REVIEW ARTICLE

Therapeutic and insecticidal potential of plant terpenes: A review

Nidhi Yadav, Ravi Kant Upadhyay

Department of Zoology, Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur, Uttar Pradesh, India

Abstract

Present article describes therapeutic and insecticidal activities of plant terpenes. Volatile terpenes and terpenophenolics were found highly active against protozoa, viruses, bacteria, and helminthes. Terpenes also display bacteriostatic, bactericidal, and virucidal activities. These potentially function like promising natural insecticides and were found active against houseflies, storage grain insects and medical pests. Terpenes are strongest anti-parasitic natural products which could be used for development of formulations for oral delivery. These quickly absorbed in the stomach, and show reducing dosage and toxic side effects. Terpenoids as largest group of bio-organic compounds are safer, show high efficacy and no side effects when applied in field or provided for therapeutic purposes. This article suggests use of various terpenoids for development of herbal drug formulations for disease control after determining clinical and therapeutic dose level.

Key words: Antimicrobial, insecticidal activities, plant essential oils, plant terpenes

INTRODUCTION

Terpenes are aromatic compounds found in many plant species. Essential oils (EOs) are major source of terpenes. These provide different or characteristic aroma or smell in different plants and herbs, such as rosemary and lavender, cannabis, pine, and fresh orange peel. Terpenes play a key role in plants, these attract pollinators, repel predators, such as insects or foraging animals. Some terpenes play a protective role in the plant, helping the plant to recover from damage; others act as a part of the plant's immune system to keep away infectious germs. In cannabis plants when terpenes oxidize these become terpenoids. The terpenoids constitute the largest class of natural products and many interesting products are extensively applied in the industrial sector as flavors, perfumes, fragrances, spices cosmetics body products, and even foods. In higher plants, the conventional acetate-mevalonic acid pathway operates mainly in the cytosol and mitochondria and synthesizes sterols, sesquiterpenes, and ubiquinones mainly. In the plastid, the non-mevalonic acid pathway takes place and synthesizes hemi-, mono-, sesqui-, and diterpenes along with carotenoids and phytol tail of chlorophyll.

Terpenes, one of the most extensive and varied structural compounds occurring in nature, display a wide range of biological and pharmacological activities. Terpenes comprise a class of diversified phytochemicals, which have beneficial effects and important functions in plants. They have shown a series of biological properties that health promoting conduct in humans. Terpenes are less toxic as compared to synthetic compounds.[1] Terpenes from marine plants show very strong antimicrobial and insecticidal activity.[2] Terpenes and their derivatives comprising hydrocarbons are usually found in EOs. These possess five-carbon (isoprene) units as their building blocks, based on presence of carbon units different terpenes are named as hemiterpenes (C5), monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), sesterterpenes (C25), triterpenes (C30), and polyterpenes (>C30). Terpenoids derivatives, that is, fatty acids and phenolics found in the leaves, bolls, stalks, and stem play diverse functional roles in plants.[3] They exhibited potent antimicrobial activity, exhibiting bacteriostatic and bactericidal effects against tested pathogens.[4] Terpenoids as secondary metabolites show broad spectrum antimicrobial properties *in vitro*.[5] β-bisabolol, a sesquiterpenoid found in flowers of cotton plants, display strong anti-inflammatory activity.[6] Other

Address for correspondence:
Dr. Ravi Kant Upadhyay, Department of Zoology, Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur, Uttar Pradesh, India. E-mail: rkupadhya@yahoo.com

Received: 27-01-2022
Revised: 15-03-2022
Accepted: 21-03-2022

important therapeutic uses of terpenoids include antimicrobial, antifungal, antiviral, anti-hyperglycemic, anti-inflammatory, antioxidants, antiparasitic, immunomodulatory, and as skin permeation enhancer.[7] Terpenoids are toxic compounds produced by plants as a defense strategy against insect herbivores.[8] Many terpenoids have biological activities and also used for medical purposes. Terpenes are also used as drugs in cancer chemotherapy. These could be used as anti-diabetic agents.[9] In the present review articles few important terpenes which show diverse therapeutic and insecticidal activity have been described [Figure 1].

SOURCE OF INFORMATION

For writing this comprehensive research review, on plant terpenes various databases were searched. For collection of relevant information specific terms such as phytochemical subject headings and key text words, such as "plant terpenes," "therapeutic and insecticidal effects," therapeutic uses" published till 2022 were used in MEDLINE. Most specially for retrieving all articles pertaining to the use of plant terpenes, electronic bibliographic databases was searched and abstracts of published studies with relevant information on the plant terpenes were collected. Furthermore, additional references were included through searching the references cited by the studies done on the present topic. Relevant terms were used individually and in combination to ensure an extensive literature search. For updating the information about a subject and incorporation of recent knowledge, relevant research articles, books, conferences proceedings and public health organization survey reports were selected and collated based on the broader objective of the review. This was achieved by searching databases, including SCOPUS, Web of Science, and EMBASE, PubMed, PMC, Publon, Swissprot, Google searches" From this common

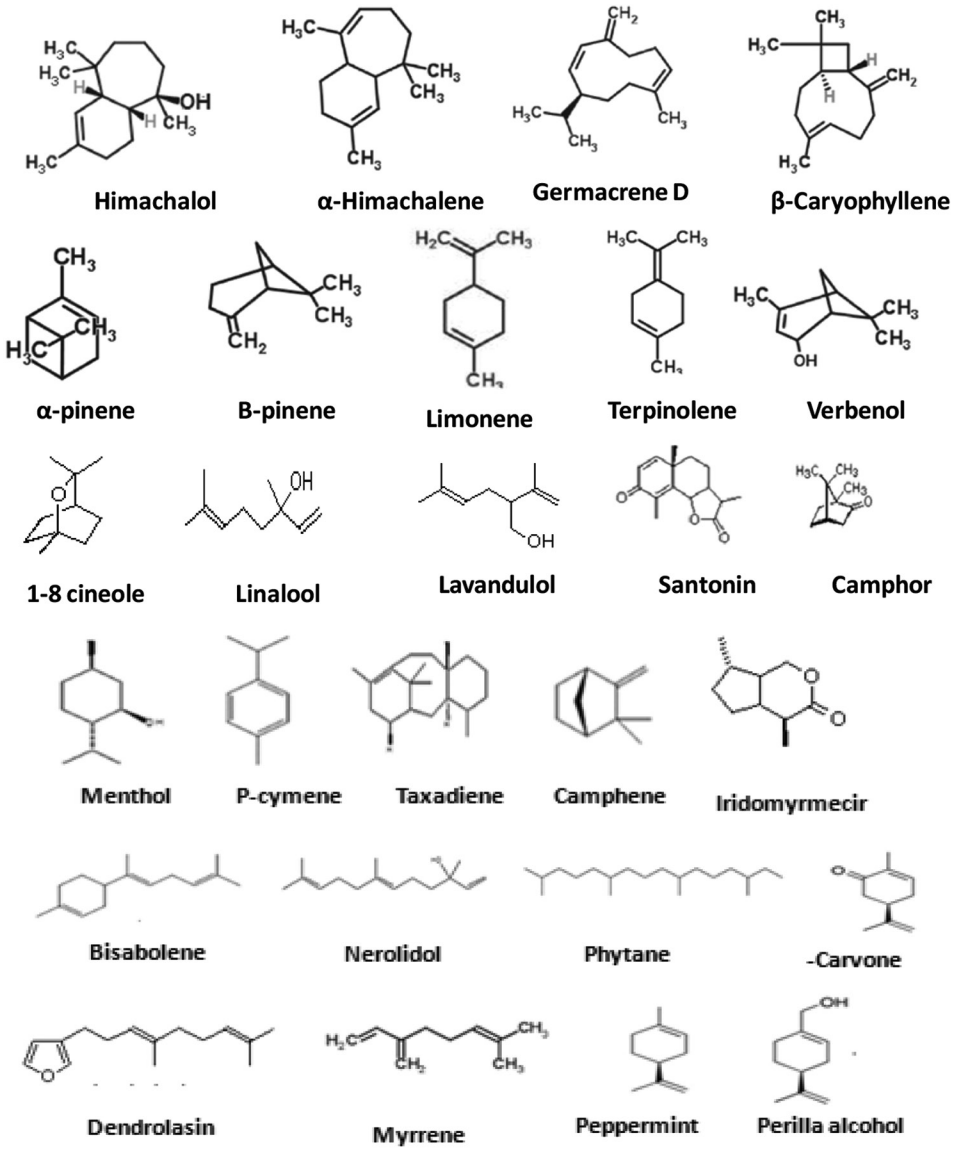

Figure 1: Chemical structures of major plant terpenes and their derivatives

methodology, discoveries and findings were identified and summarized in this final review.

ANTIMICROBIAL ACTIVITY OF TERPENES

Plant terpenes mainly monoterpenes such as a-pinene, a-bulnesene, and copaene were isolated from *Cyperus articulates* EO. It shows antimicrobial activity ability to control biofilm formation. It was found active against oral pathogens *Candida albicans*, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Streptococcus sanguis and Streptococcus mitis*.[10] Terpenes mainly p-cymene, menthol, carvacrol and thymol antibacterial, antifungal and antiparasitic, and antimycobacterial properties.[11] The plant species *Aristolochia indica*, *Melilotus indicus*, *Tribulus terrestris,* and *Cuscuta pedicellata* synthesize various terpenes and its derivatives. These were found active against *Aspergillus fumigatus*, *Aspergillus flavus,* and *Rhizopus oryzae*.[12] Few plant-derived terpenes and their derivatives β-pinene, eucalyptol, eugenol, and limonene show anti-inflammatory and antimicrobial activity[13] [Figure 1].

Various Piper species, that is, *Piper nigrum*, *Piper betle*, and *Piper auritum* synthesize different aromatic terpenes which are used as spices in the kitchen. These show diverse biological effects on human health.[14] Seaweed mainly green, brown and red algae produce secondary metabolites, that is, fatty acids, phlorotannins, pigments, lectins, alkaloids, terpenoids, and halogenated compounds which show antiviral, antiprotozoal, antifungal, and antibacterial potential.[15] EOs from *Inga laurina* possess high amounts of terpenoids (30.05%) and fatty acids (46.84%).[15] Plant extracts from *Phyllanthus muellerianus*, *Piptadeniastrum africanum* are antimicrobial phytomedicines which can be therapeutically used against infections caused by multidrug-resistant pathogens.[16]

Terpenes and their derivatives comprising of hydrocarbons, are usually found in EOs. They have been reported to have potent antimicrobial activity, exhibiting bacteriostatic, and bactericidal effects against tested pathogens.[4] Among these compounds, most terpenoids and their derivatives (51), fatty acids (four), and phenolics (six), were found in the leaves, bolls, stalks, and stems [Figure 1].

Plants synthesize tannins, terpenoids, alkaloids, and flavonoids enormously, these are well known antimicrobial phytochemicals.[5] Biological activities, such as anti-microbial and anti-inflammatory activities, are associated with some of these phytochemicals. For example, β-bisabolol, a sesquiterpenoid enriched in the flowers of cotton plants, may have anti-inflammatory product application.[6] Honey bee, *Apis mellifera* deposit plant resins which show antimicrobial activity[17] phenolic compounds 2,5-dihydroxybenzaldehyde and 2-hydroxy-5-methoxybenzaldehyde, and the plant EO compounds Similarly, carvacrol, cinnamaldehyde, and geraniol, found in plant EOs showed antimicrobial activity against both Gram-positive and Gram-negative pathogenic microorganisms.[18]

Aspergillus clavatonanicus strain MJ31, an endophytic fungi exhibit significant antimicrobial activity,[19] EOs of oregano showed both antiviral, antifungal, antioxidant, anti-inflammatory, antidiabetic, and anticancer activity.[20] Polyphenolic isolated from *Jacaranda mimosifolia* anti-inflammatory antioxidant, antimicrobial and lipoxygenase inhibitory activities, and anticancer properties.[21] Several species of Tagetes (marigold) *Tagetes minuta*, *Tagetes erecta*, *Tagetes patula*, and *Tagetes tenuifolia* EOs show broad medicinal properties and are used to treat various health problems, including dental, stomach, intestinal, emotional and nervous disorders, as well as muscular pain, across the world.[22] Plant natural products such as flavonoids, terpenoids, saponins, tannin, alkaloids, and phenol isolated from various plant parts (root, stem, and leaves) of *Ballota nigra* activity against bacteria and fungi and protozoans.[23] *Tagetes walteri* contain Thymol (22.5%), 1,8-cineole (8.2%), umbellulone (6.9%), α-bisabolol (6.3%), and camphor (5.3%) show antimicrobial activity.[24] Plant secondary natural products mainly terpenes show much potent *in vitro* antimicrobial activity against opportunistic infections in cancer patients [Table 1 and Figure 1].

TRYPANOCIDAL ACTIVITY

Due to their low toxicity, wide pharmacologic spectrum, and potential synergies, medicinal plants as *Lippia alba*, offer a promising reserve of bioactive molecules. Induction of programmed cell death in *Trypanosoma cruzi* by plant terpenes citral, limonene, and caryophyllene oxide isolated from *L. alba* EOs synergistic against *T. cruzi*, the causative agent of Chagas Disease at a very low IC50 value[25] [Table 1 and Figure 1].

ANTIMALARIAL

Plant metabolites such as alkaloids, terpenoids, flavonoids, coumarines, phenolics, polyacetylenes, xanthones, quinones, steroids, and lignans showed antimalarial activity.[26] Cryptolepine (CPE) is the major indoloquinoline isolated from the popular West African anti-malarial plant, *Cryptolepis sanguinolenta*. CPE possesses various showed potent anti-malarial activity against both chloroquine-resistant and -sensitive strains.[27] Similar antimalarial activity is reported in *Olea europaea* against *Plasmodium berghei* infected mice.[28] The ethanol extract *Himatanthus articulatus* showed anti-plasmodial activity.[29] Artemisia species, is used for treatment of many diseases such as malaria, hepatitis, cancer, inflammation and infections by fungi, bacteria, and viruses.[30] Marine compounds are well known for their antimalarial activities[31] [Table 1 and Figure 1].

Table 1: Antimicrobial activities of plant terpenes

Plant species	Family	Compound isolated	Biological effect	Source
Aspergillus clavatonanicus	Trichocomaceae	Ethyl acetate	Antimicrobial activity	[19]
Jacaranda mimosifolia	Bignoniaceae	Ethyl acetate Chloroform	Antioxidant, antimicrobial anti-inflammatory	[21]
Tagetes minuta	Asteraceae	Terpenoids	Antioxidant, anti-inflammatory, and enzyme inhibitory properties, cytotoxic and antiinflammatory activities	[22]
Tagetes erecta	Asteraceae	Terpenoids	Antioxidant, antiinflammatory, and enzyme inhibitory properties	[22]
Tagetes patula	Asteraceae	Terpenoids	Antioxidant, anti-inflammatory, and enzyme inhibitory properties	[22]
Tagetes tenuifolia	Asteraceae	Terpenoids	Antioxidant, anti-inflammatory	[22]
Verbena carolina	Verbenaceae	Terpenes	Inhibition of acetylcholinesterase	[21]
Aeglemarmelos correa	Rutaceae	Terpenes	Antioxidant, and antibacterial efficacy	[82]

ANTIFUNGAL

Volatile chemicals isolated from *Cyperus iria* leaves showed anti-fungal effects on *Fusarium graminearum*. These are sesquiterpenoids in *C. iria* which show potential as fungicides.[32] Terpenes and their derivatives showed potent antimicrobial activity.[4] Few phytoalexins both volatile and nonvolatile organic compounds show antifungal activity.[33] EO components also showed antifungal, against *A. fumigatus*, *A. flavus,* and *R. oryzae*.[12] Terpenes also showed activity against *Fusarium oxysporum*.[34] While cucumerinum, showed antifungal activity against *Physalospora piricola, Alternaria solani, and Cercospora arachidicola*.[35] Terpenoids, one of the major components of EOs, are known to exert potent antifungal activity against yeast Saccharomyces cerevisiae[36] [Table 1 and Figure 1].

ANTIBACTERIAL ACTIVITY

The oil from *C. articulates* contains a-pinene, a-bulnesene, and copaene and exhibits antimicrobial activity to control biofilm formation. It also shows antimicrobial activity against the oral pathogens *C. albicans*, *F. nucleatum*, *P. gingivalis*, *S. sanguis,* and *S. mitis*.[37] EOs and their constituents p-cymene, menthol, carvacrol, and thymol are showed antimycobacterial properties.[11] The plant species *A. indica*, *M. indicus*, *T. terrestris,* and *C. pedicellata* showed antibacterial, antifungal, cytotoxic, and anti-inflammatory potential.[12] Plant-derived compounds eugenol, β-pinene, eucalyptol, and limonene are used in treatment of acne and other skin infections.[13] Phenol group of phenolic terpenoids and its substituted derivatives against both Gram-negative *Escherichia coli* and Gram-positive *Staphylococcus aureus* bacteria[10] [Table 1].

ANTIVIRAL ACTIVITY

Plant terpenes have shown much potent effect against viral infections caused by the human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2), hepatitis virus B and C, influenza A virus, and the severe acute respiratory syndrome coronavirus 2.[33] Hyperjaponol H, a new filicinic acid-based meroterpenoid, exhibited a moderate inhibitory efficacy on lytic Epstein-Barr virus DNA replication in B95-8 cells[34] [Table 1].

PSYCHOTROPIC ACTIVITIES

Cannabinoids showed wide range of pharmaceutical effects in humans, including psychotropic activities. These are used to treat sleep disorders, attention deficit/hyperactivity disorder, and epilepsy specially Autism Spectrum Disorder patients.[38] Inhalation of the smoke of marijuana cigarettes, showed psychotropic effects in patients mainly in non-users.[39] Few terpenes and phenolic compounds, and in particular stilbenoids and lignans have high therapeutic application.[40] The phytocannabinoids Δ-9-tetrahydrocannabinol (Δ^9-THC) and cannabidiol (CBD) differentially regulate salience attribution and psychiatric risk.[41] Cannabinoid receptors are distributed in the central nervous system and many peripheral tissues including spleen, leukocytes; reproductive, urinary and gastrointestinal tracts; endocrine glands, arteries, and heart. Endogenous cannabinoids such as anandamide and 2-arachidonylglycerol are non-psychotropic CBD, its analogs and their metabolites, are antagonists at the cannabinoid receptors and modulators of the endogenous cannabinoid system. These are promising candidates for therapeutic uses.[42]

IMMUNO-MODULATORY

Terpenoids from *Chamaecyparis formosensis* (*Cupressaceae*) leaves show immunomodulatory activity on matrix metalloproteases 2 and 9. *C. formosensis*.[43] Waxy apple cultivar "Royal Gala" contain betulinic acid-3-trans-caffeateshow immunomodulatory effects.[44] Terpenes show antioxidant and/or radical scavenging and counteract the activation of redox-regulated signaling pathways.[45] Acenocoumarol had no effect in unstimulated cells but in PHA-stimulated PBMC tryptophan breakdown and the formation of neopterin, as well as IFN-γ and TNF-α, were dose-dependently suppressed at concentrations as low as 10 μg/ml.[46]

ANTI-INFLAMMATORY

Inflammation is a complex biological response in which inflammation is cause by secretion of various cytokines. Terpenes are natural products which showed anti-inflammatory activity.[47] Few terpinods such as scropolioside like iridoids have shown potential for anti-inflammatory, hepatoprotective and wound healing activity.[48] Few resin glycosides such as crypthophilic acids flavonoids, terpenoids, metabolites exhibit anti-inflammatory properties.[49] Terpenes as bioactive compounds are promising in the treatment inflammatory bowel diseases.[50] Terpenes and terpenoids are known as the main BVOCs of forest aerosols. These compounds have been shown to display a broad range of biological activities in various human disease models, these showed anti-inflammatory activities.[51] Few other volatile terpenes and terpenoids mainly monoterpenes, oxygenated terpenes, terpene esters, and sesquiterpenes showed anti-inflammatory properties.[52]

ANTICANCER ACTIVITY

Taxol is a terpene, its derivative (paclitaxel and docetaxel) are drugs which are widely used in cancer chemotherapy.[7] *Acanthopanax trifoliatus* containers-type triterpenoids, acantrifoic acid C (1) and acantrifoic acid D (2), were found to show significant inhibitory effects against SF-268, MCF-7, HepG2 and NCI-H460 cancer cells.[53] Natural bicyclic sesquiterpenes, β-caryophyllene (BCP) and BCP oxide (BCPO), show anticancer activity.[54] BCPO alters several key pathways for cancer development, such as mitogen-activated protein kinase, PI3K/AKT/mTOR/S6K1 and STAT3 pathways.[54] *Cannabis sativa* L., possess Δ^9-THC and CBD, which showed anticancer activity[55] [Table 1].

ANTIOXIDANT

Natural terpenes are strong antioxidants, due to unique behavior terpenes are provided for making protection under oxidative stress conditions in different diseases including liver, renal, neurodegenerative and cardiovascular diseases, cancer, diabetes as well as in ageing processes.[3] Quinoa Secondary Metabolites antioxidant activity.[49] Abisil is an extract of Siberian fir terpenes with antimicrobial and wound healing activities.[56] The extract of fir (*Abies sibirica*) terpenes, on normal and cancer cell lines. It was revealed that in normal fibroblasts, terpenes induced genes of stress response, apoptosis regulation, and tissue regeneration.[57] Terpenes of cannabis and hops are typically simple mono- and sesquiterpenes derived from two and three isoprene units, these are much potent anti-oxidants.[58] *Ganoderma lucidum* (Reishi) is a popular medicinal mushroom triterpenoids and polysaccharides, proteins, lipids, phenols, sterols, showed strong antioxidant and anti-acetylcholinesterase activities.[59] *Verbena carolina* L. (*Verbenaceae*) showed free radical scavenging capacity in extracts and isolated compounds.[60] Canola oil contains α-terpinene showed DPPH scavenging activity and antioxidant activity at very low IC_{50} of 0.035 Mm.[61] Dill (*Anethum graveolens*) seed EO, its nonpolar and polar compounds mainly carvone, limonene, and camphor showed antioxidant potential using different *in vitro* assays. These are natural antioxidants that are the important source of alternative medicines and can be used natural therapy in the pharmaceutical industry.[62]

ANTI-DIABETIC

Terpenoids showed anti-diabetic activity, these inhibit enzymes responsible for the development of insulin resistance, normalization of plasma glucose and insulin levels and glucose metabolism.[63] They can inhibit enzymes involved in glucose metabolism, prevent the development of insulin resistance and normalize plasma glucose and insulin levels.[64] Triterpenes can act as promising agents in the treatment of diabetic retinopathy, neuropathy and nephropathy or in impaired wound healing by inhibiting several pathways involved in the diabetes and associated complications.[63] Terpenes comprise a class of diversified phytochemicals, which have beneficial effects and important functions in plants. They have shown a series of biological properties that health promoting conduct in humans.[1] Terpenes are less toxic as compared to synthetic compounds and target insulin signaling pathways and/or the associated PI3K-AKT (protein kinase B), peroxisome proliferator activated receptor-γ, glucose transporter-4 and adenosine monophosphate-activated protein kinase pathways; pro-inflammatory cytokines and the NF-κB pathway; glycogenolysis and gluconeogenesis in Habtemariam.[65]

INSECTICIDAL ACTIVITY

Origanum vulgare terpenoids inhibit feeding behavior in *Spodoptera littoralis*.[8] *Citrus sinensis* essential oil showed insecticidal activity against the house fly *Musca domestica*.

Eucalyptus cinerea oil contains limonene (92.47%), linalool (1.43%), and β-myrcene (0.88%). EOs from *C. sinensis*, *C. aurantium,* and *E. cinerea* show promise as natural insecticides against houseflies.[66] Similarly, *O. vulgare* terpenoids carvacrol and γ-terpinene inhibit feeding in larvae feeding. Major constituents found in rosemary (*Rosmarinus officinalis*) oil, showed synergistic or antagonistic insecticidal activities with camphor in a binary mixture with 1,8-cineole. It penetrates through the larval integument and imposed severe negative effects in larvae.[67] *M. alternifolia* oil demonstrated an excellent deterrence index (0.8) at 2 g/L after 48 h. in *Myzus persicae* [Table 2].[68]

Similarly, EOs from *Zanthoxylum dissitum* leaves and roots against stored grain insect pests, that is, cigarette beetle (*Lasioderma serricorne*), red flour beetle (*Tribolium castaneum*), and black carpet beetle (*Attagenus piceus*). Both leaves and roots T contains sesquiterpenoids. *Z. dissitum* roots showed moderate contact toxicity against three species of storage pests, *L. serricorne*, *T. castaneum* and *A. piceus*, with LD50 values of 13.8, 43.7, and 96.8 μg/adult 9.[69] Similarly, EO of *Illicium pachyphyllum* fruits against two grain storage insects, *Sitophilus zeamais* and *Tribolium*. EO of *I. pachyphyllum* fruits and its constituent compounds have potential for development into natural insecticides or fumigants for the control of insects in stored grains.[70] EOs from *Cinnamomum cassia* exhibit strong insecticidal activity against *Sitophilus zeamais* Motschulsky *Maize weevils*, *S. zeamais*.[71] Similarly, trans-p-Mentha-1(7),8-dien-2-ol exhibited stronger fumigant toxicity against *S. zeamais* and *T. castaneum* adults, respectively, with LC50 values of 6.01 mg/L and 8.14 mg/L, than caryophyllene oxide (LC_{50} = 17.02 mg/L and 15.98 mg/L) and d-limonene (LC_{50} = 33.71 mg/L and 21.24 mg/L).[70] EO of *I. pachyphyllum* fruits and its constituent compounds have potential for development into natural insecticides or fumigants for the control of insects in stored grains.[72]

Cinnamosma sp. are rich in drimane sesquiterpenes, these are toxic and/or antifeedant to the yellow fever mosquito *Aedes aegypti*.[73] Further, lactone (cinnamosmolide) found in the root extract of *Cinnamosma* sp. synergized the larvicidal effects of cinnamodial plant drimane sesquiterpenes. It also shows insecticidal and repellent activity in mosquito vectors.[73] Bioactivities terpenes show antifungal effect on *Fusarium verticillioides* while S Thymoquinone showed a strong repellent effect (-77.8 ± 8.5, $P < 0.001$) against *S. zeamais*.[74] *Thymus kotschyanus* EO showed strong insecticidal activity against (*Oryzaephilus surinamensis* and *Sitophilus oryzae*). *O. surinamensis* was more susceptible to the effect of EO (LC_{50} = 4.78 μL/L air) than *S. oryzae* (LC_{50} = 13.20 μL/L air).[75] Terpenes and citronellal show synergistic toxicity in *M. domestica*).[72] *Bacopa caroliniana* contains α-Terpinolene efficient insecticidal effects.[76] Terpenes show long term effectiveness against insects similar to Piperonyl butoxide against pyrethroid-resistant mosquitoes.[77] Plant

Table 2: Insecticidal activities of plant terpenes

Plant species	Family	Compound isolated	Insecticidal activity	Source
Origanum vulgare	Lamiaceae	Carvacrol and p-cymene	*Spodoptera littoralis*	[8]
Illicium pachyphyllum Fruits	Schisandraceae	Trans-ρ-mentha-1(7),8-dien-2-ol, D-limonene and caryophyllene oxide	*Sitophilus zeamais* and *Tribolium castaneum* adults	[70]
Eucalyptus cinerea	Myrtaceae	Limonene	*Musca domestica*	[66]
Rosmarinus officinalis	Lamiaceae	1,8-cineole	*Cabbage looper, Trichoplusiani*	[67]
Melaleuca alternifolia	Myrtaceae	Terpinen-4-ol	*Myzus persicae*	[68]
Zanthoxylum dissitum	Rutaceae	Sesquiterpenoids	*Lasioderma serricorne, T. castaneum, Attagenus piceus)*	[69]
Illicium pachyphyllum	Schisandraceae	Trans-ρ-mentha-1(7),8-dien-2-ol, D-limonene and caryophyllene oxide	*S. zeamais* and *T. castaneum* adults	[70]
Cinnamomum cassia	Lauraceae	Chlorobiphenyl and 2-chlorophenylpyridine	*Aedes albopictus*	[71]
Bacopa caroliniana	Plantaginaceae	α-terpinolene	*Rice weevils*	[76]
Cinnamosma sp.	Canellaceae	Drimanesesquiterpenes	*Aedes aegypti*	[73]
Fusarium verticillioides	Nectriaceae	Terpenoids	*Arbuscular mycorrhiza*	[78]
F. verticillioides	Nectriaceae	Ketone terpenes	Repellent and insecticidal activities against the weevill *S. zeamais*	[74]
S. thymoquinone	Ranunculaceae	Ketone terpenes	*S. zeamais*	[74]

mycorrhizalterpenoids found in plants make defense against herbivory in natural communities.[78]

NEMATICDIAL ACTIVITY

Vetiver (*Vetiveria zizanioides* (L.) derived compounds showed nematotoxicity and repellency (LC_{50} = 185.9 µg/mL) against knot nematode, *Meloidogyne incognita*.[79] EO of *Agastache rugosa* aerial parts and its constituent compounds, that is, methyleugenol, thymol, eugenol, estragole, and limonene have potential for development into natural nematicides for control of the root knot nematode *Meloidogyne incognita*.[80]

MISCELLANEOUS

Genus Vitex contains monoterpenoids, sesquiterpenoids, diterpenoids and triterpenoids, anti-inflammatory, antitumor, antibacterial, and antioxidant activities.[81] *G. lucidum* contains various compounds with a high grade of biological activity, which increase the immunity and show antitumor, antimicrobial, anti-inflammatory, antioxidant, and acetylcholinesterase inhibitory activity.[59] Most of the terpenes are used in prevention and treatment of cancer. Taxol derivative (paclitaxel and docetaxel) are drugs which are widely used in cancer chemotherapy. Other important therapeutic uses of terpenoids include antihyperglycemic, and work as skin permeation enhancer.[7] Terpenes from *Aeglemarmelos Correa* (*Rutaceae*), "Bael," is used for in traditional medication for the treatment of various human ailments and possess great medicinal values.[82]

CONCLUSION

Both terpenes and derivatives were found highly active against pathogenic bacteria, mainly against drug resistant. Plant terpenes show much wider therapeutic uses antimicrobial, antifungal, antiviral, antihyperglycemic, anti-inflammatory, antioxidants, antiparasitic, immunomodulatory, and as skin permeation enhancer. Since many of these molecules are only found in very low levels in nature, their massive harvesting to obtain sufficient amounts of the drug including synthetic biology and metabolic engineering provides innovative approaches to increase the production of terpenoids. These compounds can act as direct antioxidants through free radical scavenging mechanisms and/or as indirect antioxidants by enhancing the antioxidant status (enzymatic and non-enzymatic). Plants are rich in a wide variety of secondary metabolites, such as tannins, terpenoids, alkaloids, and flavonoids, which have been found *in vitro* to have antimicrobial properties. These show much stronger insecticidal and nematicidal activities. This review attempts to find and explore effectiveness and toxicity of terpenes for its application in agriculture and pharmaceutical industries.

ACKNOWLEDGMENTS

The author is thankful to HOD Zoology for facilities.

REFERENCES

1. Panigrahy SK, Kumar A, Bhatt R. *Hedychium coronarium* rhizomes: Promising antidiabetic and natural inhibitor of α-amylase and α-glucosidase. J Diet Suppl 2020;17:81-7.
2. Choudhary A, Naughton LM, Montánchez I, Dobson AD, Rai DK. Current status and future prospects of marine natural products (MNPs) as antimicrobials. Mar Drugs 2017;15:272.
3. González-Burgos E, Gómez-Serranillos MP. Terpene compounds in nature: A review of their potential antioxidant activity. Curr Med Chem 2012;19:5319-41.
4. Mahizan NA, Yang SK, Moo CL, Song AA, Chong CM, Chong CW, *et al.* Terpene derivatives as a potential agent against antimicrobial resistance (AMR) pathogens. Molecules 2019;24:2631.
5. Cowan MM. Plant products as antimicrobial agents. Clin Microbiol Rev 1999;12:564-82.
6. Egbuta MA, McIntosh S, Waters DL, Vancov T, Liu L. Biological importance of cotton by-products relative to chemical constituents of the cotton plant. Molecules 2017;22:93.
7. Brahmkshatriya PP, Brahmkshatriya PS. Terpenes: Chemistry, biological role, and therapeutic applications. In: Ramawat K., Mérillon JM, editors. Natural Products. Berlin, Heidelberg: Springer; 2013.
8. Agliassa C, Maffei ME. *Origanum vulgare* terpenoids induce oxidative stress and reduce the feeding activity of *Spodoptera littoralis*. Int J Mol Sci 2018;19:2805.
9. Shehadeh MB, Suaifan GA, Abu-Odeh AM. Plants secondary metabolites as blood glucose-lowering molecules. Molecules 2021;26:4333.
10. Bersan SM, Galvão LC, Goes VF, Sartoratto A, Figueira GM, Rehder VL, *et al.* Action of essential oils from Brazilian native and exotic medicinal species on oral biofilms. BMC Complement Altern Med 2014;14:451.
11. Andrade-Ochoa S, Nevárez-Moorillón GV, Sánchez-Torres LE, Villanueva-García M, Sánchez-Ramírez BE, Rodríguez-Valdez LM, *et al.* Quantitative structure-activity relationship of molecules constituent of different essential oils with antimycobacterial activity against *Mycobacterium tuberculosis* and *Mycobacterium bovis*. BMC Complement Altern Med 2015;15:332.
12. Naz R, Ayub H, Nawaz S, Islam ZU, Yasmin T, Bano A, *et al.* Antimicrobial activity, toxicity and anti-inflammatory potential of methanolic extracts of four ethnomedicinal plant species from Punjab, Pakistan. BMC Complement Altern Med 2017;17:302.
13. Saviuc C, Ciubucă B, Dincă G, Bleotu C, Drumea V, Chifiriuc MC, *et al.* Development and sequential analysis of a new multi-agent, anti-acne formulation based on

plant-derived antimicrobial and anti-inflammatory compounds. Int J Mol Sci 2017;18:175.
14. Salehi B, Krochmal-Marczak B, Skiba D, Patra JK, Das SK, Das G, *et al.* Convolvulus plant a comprehensive review from phytochemical composition to pharmacy. Phytother Res 2020;34:315-28.
15. Pérez MJ, Falqué E, Domínguez H. Antimicrobial action of compounds from marine seaweed. Mar Drugs 2016;14:52.
16. Assob JC, Kamga HL, Nsagha DS, Njunda AL, Nde PF, Asongalem EA, *et al.* Antimicrobial and toxicological activities of five medicinal plant species from Cameroon traditional medicine. BMC Complement Altern Med 2011;11:70.
17. Wilson MB, Spivak M, Hegeman AD, Rendahl A, Cohen JD. Metabolomics reveals the origins of antimicrobial plant resins collected by honey bees. PLoS One 2013;8:e77512.
18. Nowotarska SW, Nowotarski KJ, Friedman M, Situ C. Effect of structure on the interactions between five natural antimicrobial compounds and phospholipids of bacterial cell membrane on model monolayers. Molecules 2014;19:7497-515.
19. Mishra VK, Passari AK, Chandra P, Leo VV, Kumar B, Uthandi S, *et al.* Determination and production of antimicrobial compounds by *Aspergillus clavatonanicus* strain MJ31, an endophytic fungus from *Mirabilis jalapa* L. using UPLC-ESI-MS/MS and TD-GC-MS analysis. PLoS One 2017;12:e0186234.
20. Leyva-López N, Nair V, Bang WY, Cisneros-Zevallos L, Heredia JB. Protective role of terpenes and polyphenols from three species of Oregano (*Lippia graveolens*, *Lippia palmeri* and *Hedeoma patens*) on the suppression of lipopolysaccharide-induced inflammation in RAW 264.7 macrophage cells. J Ethnopharmacol 2016;187:302-12.
21. Tayyab N, Lara-Issasi R, Yasmin H, Nosheen A, Keyani R, Sajjad M, *et al.* Combined seed and foliar pre-treatments with exogenous methyl jasmonate and salicylic acid mitigate drought-induced stress in maize. PLoS One 2020;15:e0232269.
22. Salehi B, Stojanović-Radić Z, Matejić J, Sharopov F, Antolak H, Kręgiel D, *et al.* Plants of Genus *Mentha*: From Farm to Food Factory. Plants (Basel) 2018;7:70.
23. Ullah N, Ahmad I, Ayaz S. *In vitro* antimicrobial and antiprotozoal activities, phytochemical screening and heavy metals toxicity of different parts of *Ballota nigra*. Biomed Res Int 2014;2014:321803.
24. Ghaderi A, Sonboli A. Chemical composition and antimicrobial activity of the essential oil of *Tanacetum walteri* (*Anthemideae-Asteraceae*) from Iran. Nat Prod Res 2019;33:1787-90.
25. Zore GB, Thakre AD, Jadhav S, Karuppayil SM. Terpenoids inhibit *Candida albicans* growth by affecting membrane integrity and arrest of cell cycle. Phytomedicine 2011;18:1181-90.
26. Moreno ÉM, Leal SM, Stashenko EE, García LT. Induction of programmed cell death in *Trypanosoma cruzi* by *Lippia alba* essential oils and their major and synergistic terpenes (citral, limonene and caryophyllene oxide). BMC Complement Altern Med 2018;18:225.
27. AmoaOnguéné P, Ntie-Kang F, Lifongo LL, Ndom JC, Sippl W, Mbaze LM. The potential of anti-malarial compounds derived from African medicinal plants, part I: A pharmacological evaluation of alkaloids and terpenoids. Malar J 2013;12:449.
28. Forkuo AD, Ansah C, Boadu KM, Boampong JN, Ameyaw EO, Gyan BA, *et al.* Synergistic anti-malarial action of cryptolepine and artemisinins. Malar J 2016;15:89.
29. Misganaw D, Engidawork E, Nedi T. Evaluation of the anti-malarial activity of crude extract and solvent fractions of the leaves of *Olea europaea* (Oleaceae) in mice. BMC Complement Altern Med 2019;19:171.
30. Vale VV, Vilhena TC, Trindade RC, Ferreira MR, Percário S, Soares LF, *et al.* Anti-malarial activity and toxicity assessment of *Himatanthus articulatus*, a plant used to treat malaria in the Brazilian Amazon. Malar J 2015;14:132.
31. Abad MJ, Bedoya LM, Apaza L, Bermejo P. The *Artemisia* L. genus: A review of bioactive essential oils. Molecules 2012;17:2542-66.
32. Mayer AM, Rodríguez AD, Berlinck RG, Hamann MT. Marine pharmacology in 2005-6: Marine compounds with anthelmintic, antibacterial, anticoagulant, antifungal, anti-inflammatory, antimalarial, antiprotozoal, antituberculosis, and antiviral activities; affecting the cardiovascular, immune and nervous systems, and other miscellaneous mechanisms of action. Biochim Biophys Acta 2009;1790:283-308.
33. Jiang Y, Ownley BH, Chen F. Terpenoids from weedy ricefield flatsedge (*Cyperus iria* L.) are developmentally regulated and stress-induced, and have antifungal properties. Molecules 2018;23:3149.
34. Lowe H, Toyang N, Steele B, Valentine H, Grant J, Ali A, *et al.* The therapeutic potential of psilocybin. Molecules 2021;26:2948.
35. Wu W, Maravelias CT. Synthesis and techno-economic assessment of microbial-based processes for terpenes production. Biotechnol Biofuels 2018;11:294.
36. Huang M, Duan WG, Lin GS, Li K, Hu Q. Synthesis and antifungal activity of novel 3-caren-5-one oxime esters. Molecules 2017;22:1538.
37. Konuk HB, Ergüden B. Phenolic -OH group is crucial for the antifungal activity of terpenoids via disruption of cell membrane integrity. Folia Microbiol (Praha) 2020;65:775-83.
38. Ergüden B. Phenol group of terpenoids is crucial for antibacterial activity upon ion leakage. Lett Appl Microbiol 2021;73:438-45.
39. Poleg S, Golubchik P, Offen D, Weizman A. Cannabidiol as a suggested candidate for treatment of autism spectrum disorder. Prog Neuropsychopharmacol Biol Psychiatry 2019;89:90-6.
40. Fitzgerald KT, Bronstein AC, Newquist KL. Marijuana

poisoning. Top Companion Anim Med 2013;28:8-12.
41. Andre CM, Hausman JF, Guerriero G. *Cannabis sativa*: The plant of the thousand and one molecules. Front Plant Sci 2016;7:19.
42. Hudson R, Renard J, Norris C, Rushlow WJ, Laviolette SR. Cannabidiol counteracts the psychotropic side-effects of δ-9-tetrahydrocannabinol in the ventral hippocampus through bidirectional control of ERK1-2 phosphorylation. J Neurosci 2019;39:8762-77.
43. Grotenhermen F. Pharmacology of cannabinoids. Neuro Endocrinol Lett 2004;25:14-23.
44. Chang ML, Mei HC, Kuo IC, Hsiao G, Kuo YH, Lee CK. New Terpenoids from *Chamaecyparis formosensis* (Cupressaceae) leaves with modulatory activity on matrix metalloproteases 2 and 9. Molecules 2018;23:604.
45. Andre CM, Larsen L, Burgess EJ, Jensen DJ, Cooney JM, Evers D, *et al.* Unusual immuno-modulatory triterpene-caffeates in the skins of russeted varieties of apples and pears. J Agric Food Chem 2013;61:2773-9.
46. Gostner JM, Ganzera M, Becker K, Geisler S, Schroecksnadel S, Überall F, *et al.* Lavender oil suppresses indoleamine 2,3-dioxygenase activity in human PBMC. BMC Complement Altern Med 2014;14:503.
47. Schroecksnadel S, Gostner J, Jenny M, Kurz K, Schennach H, Weiss G, *et al.* Immunomodulatory effects *in vitro* of Vitamin K antagonist acenocoumarol. Thromb Res 2013;131:e264-9.
48. Souza MT, Almeida JR, Araujo AA, Duarte MC, Gelain DP, Moreira JC, *et al.* Structure activity relationship of terpenes with anti-inflammatory profile a systematic review. Basic Clin Pharmacol Toxicol 2014;115:244-56.
49. Pasdaran A, Hamedi A. The genus *Scrophularia*: A source of iridoids and terpenoids with a diverse biological activity. Pharm Biol 2017;55:2211-33.
50. Lin M, Han P, Li Y, Wang W, Lai D, Zhou L. Quinoa secondary metabolites and their biological activities or functions. Molecules 2019;24:2512.
51. Araruna ME, Serafim C, Alves E Jr., Hiruma-Lima C, Diniz M, Batista L. Intestinal anti-inflammatory activity of terpenes in experimental models (2010-2020): A review. Molecules 2020;25:5430.
52. Kim T, Song B, Cho KS, Lee IS. Therapeutic potential of volatile terpenes and terpenoids from forests for inflammatory diseases. Int J Mol Sci 2020;21:2187.
53. Ji W, Ji X. Comparative analysis of volatile terpenes and terpenoids in the leaves of *Pinus* species a potentially abundant renewable resource. Molecules 2021;26:5244.
54. Li DL, Zheng X, Chen YC, Jiang S, Zhang Y, Zhang WM, *et al.* Terpenoid composition and the anticancer activity of *Acanthopanax trifoliatus*. Arch Pharm Res 2016;39:51-8.
55. Fidyt K, Fiedorowicz A, Strządała L, Szumny A. β-caryophyllene and β-caryophyllene oxide-natural compounds of anticancer and analgesic properties. Cancer Med 2016;5:3007-17.
56. Pellati F, Borgonetti V, Brighenti V, Biagi M, Benvenuti S, Corsi L. *Cannabis sativa* L. and nonpsychoactive cannabinoids: Their chemistry and role against oxidative stress, inflammation, and cancer. Biomed Res Int 2018;2018:1691428.
57. Lipatova A, Krasnov G, Vorobyov P, Melnikov P, Alekseeva O, Vershinina Y, *et al.* Effects of Siberian fir terpenes extract Abisil on antioxidant activity, autophagy, transcriptome and proteome of human fibroblasts. Aging (Albany NY) 2021;13:20050-80.
58. Kudryavtseva A, Krasnov G, Lipatova A, Alekseev B, Maganova F, Shaposhnikov M, *et al.* Effects of *Abies sibirica* terpenes on cancer- and aging-associated pathways in human cells. Oncotarget 2016;7:83744-54.
59. Nuutinen T. Medicinal properties of terpenes found in *Cannabis sativa* and *Humulus lupulus*. Eur J Med Chem 2018;157:198-228.
60. Cör D, Knez Ž, Hrnčič MK. Antitumour, antimicrobial, antioxidant and antiacetylcholinesterase effect of *Ganoderma lucidum* terpenoids and polysaccharides: A review. Molecules 2018;23:649.
61. Quiroga PR, Nepote V, Baumgartner MT. Contribution of organic acids to α-terpinene antioxidant activity. Food Chem 2019;277:267-72.
62. Kaur N, Chahal KK, Kumar A, Singh R, Bhardwaj U. Antioxidant activity of *Anethum graveolens* L. essential oil constituents and their chemical analogues. J Food Biochem 2019;43:e12782.
63. Putta S, Yarla NS, Kilari EK, Surekha C, Aliev G, Divakara MB, *et al.* Therapeutic potentials of triterpenes in diabetes and its associated complications. Curr Top Med Chem 2016;16:2532-42.
64. Nazaruk J, Borzym-Kluczyk M. The role of triterpenes in the management of diabetes mellitus and its complications. Phytochem Rev 2015;14:675-90.
65. Habtemariam S. Iridoids and other monoterpenes in the Alzheimer's brain: Recent development and future prospects. Molecules 2018;23:117.
66. Palacios SM, Bertoni A, Rossi Y, Santander R, Urzúa A. Efficacy of essential oils from edible plants as insecticides against the house fly, *Musca domestica* L. Molecules 2009;14:1938-47.
67. Tak JH, Isman MB. Penetration-enhancement underlies synergy of plant essential oil terpenoids as insecticides in the cabbage looper, *Trichoplusia ni*. Sci Rep 2017;7:42432.
68. Chohan TA, Chohan TA, Zhou L, Yang Q, Min L, Cao H. Repellency, toxicity, gene expression profiling and *in silico* studies to explore insecticidal potential of *Melaleuca alternifolia* essential oil against *Myzus persicae*. Toxins (Basel) 2018;10:425.
69. Wang CF, Yang K, You CX, Zhang WJ, Guo SS, Geng ZF, *et al.* Chemical composition and insecticidal activity of essential oils from *Zanthoxylum dissitum* leaves and roots against three species of storage pests. Molecules 2015;20:7990-9.
70. Liu P, Liu XC, Dong HW, Liu ZL, Du SS, Deng ZW.

Chemical composition and insecticidal activity of the essential oil of *Illicium pachyphyllum* fruits against two grain storage insects. Molecules 2012;17:14870-81.
71. Zhu Q, Yang Y, Zhong Y, Lao Z, O'Neill P, Hong D, *et al.* Synthesis, insecticidal activity, resistance, photodegradation and toxicity of pyrethroids (A review). Chemosphere 2020;254:126779.
72. Scalerandi E, Flores GA, Palacio M, Defagó MT, Carpinella MC, Valladares G, *et al.* Understanding synergistic toxicity of terpenes as insecticides: Contribution of metabolic detoxification in *Musca domestica*. Front Plant Sci 2018;9:1579.
73. Cui S, Inocente EA, Acosta N, Keener HM, Zhu H, Ling PP. Development of fast E-nose system for early-stage diagnosis of aphid-stressed tomato plants. Sensors (Basel) 2019;19:3480.
74. Pizzolitto RP, Herrera JM, Zaio YP, Dambolena JS, Zunino MP, Gallucci MN, *et al.* Bioactivities of ketones terpenes: Antifungal effect on *F. verticillioides* and repellents to control insect fungal vector, *S. zeamais*. Microorganisms 2015;3:851-65.
75. Ghasemi G, Alirezalu A, Ghosta Y, Jarrahi A, Safavi SA, Abbas-Mohammadi M, *et al.* Composition, antifungal, phytotoxic, and insecticidal activities of *Thymus kotschyanus* essential oil. Molecules 2020;25:1152.
76. Liu TT, Chao LK, Hong KS, Huang YJ, Yang TS. Composition and insecticidal activity of essential oil of *Bacopa caroliniana* and interactive effects of individual compounds on the activity. Insects 2019;11:23.
77. Sherrard-Smith E, Griffin JT, Winskill P, Corbel V, Pennetier C, Djénontin A, *et al.* Systematic review of indoor residual spray efficacy and effectiveness against *Plasmodium falciparum* in Africa. Nat Commun 2018;9:4982.
78. Sharma E, Anand G, Kapoor R. Terpenoids in plant and arbuscular mycorrhiza-reinforced defence against herbivorous insects. Ann Bot 2017;119:791-801.
79. Jindapunnapat K, Reetz ND, MacDonald MH, Bhagavathy G, Chinnasri B, Soonthornchareonnon N, *et al.* Activity of vetiver extracts and essential oil against *Meloidogyne incognita*. J Nematol 2018;50:147-62.
80. Li HQ, Liu QZ, Liu ZL, Du SS, Deng ZW. Chemical composition and nematicidal activity of essential oil of *Agastache rugosa* against *Meloidogyne incognita*. Molecules 2013;18:4170-80.
81. Yao JL, Fang SM, Liu R, Oppong MB, Liu EW, Fan GW, *et al.* A review on the terpenes from genus *Vitex*. Molecules 2016;21:1179.
82. Mujeeb F, Bajpai P, Pathak N. Phytochemical evaluation, antimicrobial activity, and determination of bioactive components from leaves of *Aegle marmelos*. Biomed Res Int 2014;2014:497606.

Source of Support: Nil. **Conflicts of Interest:** None declared.