G.H., Baldwin I.T., Erb M. (2016): Auxin is rapidly induced by herbivore attack and regulates a subset of systemic, jasmonate-dependent defenses. Plant Physiology, 172: 521–532.

Maeda H., Dudareva N. (2012): The shikimate pathway and aromatic amino acid biosynthesis in plants. Annual Review of Plant Biology, 63: 73–105.

Mahmood I., Imadi S.R., Shazadi K., Gul A., Hakeem K.R. (2016): Effects of pesticides on environment. In: Hakeem K.R., Akhtar M.S., Abdullah S.N.A. (eds): Plant, Soil and Microbes: Volume 1: Implications in Crop Science. Springer, Cham: 253–269.

Makoi J.H., Belane A.K., Chimphango S.B., Dakora F.D. (2010): Seed flavonoids and anthocyanins as markers of enhanced plant defence in nodulated cowpea (*Vigna unguiculata* L. Walp.). Field Crops Research, 118: 21–27.

Marchiosi R., dos Santos W.D., Constantin R.P., de Lima R.B., Soares A.R., Finger-Teixeira A., Mota T.R., de Oliveira D.M., et al. (2020): Biosynthesis and metabolic actions of simple phenolic acids in plants. Phytochemistry Reviews, 19: 865–906.

Maugh T.H. (1976): Plant biochemistry: Two new ways to fight pests. Science, 192: 874–876.

McMullen M.D., Frey M., Degenhardt J. (2009): Genetics and biochemistry of insect resistance in maise. In: Bennetzen J.L., Hake S.C. (eds): Handbook of Maise: Its Biology, Springer, New York: 271–289.

Mierziak J., Wojtasik W., Kostyn K., Czuj T., Szopa J., Kulma A. (2014): Crossbreeding of transgenic flax plants overproducing flavonoids and glucosyltransferase results in progeny with improved antifungal and antioxidative properties. Molecular Breeding, 34: 1917–1932.

Mikani A. (2019): Effect of quercetin on some digestive enzyme activity via crustacean cardioactive peptide (CCAP) content of the midgut of the diamondback moth, *Plutella xylostella* (Lepidoptera: Plutellidae). Journal of Crop Protection, 8: 33–43.

Morimoto M., Kumeda S., Komai K. (2000): Insect Antifeedant Flavonoids from *Gnaphalium affine* D. Don. Journal of Agricultural and Food Chemistry, 48: 1888–1891.

https://doi.org/10.17221/56/2025-PPS

Morkunas I., Woźniak A., Formela M., Mai V.C., Marczak Ł., Narożna D., Borowiak-Sobkowiak B., Kühn C., et al. (2016): Pea aphid infestation induces changes in flavonoids, antioxidative defence, soluble sugars and sugar transporter expression in leaves of pea seedlings. Protoplasma, 253: 1063–1079.

Murota K., Terao J. (2003): Antioxidative flavonoid quercetin: implication of its intestinal absorption and metabolism. Archives of Biochemistry and Biophysics, 417: 12–17.

Muthu C., Baskar K., Ignacimuthu S., Al-Khaliel A.S. (2013): Ovicidal and oviposition deterrent activities of the flavonoid pectolinaringenin from *Clerodendrum phlomidis* against *Earias vittella*. Phytoparasitica, 41: 365–372.

Napal G.N.D., Carpinella M.C., Palacios S.M. (2009): Antifeedant activity of ethanolic extract from *Flourensia oolepis* and isolation of pinocembrin as its active principle compound. Bioresource Technology, 100: 3669–3673.

Napoleão T.H., Albuquerque L.P., Santos N.D., Nova I.C., Lima T.A., Paiva P.M., Pontual E.V. (2019): Insect midgut structures and molecules as targets of plant-derived protease inhibitors and lectins. Pest Management Science, 75: 1212–1222.

Narciso J.A., De Souza M.S., De Carvalho M.G., Genestra M., Cabral M. (2011): Flavonoids inhibited NADPH consumption and ecdysis processes in *Oncopeltus fasciatus*. Journal of Natural Pharmaceuticals, 2: 133–133.

Navinraj S., Boopathi N.M., Balasubramani V., Nakkeeran S., Raghu R., Gnanam R., Saranya N., Santhanakrishnan V. (2023): Molecular docking of nimbolide extracted from leaves of *Azadirachta indica* with protein targets to confirm the antifungal, antibacterial and insecticidal activity. Indian Journal of Microbiology, 63: 494–512.

Nikpay A., Tiwari A.K., Vejar-Cota G., Ziaee M., Wilson B., Srivastava S., Goebel F.-R. (2023): Biotic stresses in sugarcane plants and its management. In: Agro-industrial Perspectives on Sugarcane Production under Environmental Stress. Springer, Cham: 301–359.

Nugroho L.H., Pratiwi R., Soesilohadi R., Subin E.R., Wahyuni S., Hartini Y.S., Lailaty I.Q. (2020): Repellent activity of piper spp. leaves extracts on rice ear bugs (*Leptocorisa oratorius* Fabricius) and the characters of its volatile compounds. Annual Research & Review in Biology, 35: 34–45.

O'Neill B.F., Zangerl A.R., Dermody O., Bilgin D.D., Casteel C.L., Zavala J.A., DeLucia E.H., Berenbaum M.R. (2010): Impact of elevated levels of atmospheric CO2 and herbivory on flavonoids of soybean (*Glycine max* Linnaeus). Journal of Chemical Ecology, 36: 35–45.

Ohmura W., Doi S., Aoyama M., Ohara S. (2000): Antifeedant activity of flavonoids and related compounds against the subterranean termite *Coptotermes formosanus* Shiraki. Journal of Wood Science, 46: 149–153.

Onyilagha J.C., Lazorko J., Gruber M.Y., Soroka J.J., Erlandson M.A. (2004): Effect of flavonoids on feeding preference and development of the crucifer pest *Mamestra configurata* Walker. Journal of Chemical Ecology, 30: 109–124.

Peer W.A., Murphy A.S. (2007): Flavonoids and auxin transport: modulators or regulators? Trends in Plant Science, 12: 556–563.

Petersen M., Hans J., Matern U. (2010): Biosynthesis of phenylpropanoids and related compounds. In: Wink M. (ed.):Annual Plant Reviews Volume 40: Biochemistry of Plant Secondary Metabolism, Wiley-Blackwell Oxford: 182–257.

Pratap A., Douglas C., Prajapati U., Kumari G., War A.R., Tomar R., Pandey A.K., Dubey S. (2020): Breeding progress and future challenges: biotic stresses. In: Nair R., Schafleitner R., Lee S.H. (eds): The Mungbean Genome, Springer, Cham: 55–80.

Puri H., Ikuze E., Ayala J., Rodriguez I., Kariyat R., Louis J., Grover S. (2023): Greenbug feeding-induced resistance to sugarcane aphids in sorghum. Frontiers in Ecology and Evolution, 11: 85.

Ramaroson M.-L., Koutouan C., Helesbeux J.-J., Le Clerc V., Hamama L., Geoffriau E., Briard M. (2022): Role of phenylpropanoids and flavonoids in plant resistance to pests and diseases. Molecules, 27: 8371.

Ramesh P., Jagadeesan R., Sekaran S., Dhanasekaran A., Vimalraj S. (2021): Flavonoids: classification, function, and molecular mechanisms involved in bone remodelling. Frontiers in Endocrinology, 12: 779638.

Ramputh A.-I. (2002): Soluble and Cell Wall Bound Phenolic-Mediated Insect Resistance in Corn and Sorghum [PhD. thesis].University of Ottawa, Ottawa.

Rani L., Thapa K., Kanojia N., Sharma N., Singh S., Grewal A.S., Srivastav A.L., Kaushal J. (2021): An extensive review on the consequences of chemical pesticides on human health and environment. Journal of Cleaner Production, 283: 124657.

Salunke B., Kotkar H., Mendki P., Upasani S., Maheshwari V. (2005): Efficacy of flavonoids in controlling *Callosobruchus chinensis* (L.) (Coleoptera: Bruchidae), a post-harvest pest of grain legumes. Crop Protection, 24: 888–893.

Santos-Sánchez N.F., Salas-Coronado R., Hernández-Carlos B., Villanueva-Cañongo C. (2019): Shikimic acid pathway in biosynthesis of phenolic compounds. Plant Physiological Aspects of Phenolic Compounds, 1: 1–15.

Sharma H., Norris D.M. (1991): Chemical basis of resistance in soya bean to cabbage looper, *Trichoplusia ni*. Journal of the Science of Food and Agriculture, 55: 353–364.

Sharma N., Singhvi R. (2017): Effects of chemical fertilisers and pesticides on human health and environment: A review. International Journal of Agriculture, Environment, and Biotechnology, 10: 675–680.

Shen N., Wang T., Gan Q., Liu S., Wang L., Jin B. (2022): Plant flavonoids: Classification, distribution, biosynthesis, and antioxidant activity. Food Chemistry, 383: 132531.

https://doi.org/10.17221/56/2025-PPS

Shonouda M., Farrag R., Salama O. (2000): Efficacy of the botanical extract (myrrh), chemical insecticides and their combinations on the cotton leafworm, *Spodoptera littoralis* boisd (Lepidoptera: Noctuidae). Journal of Environmental Science & Health Part B, 353: 347–356.

Simmonds M.S. (2001): Importance of flavonoids in insect–plant interactions: feeding and oviposition. Phytochemistry, 56: 245–252.

Simmonds M.S. (2003): Flavonoid–insect interactions: recent advances in our knowledge. Phytochemistry, 64: 21–30.

Stafford H. (1974): Possible multienzyme complexes regulating the formation of C6-C3 phenolic compounds and lignins in higher plants. In: Runeckles V.C., Conn E.E. (eds): Recent Advances in Phytochemistry, Academic Press New York, 8: 53–79.

Stenberg J.A., Heil M., Åhman I., Björkman C. (2015): Optimising crops for biocontrol of pests and disease. Trends in Plant Science, 20: 698–712.

Suganthy M., Sakthivel P. (2013): Field evaluation of biopesticides against tobacco caterpillar, *Spodoptera litura* Fab. infesting *Gloriosa superba* (Linn.). Journal of Biopesticides, 6: 90.

Thaler J.S., Bostock R.M. (2004): Interactions between abscisic-acid-mediated responses and plant resistance to pathogens and insects. Ecology, 85: 48–58.

Tiwari A.K. (2024): IPM Essentials: Combining biology, ecology, and agriculture for sustainable pest control. Journal of Advances in Biology & Biotechnology, 27: 39–47.

Treutter D. (2005): Significance of flavonoids in plant resistance and enhancement of their biosynthesis. Plant Biology, 7: 581–591.

Treutter D. (2006): Significance of flavonoids in plant resistance: A review. Environmental Chemistry Letters, 4: 147–157.

Vihakas M. (2014): Flavonoids and Other Phenolic Compounds: Characterisation and Interactions with Lepidopteran and Sawfly Larvae [PhD. thesis]. University of Turku, Turku.

Wang L., Chen M., Lam P.-Y., Dini-Andreote F., Dai L., Wei Z. (2022a): Multifaceted roles of flavonoids mediating plant-microbe interactions. Microbiome, 10: 1–13.

Wang L., Xu D., Yang Y., Liu W., Cong S., Li W., Yang N., Yin H., et al. (2024): Impact of rutin on growth, development and oviposition of Bt-susceptible and Bt-resistant pink bollworm. Entomological Research, 54: e12702.

Wang Q., Liu X., Liu H., Fu Y., Cheng Y., Zhang L., Shi W., Zhang Y., et al. (2022b): Transcriptomic and metabolomic analysis of wheat kernels in response to the feeding of orange wheat blossom midges (*Sitodiplosis mosellana*) in the field. Journal of Agricultural and Food Chemistry, 70: 1477–1493.

Wang Z., Zhao Z., Cheng X., Liu S., Wei Q., Scott I.M. (2016): Conifer flavonoid compounds inhibit detoxification enzymes and synergise insecticides. Pesticide Biochemistry and Physiology, 127: 1–7.

War A.R., Paulraj M.G., Ahmad T., Buhroo A.A., Hussain B., Ignacimuthu S., Sharma H.C. (2012): Mechanisms of plant defense against insect herbivores. Plant Signaling & Behavior, 7: 1306–1320.

Watkins J.M., Hechler P.J., Muday G.K. (2014): Ethylene-induced flavonol accumulation in guard cells suppresses reactive oxygen species and moderates stomatal aperture. Plant Physiology, 164: 1707–1717.

Williams J.S., Thomas M., Clarke D.J. (2005): The gene stlA encodes a phenylalanine ammonia-lyase that is involved in the production of a stilbene antibiotic in *Photorhabdus luminescens* TT01. Microbiology, 151: 2543–2550.

Winkel-Shirley B. (2001): Flavonoid biosynthesis. A colorful model for genetics, biochemistry, cell biology, and biotechnology. Plant Physiology, 126: 485–493.

Woch N., Laha S., Gudipalli P. (2023): Salicylic acid and jasmonic acid induced enhanced production of total phenolics, flavonoids, and antioxidant metabolism in callus cultures of *Givotia moluccana* (L.) Sreem. *In Vitro* Cellular & Developmental Biology - Plant: 1–22.

Wohl J., Petersen M. (2020): Functional expression and characterisation of cinnamic acid 4-hydroxylase from the hornwort Anthoceros agrestis in *Physcomitrella* patens. Plant Cell Reports, 39: 597–607.

Zain W., Hamid N., Nazihah N., Izzah N., Azaman N., Ramli N., Yamin B., Musa S. (2022): Phytochemical screening, total phenolic and flavonoid content of jupiter variety leaves extract and their antioxidant and insecticidal activity. IOP Conference Series: Earth and Environmental Science, IOP Publishing, Cham.

Zhang K.-X., Li H.-Y., Quandahor P., Gou Y.-P., Li C.-C., Zhang Q.-Y., Haq I. U., Ma Y., et al. (2022): Responses of six wheat cultivars (*Triticum aestivum*) to wheat aphid (Sitobion avenae) infestation. Insects, 13: 508.

Zhao A., Li Y., Leng C., Wang P., Li Y. (2019): Inhibitory effect of protease inhibitors on larval midgut protease activities and the performance of *Plutella xylostella* (Lepidoptera: Plutellidae). Frontiers in Physiology, 9: 1963.

Zhao W., Zhuang Y., Chen Y., Lou Y., Li R. (2023): Enhanced chemical and physical defense traits in a rice cultivar showing resistance to leaffolder infestation. Crop Health, 1: 10.

Zhou Y.-S., Hao P.-Y., Yu X.-P. (2011): Flavonoids in rice: Ultrasonic extraction and its insecticidal effect on the brown planthopper *Nilaparvata lugens* Stål. 2011 IEEE International Symposium on IT in Medicine and Education.

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