



Valorization of horticultural by-products as sources of natural agents for biological control of disease vectors



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ABSTRACT

Synthetic pesticides are widely used for disease vector control, but their repeated application poses risks to human health, environmental quality, non-target organisms, and may contribute to pesticide resistance. These limitations have increased the need for safer, sustainable, and locally available alternatives. Horticultural wastes, including fruit peels, seeds, pulp, leaves, pruning residues, and processing by-products, represent an abundant and underutilized source of bioactive compounds with potential for vector management. However, existing evidence is fragmented across different waste sources, bioactive constituents, target vectors, mechanisms of action, and application technologies, highlighting the need for an integrated assessment of their potential and practical limitations. This review synthesizes current knowledge on horticultural by-products as natural vector-control agents, with emphasis on their bioactive compounds, mechanisms of action, efficacy, extraction and formulation technologies, environmental considerations, and future applications. Citrus wastes have received considerable attention because of their strong larvicidal activity associated with limonene, citral, and other terpenoids. Pomegranate peel, mango waste, grape pomace, and garlic residues also show promising activities due to their polyphenols, tannins, sulfur-containing compounds, and other metabolites. The review further identifies key research gaps, including the need for standardized extraction and formulation methods, field validation, safety assessment, and evaluation of long-term efficacy. Finally, region-specific utilization of horticultural and agricultural residues is proposed as a promising strategy for developing sustainable and economically viable vector-control products while supporting waste valorization and circular bioeconomy approaches.

Keywords: botanical insecticide, essential oils, green extraction, limonoids, nanoformulation, vector-borne diseases.

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Introduction

Vector-borne diseases such as malaria, dengue, chikungunya, Zika, lymphatic filariasis, and yellow fever continue to pose significant global health challenges. Mosquitoes belonging to the genera *Aedes*, *Anopheles*, and *Culex* remain the primary vectors responsible for transmitting these pathogens (23). Conventional vector management programs rely heavily on synthetic insecticides; however, extensive use of these chemicals has resulted in resistance development, environmental contamination, and adverse effects on non-target organisms (45, 33). Simultaneously, horticultural industries generate substantial quantities of by-products during harvesting, processing, storage, and marketing

operations. Fruit peels, seeds, pomace, leaves, stems, and pruning residues are often discarded despite containing valuable bioactive compounds. The concept of valorization involves converting these agricultural wastes into value-added products. In recent years, increasing attention has focused on utilizing horticultural by-products as sources of botanical insecticides and mosquito control agents (38).

1. Horticultural By-Products as Reservoirs of Bioactive Compounds

Horticultural residues contain a broad spectrum of secondary metabolites that play defensive roles in plants and possess insecticidal activities (20).

Major groups include below compounds:

1.1. Phenolic Compounds

Fruit peels and pomaces from grapes, pomegranates, apples, berries, and citrus fruits are rich in phenolic acids and flavonoids. These compounds may interfere with larval metabolism, feeding behavior, and oxidative balance (20, 1).

1.2. Terpenoids

Terpenes such as limonene, thymol, carvacrol, linalool, and α -humulene exhibit strong larvicidal and repellent activities against mosquito vectors (39).

1.3. Essential Oils

Essential oils from citrus peels, mint, basil, rosemary, and other horticultural wastes contain volatile compounds such as limonene, linalool, citral, α -pinene, β -pinene, thymol, and carvacrol. These compounds exhibit larvicidal and repellent activities mainly by disrupting neurotransmission, inhibiting acetylcholinesterase, affecting octopamine receptors and ion channels, and inducing oxidative stress. Their multiple modes of action may contribute to broad-spectrum activity against mosquito vectors (1, 3, 7, 17, 18, 35, 39).

1.4. Alkaloids

Alkaloids are nitrogen-containing secondary metabolites with important insecticidal potential. Compounds such as nicotine, caffeine, quinine, quinidine, and berberine can interfere with insect neurotransmission, acetylcholine receptors, ion channels, and metabolic processes, resulting in paralysis, mortality, or developmental disruption. Their concentration varies among plant species and tissues, highlighting the importance of chemical characterization of horticultural wastes (1, 20, 25).

1.5. Limonoids

Limonoids are highly oxygenated tetranortriterpenoids found particularly in citrus and other horticultural residues. Important limonoids include limonin and related compounds that exhibit insect growth-regulating, antifeedant, and developmental effects. These compounds can interfere with endocrine pathways involved in molting and metamorphosis, particularly the ecdysteroid and juvenile-hormone systems. Consequently, exposure may result in delayed larval development, abnormal molting, impaired pupation, reduced adult emergence, and decreased reproductive fitness. The growth-

regulating activity of limonoids complements the rapid toxic effects of many essential-oil constituents, making citrus wastes particularly promising sources of multifunctional botanical vector-control agents (20, 24, 30).

2. Major Horticultural By-Products with Vector Control Potential

2.1. Citrus Processing Wastes

Citrus fruits are among the most extensively cultivated horticultural crops worldwide, generating large quantities of peel residues during juice and food processing. Citrus peels contain a diverse array of bioactive compounds, including limonene, citral, linalool, β -pinene, flavonoids, and limonoids. These compounds exhibit insecticidal, larvicidal, repellent, and growth-regulating activities against disease vectors. Several studies have demonstrated that essential oils extracted from orange (*Citrus sinensis*), lemon (*Citrus limon*), and grapefruit (*Citrus paradisi*) peels are highly toxic to larvae of *Aedes aegypti*, *Anopheles stephensi*, and *Culex quinquefasciatus* (35, 28, 13, 32, 20). The biological activity of citrus-derived compounds is primarily associated with monoterpenes that disrupt neural transmission and interfere with respiratory processes in mosquito larvae. Limonene has been reported to penetrate the insect cuticle, causing paralysis and mortality, while limonoids act as insect growth regulators by disrupting molting and metamorphosis. In addition, citrus extracts may function as oviposition deterrents, reducing mosquito breeding in treated habitats (24, 33, 7, 21).

2.2. Grape Pomace

Grape pomace, consisting of skins, seeds, and stems remaining after juice and wine production, is among the largest agro-industrial residues generated worldwide. It contains high concentrations of resveratrol, catechins, anthocyanins, proanthocyanidins, and phenolic acids. These compounds possess biological activities that may negatively affect insect survival and development (44, 36, 10).

Recent studies suggest that grape-derived phenolics induce oxidative stress and impair cellular metabolism in insects. Although direct mosquito control applications remain relatively limited compared with citrus and neem products, preliminary evidence indicates substantial potential for the development of novel vector

management tools based on grape processing residues (9, 34).

2.3. Pomegranate Peels

Pomegranate (*Punica granatum*) processing generates considerable quantities of peel waste, representing approximately 30–40% of the fruit weight. The peel contains substantial amounts of ellagic acid, punicalagin, gallic acid, tannins, and flavonoids. These compounds possess strong antioxidant and insecticidal properties and have shown activity against mosquito larvae and other insect pests. Several studies have demonstrated significant larval mortality following exposure to pomegranate peel extracts, particularly against *Aedes aegypti* and *Culex quinquefasciatus* (16, 46, 42). The mode of action of pomegranate-derived phytochemicals is thought to involve oxidative stress induction, disruption of digestive enzyme activity, and interference with larval metabolism. Furthermore, the synergistic effects among polyphenols and tannins may enhance toxicity while reducing the likelihood of resistance development. Such characteristics make pomegranate waste an attractive source of environmentally compatible bio-pesticides (14, 24, 9).

2.4. Mango Seed Kernels and Peels

The mango (*Mangifera indica*) industry generates substantial quantities of peels and kernels, accounting for approximately 35–60% of the fruit biomass. Mango residues are rich in mangiferin, quercetin, catechins, tannins, and gallic acid derivatives. These compounds have attracted considerable attention because of their antimicrobial, antioxidant, and insecticidal properties. Several laboratory investigations have reported significant larvicidal activity of mango peel and kernel extracts against *Aedes aegypti*, *Anopheles stephensi*, and *Culex quinquefasciatus* (3, 41, 43, 34).

Research indicates that mangiferin and associated phenolic compounds can interfere with insect digestive physiology, alter feeding behavior, and inhibit larval development. In addition, mango waste extracts may induce oxidative stress and disrupt endocrine pathways involved in insect growth regulation. These multiple mechanisms may contribute to improved effectiveness and reduced resistance development (24, 7, 20).

2.5. Avocado Wastes

Avocado (*Persea americana* Mill.) seeds and peels contain bioactive compounds such as phenolic acids, flavonoids, tannins, proanthocyanidins, and fatty acid derivatives. Compounds including catechin, epicatechin, chlorogenic acid, gallic acid, and caffeic acid may contribute to insecticidal activity through oxidative stress, disruption of digestive and metabolic enzymes, impairment of cellular membranes, and interference with nutrient utilization. Recent screening studies have reported insecticidal potential of avocado seed and peel extracts, although their activity against specific mosquito vectors remains less extensively investigated than that of citrus and *Allium* wastes (27).

2.6. Onion and Garlic Processing Wastes

Onion (*Allium cepa*) skins and garlic (*Allium sativum*) residues contain sulfur-containing compounds such as allicin, diallyl sulfides, and flavonoids including quercetin. These compounds have demonstrated insecticidal, antimicrobial, and repellent properties against a wide range of insect pests and mosquito vectors. Extracts from onion and garlic wastes have shown larvicidal effects against *Aedes* and *Culex* species under laboratory conditions (26, 22, 8, 35).

The insecticidal activity of *Allium*-derived compounds may involve multiple mechanisms, including modification of sulfhydryl-containing proteins, inhibition of essential enzymes, disruption of cellular respiration and membrane integrity, and induction of oxidative stress. Quercetin and related flavonoids may additionally interfere with digestive and detoxification enzymes, while volatile sulfur compounds can contribute to fumigant and repellent effects by affecting insect chemosensory and host-seeking behavior. However, efficacy may vary with waste type, extraction method, compound stability, and target species, emphasizing the need for standardized extraction, formulation, safety, and field-efficacy studies (32, 24, 34).

3. Mechanisms of Action of Horticultural Waste-Derived Bioactive Compounds Against Disease Vectors

Botanical compounds derived from horticultural wastes affect vectors through multiple pathways. The effectiveness of

horticultural by-products as vector control agents is largely attributed to the diverse phytochemicals present in fruit and vegetable residues. Unlike conventional insecticides that often act through a single target site, plant-derived compounds possess multiple modes of action, thereby reducing the probability of resistance development. Secondary metabolites such as terpenoids, flavonoids, alkaloids, tannins, phenolic acids, limonoids, and sulfur-containing compounds can affect various physiological and biochemical processes in insects (25, 35, 34, 7).

Neurotoxicity

Many terpenoids inhibit acetylcholinesterase activity, resulting in paralysis and mortality of mosquito larvae (39). Many phytochemicals isolated from horticultural wastes exhibit neurotoxic effects against mosquito larvae and adults. Monoterpenes such as limonene, linalool, citral, eugenol, and thymol interfere with neurotransmission by affecting octopamine receptors, acetylcholinesterase activity, and ion channels. Essential oils derived from citrus peels and other horticultural residues can induce paralysis, loss of coordination, and eventual mortality in mosquito larvae. Such effects are particularly important because octopamine receptors are absent in vertebrates, providing selective toxicity toward insects (17, 32, 35, 20). Several studies have demonstrated significant inhibition of acetylcholinesterase activity in *Aedes aegypti* and *Culex quinquefasciatus* following exposure to plant-derived essential oils. Acetylcholinesterase inhibition results in accumulation of acetylcholine at synaptic junctions, causing overstimulation of the nervous system and eventual death. Similar mechanisms have been reported for citrus peel oils rich in limonene and linalool (37, 24, 9).

Growth Regulation

Certain phytochemicals interfere with molting hormones and developmental processes, preventing successful metamorphosis (20). Numerous phytochemicals found in horticultural by-products function as insect growth regulators. Limonoids present in citrus peels interfere with ecdysteroid and juvenile hormone pathways that regulate molting and metamorphosis. Exposure to these compounds can result in delayed development, abnormal pupation, malformed adults, and reduced emergence rates (30, 25, 34).

Mango seed kernels and peels contain mangiferin and related phenolic compounds that have also been reported to affect larval development. Similar observations have been reported for pomegranate peel extracts rich in hydrolyzable tannins. These compounds may disrupt endocrine regulation, thereby reducing reproductive fitness and population growth of mosquito vectors (41, 7).

Respiratory Disruption

Essential oil constituents may impair mitochondrial function and energy production in larvae (39). Phenolic compounds present in grape pomace, pomegranate peels, apple pomace, and onion skins may induce oxidative stress in mosquito larvae. Excessive production of reactive oxygen species (ROS) damages proteins, lipids, and nucleic acids, ultimately leading to cellular dysfunction and mortality. Research has shown that exposure to plant-derived phenolics can significantly alter antioxidant enzyme activities, including catalase, superoxide dismutase, and Glutathione-S-transferase (14, 44, 36). Recent investigations suggest that oxidative stress induction may act synergistically with neurotoxic and endocrine-disrupting mechanisms. Such multifaceted actions could explain the broad-spectrum effectiveness observed in many botanical extracts derived from horticultural wastes (9, 20).

Oxidative Stress

Phenolics and related compounds can induce oxidative imbalance, cellular damage, and mortality (20).

4. Green Extraction Technologies

Efficient recovery of bioactive compounds is essential for converting horticultural wastes into commercially viable natural vector-control products. Green extraction technologies aim to improve compound recovery while reducing solvent use, energy consumption, processing time, and degradation of sensitive phytochemicals. These approaches are particularly useful for recovering phenolics, flavonoids, terpenoids, and other bioactive compounds from horticultural residues (17).

Ultrasound-Assisted Extraction

Ultrasound-assisted extraction (UAE) enhances phytochemical recovery through acoustic cavitation. The formation and collapse of

microscopic bubbles generate shear forces and microjets that disrupt plant cell walls, increase tissue permeability, and improve mass transfer between the plant matrix and solvent. UAE can therefore increase extraction efficiency while reducing solvent consumption and processing time. Its performance depends on ultrasound power, frequency, temperature, solvent composition, and extraction time; excessive treatment may degrade sensitive compounds. UAE is particularly promising for recovering phenolics, flavonoids, and terpenoids from horticultural wastes (38).

Microwave-Assisted Extraction

Microwave-assisted extraction (MAE) uses electromagnetic energy to rapidly heat plant tissues through molecular rotation and ionic conduction. This internal heating increases cellular pressure and promotes cell-wall disruption, facilitating the release and diffusion of phytochemicals into the solvent. MAE can provide rapid extraction with lower solvent consumption and high recovery of phenolic and flavonoid compounds. However, microwave power and extraction time must be carefully optimized to prevent thermal degradation of sensitive compounds (38).

Supercritical Fluid Extraction

Supercritical CO₂ extraction is an environmentally favorable method for selectively recovering essential oils, terpenoids, and other lipophilic bioactive compounds from horticultural wastes. Above its critical point, CO₂ combines high diffusivity with effective solvating properties, facilitating penetration into plant tissues and efficient extraction. Pressure and temperature can be adjusted to control selectivity, while CO₂ can be readily removed by depressurization, leaving minimal solvent residues. However, relatively high equipment and operating costs may limit large-scale application (15).

5. Nanotechnology-Based Formulations

Recent studies have combined plant-derived compounds with nanotechnology to improve efficacy and stability. Plant-extract-mediated nanoparticles have demonstrated enhanced larvicidal activity against *Aedes* mosquitoes compared with crude extracts alone (31). Nano-emulsions prepared from essential oils increase bioavailability and prolong field persistence

while reducing required dosages (18).

6. Environmental and Economic Benefits

6.1. Advantages

The valorization of horticultural by-products for vector control supports circular economy and circular bioeconomy principles by converting low-value residues into value-added products while reducing waste disposal and environmental pollution (38). Fruit and vegetable processing generates large quantities of peels, seeds, pomace, and pruning residues, and their conversion into botanical vector-control agents can reduce landfill waste and associated greenhouse gas emissions (19, 30).

Botanical insecticides derived from horticultural wastes are generally biodegradable and may have lower environmental persistence and reduced toxicity toward non-target organisms than many conventional synthetic insecticides. This characteristic may reduce risks to beneficial insects, aquatic organisms, and other non-target species, although safety must be evaluated for each extract and formulation (45, 24, 7, 34).

From an economic perspective, horticultural residues provide relatively inexpensive and locally available raw materials for developing botanical insecticides. Their utilization by juice, wine, canning, and fresh-produce industries can create additional revenue streams, reduce waste-management costs, and support local bio-based industries. This approach may be particularly valuable in regions where vector-borne diseases are prevalent and resources for vector management are limited (10, 40, 12).

6.2. Challenges

Despite their potential, several challenges limit the large-scale commercialization of horticultural waste-derived vector-control products. The phytochemical composition of plant residues can vary considerably according to cultivar, geographical origin, growing conditions, maturity, and processing methods, making standardization, reproducibility, and quality control difficult (12). In addition, most available studies have been conducted under laboratory conditions using crude extracts, whereas field validation remains limited. Environmental factors such as temperature, ultraviolet radiation, rainfall, and water chemistry may substantially influence efficacy under natural conditions, emphasizing the need for large-scale field trials (4, 34).

Advanced formulation technologies, including nano-emulsions, polymeric nanoparticles, and liposomal systems, offer potential solutions by improving the stability, controlled release, and residual activity of botanical compounds. However, their economic feasibility, environmental safety, and scalability require further investigation (5, 11, 21). Future research should also examine synergistic interactions among bioactive compounds from different horticultural residues and employ metabolomics, transcriptomics, and molecular approaches to clarify mechanisms of action and identify the most effective compound combinations (24, 20).

Conclusion

Horticultural by-products represent promising and sustainable sources of natural agents for disease-vector management. Citrus wastes are currently among the most extensively studied and consistently effective materials, while pomegranate peels, mango residues, grape pomace, and onion and garlic wastes provide additional sources of bioactive compounds with larvicidal, repellent, and growth-regulating activities. Their valorization can simultaneously contribute to vector control and sustainable waste management within a circular bioeconomy framework.

However, most available evidence remains based on laboratory-scale studies, and variations in phytochemical composition, extraction methods, formulation, and environmental conditions limit direct comparison and practical application. Future research should therefore prioritize standardized extraction and characterization, field validation, toxicological and non-target assessments, formulation stability, and economic feasibility. Advances in green extraction and formulation technologies may facilitate the development of effective, environmentally responsible, and commercially viable vector-control products from horticultural residues (20).

Author's contribution

Parts 1, 2, and 3 of the article were written by Dr. Fatemeh Bidarnamani, parts 4 and 5 by Dr. Mohammad Forouzandeh, and part 6 and the discussion were written by Dr. Maryam Kamali.

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Artificial intelligence (AI)-assisted technology

In this article, artificial intelligence has only been used to provide general information about the benefits of polyphenols, approximately 20%.

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