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REVIEW ARTICLE

Harnessing essential oils as neurotoxic biopesticides against stored product pests

S Paripoorani[1], M Shanthi[2*], M Murugan[1], N Senthil[3], S Haripriya[4], M Jayakanthan[5] & N Vijayakumari[1]

[1]Department of Agricultural Entomology, Agricultural College and Research Institute, Tamil Nadu Agricultural University, Coimbatore 641 003, India
[2]Directorate of Centre for Plant Protection Studies, Tamil Nadu Agricultural University, Coimbatore 641 003, India
[3]Directorate of Centre for Plant Molecular Biology and Biotechnology, Tamil Nadu Agricultural University, Coimbatore 641 003, India
[4]Department of Vegetable Science, Horticultural College and Research Institute, Tamil Nadu Agricultural University, Coimbatore 641 003, India
[5]Department of Plant Molecular Biology and Bioinformatics, Agricultural College and Research Institute, Tamil Nadu Agricultural University, Coimbatore 641 003, India

*Correspondence email - mshanthiento@tnau.ac.in

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Abstract

The search for sustainable solutions in pest management, particularly for stored-product pests, has accelerated due to growing concerns about food safety, environmental contamination and the development of resistance to synthetic pesticides. Essential oils (EOs), extracted from aromatic plants, possess strong neurotoxic properties and offer ecological safety. These attributes contribute to their significant potential as natural biopesticides. The review highlights current insights into the neurotoxic mechanisms of EOs, particularly their interactions with acetylcholinesterase (AchE), octopaminergic receptors, ion channels and other critical components of insect nervous systems. The efficacy of various EOs against key storage pests such as *Sitophilus* spp., *Tribolium* spp. and *Callosobruchus* spp. is discussed, highlighting their fumigant, contact and repellent activities. Despite their potential, their actual usage is limited due to several issues, including volatility, inconsistent chemical composition and limited residual activity. To address these obstacles, advancements in standardization, molecular understanding and formulation technologies are necessary. The review also emphasizes regulatory challenges and outlines future research directions for integrating EO-based neurotoxic agents into sustainable post-harvest pest management strategies. In conclusion, EOs offer a viable and environmentally sustainable approach to protecting agricultural commodities.

Keywords: biopesticides; essential oils; neurotoxin; pest management; storage pest

Introduction

Essential oils (EOs), also known volatile or ethereal oils, are complex natural mixtures derived from aromatic plants. These oils are made up of volatile compounds that plants produce as secondary metabolites (1). Globally, there are over 17500 species of aromatic plants, mostly found in tropical areas and over 3000 of their chemical components have been identified to date (2). Approximately 300 essential oils have been utilized commercially, primarily in pharmaceuticals, cosmetics, perfumery and pest control. The main structural components of essential oils-phenolic compounds, monoterpenes and sesquiterpenes-play distinct functional roles: phenolics are primarily responsible for antimicrobial and antioxidant activities, monoterpenes contribute to high volatility and rapid insecticidal action, while sesquiterpenes are associated with longer-lasting effects and lower volatility (3). Plants, bacteria, viruses, fungi and even worms are all natural sources of biopesticides, which have unique biological features. Among these, plant-derived biopesticides are increasingly favoured in integrated pest management systems to minimize the presence of synthetic chemical residues in the food supply chain. Research indicates that only around 10 % of traditional chemical pesticides are successful at controlling pests; the other 90 % remain in the environment and may contaminate human resources through runoff and leaching. In light of this, recent scientific attention has switched to sustainable agriculture practices, with biopesticides emerging as promising options to reducing chemical pesticide burdens in soils (4).

Bioactive compounds in essential oils affecting the nervous system

The use of EOs in pest control has two advantages: first, their low toxicity on mammals, birds and fish, which translates into safer products; and second, the great structural diversity of their components, making them a potential source of multi-target bioactive molecules (5). EOs are complex blends of bioactive compounds, primarily composed of monoterpenes, sesquiterpenes and their oxygenated derivatives, contributing to their diverse biological activities (6, 7). Most notably, citronellal, geraniol, limonene, 1,8-cineole and eugenol are active compounds that frequently occurring (8). Monoterpenes, which are lipophilic liquids with high volatility, are common secondary metabolites in plants. Hydrodistillation or solvent extraction isolates EOs from aromatic plants.

Essential oils (EOs) exhibit insecticidal activity through multiple biochemical pathways. These include neurotoxic actions such as disrupting synaptic transmission involving gamma-aminobutyric acid (GABA), inhibiting the function of acetylcholinesterase, altering the octopaminergic signaling system and suppressing the activity of cytochrome P450 enzymes (9). Bioactive compounds, such as terpenes, phenols and aldehydes, interact with neurotransmitter systems and modulate ion channels, thereby exerting profound effects on the insect nervous system. Consequently, EOs exhibit multiple insecticidal actions, including ovipositional deterrents, larvicidal effects, fumigant toxicity, repellency and antifeedant activity.

The unique toxic effects of the vapours of compounds present in EOs against stored product insects cause fumigant toxicity. In the case of *Sitophilus oryzae*, pulegone (LC_{50} = 0.70 µL/L), borneol (0.1 µL/720 mL), citral (LC_{50} = 7.75 mL/L) and 1,8-cineole (LC_{50} = 14.19 mg/L) caused 100 % mortality (10, 11). Similarly, linalool (LC_{50} = 0.016 mg/cm^3), limonene (LC_{50} = 0.122 mg/cm^3), α-pinene (LC_{50} = 0.264 mg/cm^3) and β-myrcene (LC_{50} = 0.274 mg/cm^3) were found to be potent effective fumigants against *Sitophilus zeamais*.

***Eucalyptus dundasii* EO**: Strong fumigant and repellent activity against *O. surinamensis*; antifeedant against *R. dominica*; attributed to 1,8-cineole (12).

***Artemisia annua* EO**: Highly repellent to *T. castaneum* and *L. serricorne*, exceeding DEET; due to α-caryophyllene and α-pinene (13).

***A. princeps* + *C. camphora* EOs**: Enhanced repellency against *S. oryzae* through synergistic interaction (14).

***Carum copticum* EO**: Potent fumigant, ovicidal and larvicidal action on C. maculatus; linked to monoterpenoid neurotoxins (15).

***Vitex pseudo-negundo* EO**: Similar effects on *C. maculatus*, though less active than *C. copticum* (15).

***Alpinia katsumadai* EO**: Strong contact toxicity and repellency against *T. castaneum*, *L. bostrychophila* and *L. serricorne*; due to methyl cinnamate (16).

***Cymbopogon citratus* EO**: Effective contact and fumigant toxicity against P. truncatus, causing 95 % mortality within 48 hr (17).

EOs have been extensively evaluated for their repellent properties, particularly against coleopteran storage pests. Limonene and menthol exhibited 83.3 % and 78 % repellency, respectively, against S. oryzae at doses of 75 µL/cm^2 and 0.353 µg/cm^2 (18, 19). Carvacrol and geraniol exhibited higher repellency against *R. dominica*, with 96 % and 92 % repellency at 12.5 and 25 µg/cm^2, respectively. Geraniol showed the highest repellent effect against *L. serricorne* (94.0 % repellence at 50.0 µg/cm^2) (20). Additionally, β-pinene induced 52.0% repellence at 0.63 µL/cm^2 (21). The toxicity of the EOs against storage pests and the main bioactive compounds in EOs are listed in Table 1.

Overall, these findings highlight the promise of EOs as natural alternatives for managing stored-product pests via neurotoxic mechanisms. However, further research is essential to address challenges related to formulation, stability, standardization and field efficacy.

Mechanisms of action of essential oils on insect neural pathways

Due to their well-known insecticidal properties, monoterpenoids such as menthol, citronellal, linalool and D-limonene are frequently used in commercial formulations as insecticides or insect repellents. The bioactivity of EOs largely stems from their mono- and sesquiterpenes components, which can target critical insect molecular receptors, including the Methoprene-tolerant receptor (MET), Juvenile Hormone Binding Protein (JHBP) and the Octopamine receptor (36).

Monoterpenes exert their insecticidal effects through multiple neurophysiological pathways. Their neurotoxicity has been attributed to interfering with key targets, including acetylcholinesterase (AChE), gamma-aminobutyric acid (GABA) receptors, octopaminergic receptors, voltage-gated sodium channels and glutamate-gated chloride channels (37, 38). In addition to disrupting neural function, monoterpenes inhibit detoxification enzymes, such as glutathione-S-transferase and

Table 1. Toxicity of essential oils and their bioactive compounds against storage pests

Essential oil	Major bioactive compounds	Insect pests	Reference
Eucalyptus sp	1,8-cineole	*S. zeamais*	(22)
Ocimum basilicum	Linalool, methyl chavicol, Linalool and estragole	*S. zeamais*	(23, 24)
Citrus aurantifolia	(S)-Limonene	*S. zeamais*	(25)
Mentha piperita	Menthol	*S. oryzae*	(26)
Rosmarinus officinalis	α-pinene	*S. oryzae*	(26)
Ocimum tenuiflorum	Eugenol	*S. oryzae*	(27)
Melaleuca bracteata	Methyl eugenol	*S. oryzae*	(28)
Syzygium aromaticum	Eugenol	*S. oryzae*	(29)
Ocimum basilicum	Linalool and estragole	*R. dominica*	(30)
Mentha spicata	Menthol, isomenthone and menthyl acetate	*R. dominica*	(30)
Citrus aurantium	Limonene and myrcene	*R. dominica*	(30)
Myristica fragrans	Eugenol, methylisoeugenol, methyleugenol	*L. serricorne*	(31)
Elsholtzia ciliata	Limonene, *β*-ocimene, Carvone	*L. serricorne*	(32)
Bupleurum bicaule	trans-2-isopropyl bicyclo [4.3.0] non-3-en-8-one, 4,5-dimethyl-1,2,3,6,7,8,8a,8b- octahydrobiphenylene and 1,4-dimethoxy-2-tert-butylbenzene	*L.serricorne* and *L. bostrychophila*	(33)
Tetradium ruticarpum	3-carene	*L. serricorne*	(34)
Artemisia lavandulaefolia	Chamazulene, 1,8-cineole and β-caryophyllene	*L. serricorne*	(35)

cytochrome P450 and interfere with growth regulation and metabolic processes essential for insect survival (39, 40).

Insect acetylcholinesterase (AChE) differs from its mammalian counterpart by a unique cysteine residue, making it a promising target for selective insecticides with minimal risk to non-target vertebrates (41). Research indicates that their symptoms on pests were similar to those of organophosphate and carbamate insecticides, suggesting that AChE could be the primary target for monoterpenes. Around 28 chemicals were evaluated for their effect on insect AChE and 23 of them inhibited the enzyme. α-pinene, β-pinene, β-phellandrene, carvacrol, limonene, menthol, menthone, 1,8-cineole, cis-ocimene and niloticin were the most effective among them (42).

Eleven monoterpenes had an inhibitory effect on the activity of AChE of *T. castaneum* and *S. oryzae* (11). Many essential oil components inhibit AChE; however, they have lower potency than synthetic inhibitors (42). Similarly, crucial oil-based compounds have shown promise as anticholinesterase insecticides (43). The essential oil of *Lippia turbinata* contributes to the mortality of bruchid pests and efficiently inhibits AChE in vitro. Cuminaldehyde 1,8-cineole and (-) limonene were the most successful inhibitors of *S. oryzae* (44). Phytol has neurotoxic effects on the nervous system of insects, mainly via inhibiting the activity of acetylcholinesterase (AChE) (45). Moreover, researches indicates that phytol disrupts the usual growth cycle and impedes normal insect development. Additionally, retinol and phytol disrupt insect growth cycled, significantly prolonging the larval stage and causing developmental delays (46).

Several EO components, such as thymol, carvacrol and eugenol, modulate the GABAergic system, which regulates C^{1-} ion flow in inhibitory synapses. This modulation affects membrane hyperpolarisation, leading to either excessive inhibition or disinhibition, which disrupts the nervous system. Thus, EOs alter GABA ion channels as part of their neurotoxic mechanism (47). Insecticidal properties of various EOs suggest that their mode of action often involves disruption of neural signalling, possibly by interfering with GABA receptors (48). The role of GABAergic pathways in the efficacy of EOs was emphasized, with a call for further electrophysiological research to clarify their specific receptor-binding mechanisms (49). In the housefly, carvacrol, pulegone and thymol were shown to modulate GABA receptors (50).

EOs such as eugenol, α-terpineol and cinnamic alcohol have been shown to increase heart rate and cAMP levels at specific doses, binding to octopamine receptors, altering normal neural signalling and causing hyperactivity, paralysis and death (51). EOs elevate intracellular cAMP and calcium levels, indicating octopaminergic modulation that supports their role as bioinsecticides (42). Exposure to EO from *M. alternifolia* caused mitochondrial dysfunction and neurotoxicity in *S. zeamais* (52). Detailed evidence was provided on how essential oil components, particularly monoterpenes, act on voltage-gated sodium channels (53). Other neural targets include the GABA receptor, the octopamine receptor, the tyramine receptor and the nicotinic acetylcholine receptor (nAChR). Among these, GABA remains the primary inhibitory neurotransmitter in the insect nervous system.

Challenges and limitations of essential oils as neurotoxic biopesticides

EOs limitations and difficulties as neurotoxic biopesticides Although EOs are considered environmentally friendly alternatives to synthetic pesticides, several challenges limit their widespread adoption in pest control. Reduced residual activity and short-term efficacy in storage conditions are frequently the result of their high volatility and vulnerability to deterioration upon exposure to light, heat and oxygen (54). Furthermore, depending on the type of plant, the region of origin and the extraction technique, the chemical makeup of EOs can differ greatly, resulting in inconsistent insecticidal efficacy (55). Because of their hydrophobic nature, they are challenging to formulate and supply, making it difficult for EOs to penetrate insect cuticles or adhere effectively to stored grain surfaces. Although new delivery methods, such as microencapsulation and nanoemulsions, have potential, they are often costly and have not yet gained widespread use (56). Although EOs are generally considered benign, some can be hazardous to people and non-target creatures, particularly at higher concentrations (57). The approval process for biopesticides is complex and varies across nations and many formulations lack thorough toxicological and environmental data, which pose regulatory obstacles that further hinder their commercialization (58, 59). These restrictions highlight the need for improved formulations, standardization and policy frameworks that enable the use of EOs in pest management.

Formulation and delivery strategies for essential oil-based biopesticides

Scaling up the use of EO in agriculture is hindered by variability in active component concentrations and supply inconsistencies of plant-derived materials. Additionally, EOs have significant limits due to their physicochemical features, such as high volatility, limited stability and susceptibility to rapid evaporation and degradation. These issues reduce their effectiveness in field conditions. To overcome such limitations, significant research has focused on developing advanced formulations such as micro- and nano-encapsulation in both liquid and solid matrices that can enhance EO stability, protect active constituents from degradation and provide controlled release mechanisms for improved efficacy and usability (60). These encapsulation methods create protective carriers around EO molecules, reducing degradation and allowing controlled release.

A major challenge with EOs is the poor protection of their volatile organic compounds (VOCs). The total VOC abundance depends on the release kinetics, which are influenced by the formulation. While pure EOs exhibit higher VOC release, formulated EOs ensure a more gradual and controlled release (61). To address these challenges, various formulation strategies have been explored. A gel-based essential oil (EO) formulation using nanoemulsions was developed by incorporating agarose and sodium polyacrylate to enhance stability and controlled release (62). This formulation demonstrated the high efficacy of a garlic EO-based formulation against *Tribolium confusum*, with an LC_{50} of 0.486 mg/L (62). The formulation maintained its bioactivity over an extended period, ensuring prolonged effectiveness.

The use of nanoemulsions of *M. piperita* essential oil (EO) for stored grain pest management revealed that nano-formulations significantly enhanced insecticidal efficiency while reducing the required EO concentration. The LC_{50} at 24 hr post-exposure was 0.332 μL/cm² for the EO, while the nanoemulsion exhibited a lower LC_{50} of 0.192 μL/cm², indicating a more effective formulation with reduced EO usage (63). Studies on EO-based nano-biopesticides have shown promising results, especially in repelling *R. dominica*, demonstrating strong repellent properties (64). Eucalyptus oil nanoemulsions exhibited superior insecticidal efficacy against *S. oryzae* and *T. castaneum* (65). The nanoemulsions provided enhanced stability, reduced volatility and prolonged residual activity, making them a promising alternative to synthetic pesticides for protecting stored rice. Chitosan nanoparticle-encapsulated peppermint essential oil was formulated, exhibiting improved stability, controlled release and high insecticidal efficacy against stored-grain pests (66). This formulation presents a promising alternative for sustainable pest management. A sustained-release cinnamon essential oil microemulsion was developed, demonstrating enhanced insecticidal efficacy and prolonged residual activity while reducing volatility and improving stability thereby minimizing environmental loss and contributing to a reduced ecological footprint (67).

Conclusion

EOs are gaining significant attention for their potential as neurotoxic biopesticides due to their diverse mechanisms of action and ecologically safe properties. Targeting vital components of the insect nervous system, such as AchE inhibition, interference with neurotransmitter receptors and ion channel disruption, EOs exhibit substantial insecticidal potential while lowering the risk of resistance development. These are particularly appealing for integrated pest management (IPM) and sustainable agriculture due to their low toxicity to non-target organisms, quick degradation and natural origin. However, their broad use in commercial pest management is still hampered by drawbacks such as low persistence, formulation issues and inconsistencies in chemical composition.

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Authors' contributions

SP, MS, MM, NS, SH, MJ and NV contributed equally to the conceptualization of the review, literature collection, critical analysis of the findings, and manuscript preparation.

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