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Botanical Nematicides: A Review

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ABSTRACT: Despite the uselfuness of nematicidal compounds in agricultural practices, some serious concerns are raised today about their excessive use leading to enhancement of biodegradation mechanisms in soil expressed as lack of efficacy under field conditions and resistance development. Moreover, the phase-out of methyl bromide has led to the need for a valid alternative to organophosporous and carbamate compounds, such us fosthiazate, fenamiphos, oxamyl, and aldicarb. In the past years, intregated pest management strategies have been practised worldwide to maximize crop production while maintaining and contributing to agriculture sustainability. Biopesticides and specifically bionematicides constitute a desirable component of pest management technology and practices. Particularly, in the frame of our ongoing research on natural nematicides of botanical origin, we have reviewed the international bibliography for candidate nematicidal compounds. We report herein the nematicidal activity of plant metabolites on the basis of their chemical characteristics and structure.

KEYWORDS: *nematicidal compounds, biopesticides, bionematicides*

1. INTRODUCTION

Phytonematodes are among the most known crop pests, and their control is achieved mainly by cultural practices, crop rotation, and resistant cultivars, combined with a few available chemical nematicides that are still authorized. *Meloidogyne* sp. are probably the most notorious phytonematodes living in soil in protected areas. Inside the host tissues, *Meloidogyne* pass through an embryonic stage, four juvenile stages (J1−J4), and an adult stage (Figure 1). Juvenile *Meloidogyne* species hatch from eggs as second-stage juveniles (J2), while the first molt occurs within the egg. Newly hatched juveniles live for a short period of time in the rhizosphere of the host plants without feeding. Then J2s invade host root in the root elongation region and migrate until they find a place to settle and feed. In that area, parenchyma cells near the head of the J2 become multinucleate giant cells, from which the J2s and later the adults feed. After further feeding, the J2s undergo morphological changes, and then without further feeding, they molt three times and eventually become adults. In females, the reproductive system develops, and they can produce hundreds of eggs, while male adults leave the root and do not harm the host. The length of the life cycle is temperature-dependent.

The need for discovering less toxic and environmentally acceptable substitutes for commercial nematicides is amplified, creating a significant market opportunity for alternative and biorational products such as botanical nematicidals. However, the economic cost of research and registration of a prospective new synthetic nematicide is an enormous hurdle to overcome that the industry rarely sustains.[1] For this reason, at present there are only few commercial nematicides left in use, and their repeated applications lead to the enhancement of biodegradation mechanisms in soil[2−4] and the development of pest resistance,[5] both expressed as a lack of efficacy under field conditions. It is therefore very important to study new and alternative nematode control methods[1] like the biorational pesticides by screening naturally occurring compounds in plants.[6,7] Since plants are long-lived stationary organisms, they must resist attackers over their lifetime by producing and exuding secondary metabolites. Research of phytochemicals has its roots in allelochemistry, involving the chemical-mediated interactions between a plant and other organisms in its environment.[1] The development of PSMs as tools in crop protection evolved through the observation of their activities when they were used in traditional practices and eventually by the identification of the active molecules as well as by the systematic screening of botanical families followed by biological tests in order to discover potential active molecules. Pyrethroids, synthetic molecules analogous to pyrethrum, and neem products (Meliaceae) are characteristic examples of commercial plant protection products based on botanical sources. The OECD (Organization for Economic Cooperation and Development) defines the botanical substances as semiochemicals, including chemicals involved in species communication (pheromones, but also plant extracts, plant volatiles, and natural oils) that exhibit pest control activities, while recently, the concept of biocontrol agents has been preferred to that of biopesticides.[8] Bioactive PSMs may be developed for use as pesticides themselves, or they can be used as model compounds for the development of chemically synthesized derivatives. Some botanicals used as pesticides pose less risk to humans and animals than their synthetic ancestors did, have a selective mode of action, are environmentally friendly, and avoid the emergence of resistant races of pest species and therefore can be used in integrated pest management (IPM) programs.[6] Stability concerns under field conditions have been raised as a result of sorption in the soil organic matter which results in the reduction of their

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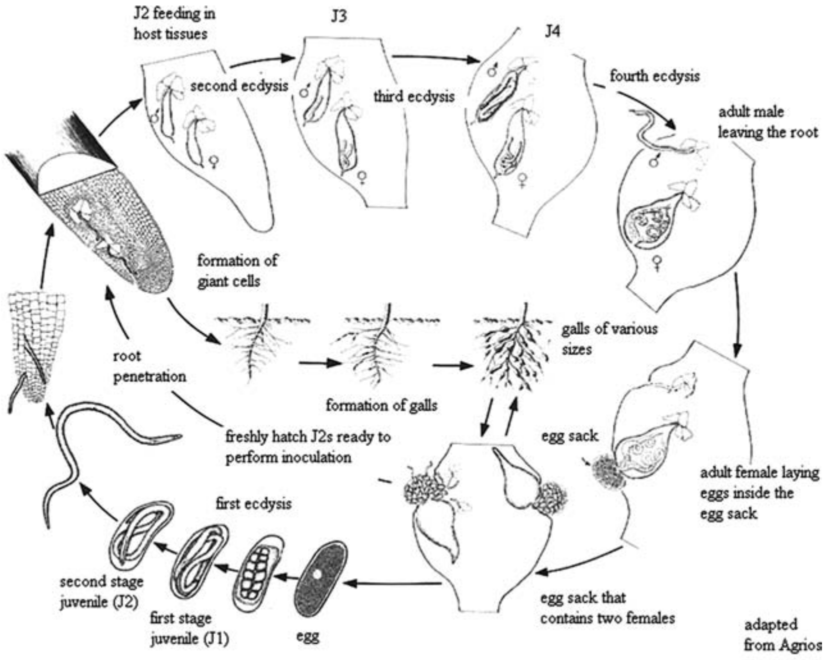

Figure 1. Biological cycle of *Meloidogyne* sp.

availability. Current studies investigate the encapsulation of essential oils as a potential controlled release vehicle with site-specific delivery to maximize the properties of the oils.[9] In recent years, the only commercial botanical registered for phytomenatodes control had been azadirachtin. This is a short review encompassing the main chemical classes of PSMs that have been used or have the potential of use as nematicides on crop protection, specifically against *Meloidogyne* species. We report on the natural substances of plant origin that have been found to exhibit, among others, nematicidal activity tested alone or in mixtures and the mode of action of single compounds against target pests (nematodes or others; if no data is available on nematodes), as well as on the current trend of use of the botanical nematicides in field practice along with their future perspective.

2. CHEMICAL CLASSES OF BOTANICAL NEMATICIDALS

2.1. Aldehydes and Ketones. Aldehydes like phenols and alcohols induce cytotoxicity, damage the cellular and organelle membranes, act as prooxidants on proteins and DNA, and produce reactive oxygen species. The activity of *Melia azedarach* against *Meloidogyne* sp. is attributed to the defatted methanol fruit extract (polar fraction) and specifically to its organic acids, aldehydes, and alcohol contents.[10,11] *Meloidogyne* species live in soil in protected areas and usually reside at a fair distance from the target of nonfumigant nematicides. In fact, furfural exhibited the highest nematicidal activity similar to that of the commercial nematicide fosthiazate, both when J2s are immersed in test solutions and exposed to its vapors (fumigant activity). Also, Rodriges-Kabana has reported on the strong nematicidal fumigant activity of furfural against *M. incognita*, when tested in greenhouse and microplot conditions,[12] but no correlation has been made so far with its contents in chinaberry. The fumigant activity is of extreme importance for a nematicide because it enhances its activity in the nontreated soil layers. The aromatic aldehyde benzaldehyde, found as a component of the essential oil (EO) from *Eucalyptus meliodora*, exhibits high nematicidal activity (EC_{50} = 9 μg/mL).[13] Aldehydes and ketones such as *p*-anisaldehyde, benzaldehyde, *trans*-cinnamaldehyde, (*R*)-(+)-pulegone, and furfural exhibit high nematicidal activities against *Meloidogyne javanica*. Specifically, the EC_{50} values of *trans*-cinnamaldehyde for juvenile immobilization and hatching inhibition in vitro were as low as 15 and 11.3 μL/L, respectively. In pot experiments, *trans*-cinnamaldehyde, furfural, and benzaldehyde at a concentration of 100 mg/kg greatly reduced the root galling of tomato. Under field conditions, soil treatment with *trans*-cinnamaldehyde (50 mL/m^2) reduced the galling index and increased the shoot weight of tomato plants.[14] In our previous studies, we have demonstrated that among oxygenated compounds, ketones were generally more active and that their activity against *M. incognita* exhibited EC_{50} values of 115 and 150 μg/mL for L-carvone and pulegone, respectively.[13,15] Similarly, (*E*,*E*)-2,4-decadienal, (*E*)-2-undecenal, (*E*)-2-decenal, hexanal, nonanal, and furfural were proved as the most prominent nematicidal constituents of *Ailanthus altissima*. (*E*,*E*)-2,4-decadienal, (*E*)-2-decenal, and furfural showed the highest nematicidal activity against *M. javanica*, with $EC_{50/1d}$ values of 11.7, 20.43, and 21.79 mg/L,[16] while 2-undecanone EC_{50} values were calculated at 20.6 and 22.5 mg/L for *M. incognita* and *M. javanica*, respectively.[17] Finally, synergistic effects in suppressing initial and final soil populations of *M. arenaria* are reported when thymol is applied at 0, 50, 100, and 150 mg/kg to soil in combination with 0, 50, and 100 mg/kg benzaldehyde at 100 mg/kg.[18]

2.2. Alkaloids. Alkaloids are PSMs containing nitrogen atoms and are derived from various botanical families among which is Solacaneae. 2,5-Dihydroxymethyl-3,4-dihydroxypyrrolidine is a pyrrolidine alkaloid contained in the genera *Loncocarpus* and *Derris*, exhibiting nematicidal activity. It is downwardly mobile in plant phloem, and its applications on plant foliar appendages decrease galling in roots, but the mode of action is under investigation.[19] *Tithonia diversifolia* (Hemsl.) A. Gray, rich in alkaloids, suppresses egg hatching of *M. incognita* by 98% from 2 days after incubation and 100%

inhibition at 9 days. *Tithonia* residue treatment at the rate of 30 tons/ha on yam (*Discoria rotundata*) in the greenhouse experiments significantly suppressed *M. incognita* (5000 eggs/plant) reproduction, number of eggs, and juveniles, as well as galling.[20] 1,2-Dehydropyrrolizidine alkaloids (PAs), representing a class of secondary plant metabolites that are active in defense against herbivores, are present in *Chromolaena odorata*, one of the most invasive weeds in Asia and Africa. In vitro studies demonstrate that pure PAs from *C. odorata* roots have nematicidal effects on *M. incognita*, even at concentrations of 70−350 mg/L. In vivo experiments show that mulch or aqueous crude extracts from *C. odorata* roots reduce *M. incognita* infection on lettuce.[21] *Crotalaria* is a PA-producing plant that is used for nematode control since it yields different structural types of PAs, although of no conclusive ranking in toxicity. The effects are more pronounced for the tertiary than for the oxidized form. Additionally, large differences are observed in the susceptibility of different nematode species to PAs.[22] In pot experiments with the commercially available PA-containing plants *Ageratum houstonianum*, *Borago officinalis*, *Senecio bicolor*, and *Symphytum officinalis*, it was demonstrated that although *Meloidogyne hapla* is not repelled per se by these plants, the nematodes' juveniles development was completely suppressed on *A. houstonianum* and *S. bicolor*. In fact, the soil in which *A. houstonianum* and *S. bicolor* were cultivated and incorporated contained 200−400 times less nematodes than the soil treated with *Lycopersicon esculentum*.[22] The brimstone (*Morinda lucida*) leaf crude extract (50 and 100% concentrations) and brimstone leaf powder (1 and 2 t/ha), rich in saponins and flavonoids, significantly increase the number of leaves, plant height, number of branches, and fresh leaf and root weight of *Celosia argentea* (L.), and also significantly reduce the gall index due to *M. incognita*.[23] When *Acacia gummifera*, *Ceratonia siliqua*, *Ononis natrix*, *Tagetes patula*, and *Peganum harmala* were evaluated for their nematicidal effect through their aqueous extract used directly in the in vitro test, and the nematicidal effect ranged between 67% and 95%. *P. harmala* had an effect similar to that of the commercial nematicide (Vydate, a.i. oxamyl), while phytochemical analysis of this species revealed that this plant is rich in alkaloids. *A. gummifera* and *T. patula* extracts exhibited a high nematicidal effect of 84% and 82%, and they were found to contain significant concentrations of flavonoids. The extract of *O. natrix* and *C. siliqua* had a nematicidal effect against *Meloidogyne* spp., with 67% and 71% of mortality, respectively.[24] *Peganum harmala* aqueous extracts, rich in alkaloids, have an effect similar to that of the commercial nematicidal Vydate.[24]

2.3. Glycosides. Cyanogenic glycosides are amino acid derived PSMs present in more than 2500 plant species, playing an important role in plant defense against herbivores due to their bitter taste and release of toxic hydrogen cyanide. Upon tissue disruption (e.g., by chewing insects), the cyanogenic glucosides are released from the vacuoles and hydrolyzed by specific β-glucosidases to yield glucose, a ketone or an aldehyde, and toxic HCN. This process is called cyanogenesis and serves to facilitate a rapid nematicidal HCN release.[1,25−28] Cyanogenic glycosides, through the action of cyanide, prevent oxygen utilization by the inhibition of cytochrome oxidase.[29] Sudangrass cv. Trudan 8 has been demonstrated to suppress the infection of vegetables by *M. hapla* due to hydrogen cyanide released from the degradation of the cyanogenic glucoside (dhurrin) during decomposition. This results in a reduction in severity of root gall infection up to 54%, which suggests that cyanogenic plants have potential as nematicidal green manure.[30] The liquid extract (manipueira) obtained through the pressing of cassava roots for the production of starch and cassava flour is rich in proteins, carbohydrates, and several PSMs, thus exhibiting toxicity against nematodes and insects. Particularly, the leaves and roots of cassava are rich in cyanogenic glycosides, namely, linamarin and lotoaustralin. The breakdown of linamarin by the enzyme linamarase is very rapid, releasing glucose and an intermediate cyanohydrin. At high pH or at high temperatures, the cyanohydrin decomposes spontaneously, producing a ketone together with volatile hydrogen cyanide that is very toxic to a wide range of organisms.[31] Soybean greenhouse experiments were conducted to evaluate the nematicidal activity of thymol at rates of 25−250 mg/kg along with its activity when applied at 0, 50, 100, and 150 mg/kg to soil in combination with 0, 50, and 100 mg/kg benzaldehyde. When benzaldehyde was applied at 100 mg/kg, it showed synergistic effects in suppressing initial and final soil populations of *M. arenaria*, while significant reductions in root galling on soybean were attributable to thymol at ≥50 mg/kg.[32] Treatment of tomato and cucumber plants with furostanol glycosides obtained from cell cultures of *Dioscorea deltoidea* Wall. decreased their susceptibility to infection by the root-knot nematode *M. incognita*. In treated plants, the fecundity of the nematode was decreased 5-fold, females were smaller, and the sex ratio shifted toward an increase in males.[33] In fact, furostanol glycosides extracted from *Dioscorea deltoidea* Wall. cell cultures under the conditions of biotic stress cause nonspecific defense reactions resulting in the formation of systemic acquired resistance in tomato plants *Lycopersicon esculentum* Mill, evidenced by the comparison of changes in isoprene content (phytosterines, tomatin, and carotenoids) and in the rate of oxidative processes in the leaves and roots of intact and treated plants. This formation is presented by the enhancement in the photosynthetic apparatus pigment fund, pigments of the violaxanthin cycle in particular, by activation of the processes related to POL, and by the increase in peroxidase activity, which is an enzyme of antioxidant protection.[34] When the effects of certain plant steroids (belonging to furostanol glycosides or glycoalkaloids) and α-ecdysone were studied, on the growth and development of *M. incognita*, it was shown that a steroid molecule exhibits significant nematicidal activity if it contains a carbohydrate moiety and an additional heterocycle in the steroid core. The maximum nematicidal activity is inherent in glycosides containing chacotriose as the carbohydrate moiety of the molecule.[35] The ethanol extract of *Arisaema erubescens* (Wall.) Schott tubers possess significant nematicidal activity against the root-knot nematode (*M. incognita*) due to its flavone-C-glycosides, namely, schaftoside and isoschaftoside. Both possess strong nematicidal activity against *M. incognita* (LC_{50} = 114.66 μg/mL and 323.09 μg/mL, respectively), while the crude extract of *A. erubescens* exhibited nematicidal activity against the root-knot nematode with an LC_{50} value of 258.11 μg/mL.[36]

2.4. Glucosinolates and Isothiocyanates. Glucosinolates (GLSs) are PSMs produced by mustards (*Brassica* and *Sinapis* sp.) and another genus of the order Capparales; they contain sulfur and nitrogen and β-D-thioglucose as well as sulphonated oxime moieties. These include thioglucosides, characterized by a side chain with varying aliphatic, aromatic and heteroaromatic carbon skeletons. Glucosinolates get converted into various degradation products (isothiocyanates, thiocyanates, and indoles) after cutting or chewing of the plant parts that contain them because through this process, they come in contact with the vacuolar enzyme myrosinase (Myr). Biofumigation is a practice by which nematicidal isothiocyanates (ITCs) are released in soil after incorporating glucosinolate-containing plant material. This practice is considered an ecological substitution of the soil fumigation with toxic fumigants such as methylbromide because these substances are fully biodegradable and less toxic.[37,38] Glucosinolate degradation products trigger the plant's defense mechanism, produce toxins, and create defensive barriers around the roots of the host plant, thus preventing harmful pathogens like fungi to enter the host (hyrpesensitive response).[39] The ITCs' (−N=C=S) fate in soil is fundamental for the efficacy of biofumigation. The maximum hydrolysis of the glucosinolates in the plant tissue that generates high isothiocyanate concentrations in the soil after incorporation is favored by maximum cell disruption, by addition of water, and by high soil temperatures. Residual glucosinolates are very weakly adsorbed, readily leached, and are microbially degraded and mineralized in soil. In contrast, isothiocyanates are strongly adsorbed by the organic matter in soil, react strongly with soil compounds bearing a nucleophilic group, and are prone to volatilization losses and microbial degradation and mineralization minimizing the risks of persistence in the environment or leaching.[40] A formulated product named Dazitol, a commercialized nematicide in the USA, contains 4.37% ITCs extracted from plant material (mustard seeds).[41] However, metam sodium and dazomet, both being methyl isothiocyanate precursors, are rapidly degraded (85% in 10 days) in soils treated with these substances, indicating that there is an induced cross-accelerated degradation with both fumigants.[42,43] During recent years, extensive reviews have concerned the chemical ecology of various *Brassica* toward parasitoids, predators, herbivores, and nematodes emphasizing GLSs and ITCs, their potential of integration in insect-pest management, and the physiological and biochemical implications underlying hydrolysis mechanisms.[44−47] Seed meals obtained from *Brassica juncea* 'Pacific Gold', *B. napus* 'Dwarf Essex' and 'Sunrise', and *Sinapis alba* 'IdaGold' were found to exhibit nematode-suppressive abilities in *Pratylenchus penetrans* and *M. incognita* second-stage juveniles.[48] Currently, it has been found that 3-methoxybenzyl isothiocyanate, the predominant enzyme degradation product of glucosinolate glucolimnanthin contained in Meadowfoam (*Limnanthes alba* L.), was very toxic to *M. hapla* ($EC_{50} = 2.5 \pm 0.1$ to 2.7 ± 0.1 mg/L) and care was taken to manipulate meadowfoam seed meal to promote its production.[49] Moreover, defatted seed meal application (*Raphanus sativus* ssp. *oleiformis* and *Eruca sativa* ssp. *oleiformis*), compared with oxamyl drip irrigation, limited nematode infestation and allowed cucumber roots with a lower root gall index (2.0 to 3.5 versus 3.5 to 4.5). The zucchini yield in the biocidal seed meal treated plot was 9% higher in the second month of harvesting due to the lower infestation of zucchini roots, and the harvesting time was one week longer with a final 14% total yield improvement.[50] It has been proven that cultivation followed by soil incorporation of broccoli reduced *M. incognita* damage in tomato.[51] For that which concerns the delineation of activity among ITC components, various studies have been made. In a study where 11 hydrolysis products of glucosinolates were tested for their nematicidal properties, 2-phenylethyl, benzyl, 4-methylthiobutyl, and prop-2-enyl isothiocyanate showed the stronger activity, with an LD_{50} at concentrations of 11, 15, 21, and 34 μM, respectively. On the basis of this study, new genotypes of Brassicaceae are selected for high content in the roots of the glucosinolates generating these most active isothiocyanates, and their agronomic performances are verified under field conditions as catch crop plants.[52] According to Wu et al., some of the most potent ITCs compounds are allyl isothiocyanate (Allyl-ITC), acryloyl isothiocyanate (Ac-ITC), ethyl isothiocyanate (Et-ITC), benzyl thiocyanate (Bz-TC), benzyl isothiocyanate (Bz-ITC), 1-phenylethyl isothiocyanate (1-PE-ITC), and 2-phenylethyl isothiocyanate (2-PE-ITC), showing in vitro irreversible nematicidal activity against second-stage juveniles of *M. javanica*, following exposure for 72 h at concentrations as low as 5 μg/mL. In pot experiments, 1.0 mL of Allyl-ITC and 1.1 mL Ac-ITC per kg of soil inhibited *M. javanica* in a manner similar to or better than metam sodium at its recommended application dose. Similar results were obtained in the field experiments using 1.0 kg Allyl-ITC or 1.0 kg Ac-ITC per ha.[53] Nonetheless, the significant interference between biofumigation and biocontrol agents in the soil, presents challenges in combining these two environmentally friendly approaches to managing plant-parasitic nematodes. Specifically, it was found that although both the seed meals high in glucosinolates and the entomopathogenic nematodes *Steinernema* spp. reduced root-knot nematode damage to potato tubers and increased marketable tuber yields, their combination did not further improve the suppression of plant-parasitic nematodes.[54]

2.5. Limonoids, Quassinoids, and Saponins. Limonoids are metabolically altered triterpenes and have a prototypical structure either containing or derived from a precursor with a 4,4,8-trimethyl-17-furanylsteroid skeleton. They can be found as constituent compounds in the order Rutales and more specifically in the families Meliaceae and Rutaceae, or less frequently in Cneoraceae and *Harrissonia* sp. of Simaroubaceae.[55] To date, 300 limonoids are known, one-third of which (meliacins) is obtained from Meliaceae species (*Azadirachta indica* and *Melia azedarach*) corresponding to structurally rather complex substances.[56−60] The plant family Meliaceae (mahogany family) has received much attention especially because of the presence of limonoid triterpenes[61] among which focus has been predominately on azadirachtin. Azadirachtin, a tetranortriterpenoid limonoid found in the Indian Neem tree (*Azadirachta indica* L., Meliaceae), is used for the production of a wide range of commercial formulations registered for nematode control.[62,63] Apart from azadirachtin, neem also contains more than 100 different limonoids exhibiting repellence, feeding deterrence, and insect growth inhibition activities.[61] In India, neem (*Azadirachta indica*) extracts have been introduced in pest management as a part of traditional practice for many years. It is of high importance that limonoids do not have direct negative effects on beneficial insects,[64,65] and for this reason, they can be combined in integrated pest management. Specifically, azadirachtin is classified as highly toxic to insects and mildly toxic to nontoxic to mammals due to the ability of mammalian cells to remove azadirachtin from the body.[66] Azadiractin is therefore classified as class IV (no mammalian toxicity) by the U.S. Environmental Protection Agency (EPA); it is not persistent in the environment principally due to photodegradation;[67,68] it has no effects on skin sensitization and eye irritation, and is not mutagenic.[69] Moreover, azadirachtin is the most studied biopesticide because it exhibits a wide range of biological activities against agricultural pests and pathogens.[70] Its chemical structure elucidation took 18 years to solve, while its total synthesis took almost 22 years.[66] Azadirachtin effects on insects are (i) antifeedancy due to deterrent effects on chemoreceptors; (ii) endocrine system disruptance (ecdysteroid and juvenile titers); and (iii) direct effects on tissues resulting in loss of fitness.[71] The insect growth regulation and development activities are caused by the decalin fragment of the molecule, while the hydroxyl-furan fragment affects the antifeedant effects.[72] Recently, it has been reported that azadirachtin induces a rapid increase in the mitotic index of insect cells, the appearance of many aberrant mitotic figures, and the prevention of polymerization in vitro of mammalian tubulin.[73]

Although several reports suggest that neem products, such as seed powder, seed kernel powder, seed cake powder, dry leaf powder, and aqueous neem extracts, exhibit good efficacy against root-knot nematodes,[74−78] it seems that azadirachtin activity, when used individually, is less fast and less high.[79] In fact, azadirachtin (Neemazal 1% EC, Intrachem Hellas) acts against *Meloidogyne* sp. at very high concentrations both concerning paralysis effects and biological cycle arrest (12.8 mg/L and 30.72 μg/g), and the recommended dose for nematode control in field does not provide adequate control.[80] According to our results, meliacins do not seem to be characteristic of nematicidal activity[81] contrary to Saha et al., sustaining synergism in a binary mixture (1:1) of azadirachtin and salannin, nimbin, and desacetylnimbin against *M. incognita* (LC_{50} 70.9 μg/mL).[82] *Melia azedarach* L. is another Meliaceae plant species, also known as chinaberry, demonstrating strong biofumigant properties when incorporated as a powder in *M. incognita* infested soil (EC_{50} = 0.34% w/w). Quassinoids and saponins also fall in the PSMs' category of triterpenoids, but they are much less studied contrary to limonoids. Quassinoids are the bitter principles of the Simaroubaceae family (*Quassia amara*, *Cassia camara*, and *Picrasma excelsa*) and constitute a group of structurally complex and highly oxygenated degraded triterpenes,[83] divided into five groups according to the basic skeleton (C-18, C-19, C-20, C-22, and C-25); they possess nematicidal properties,[1] while no data is available at present of their fate in the environment. Quassinoids act as noncompetitive antagonists of the ionotropic GABA receptor to stabilize the closed conformation of the channel, resulting in the inhibition of the action of GABA.[84] The quassinoid fraction extracted from seeds of *Hannoa undulata* composed of a mixture of three polycyclic lactones chaparrinone, glaucarubolone, and klaineanone reduces the penetration and reproduction of *M. javanica.* Full inhibition of penetration occurred during three days of nematode exposure to a 5 mg/kg quassinoid solution in the soil−water, while soil amendment of crude powder of *H. undulata* seeds fully inhibited the reproduction of *M. javanica* on tomato roots.[85] Quassinoids, C19 or C20 compounds isolated from Simaroubaceae, revealed nematicidal activities against Diplogastridae (Nematoda). Of the various quassinoids tested, samaderines B and E displayed the most potent nematicidal activity with a minimum lethal concentration (MLC) of 2.0×10^{-5} M. The nematicidal activities of samaderines B and E were 15-fold greater than that of albendazole (3.0×10^{-4} M), 10-fold greater than that of thiabendazole (2.0×10^{-4} M), and 7.5-fold greater than that of avermectin (1.5×10^{-4} M). Thus, samaderines B and E may eventually be used as lead nematicides.[86] Saponins are triterpene glycosides obtained from *Quillaja saponaria* (Quillajaceae) and various other plant species of the families Alliaceae, Asteraceae, Polygalaceae, and Agavaceae. Their side chains of hydrophilic carbohydrates provide them with surfactant properties, but they also possess significant nematicidal properties.[1,87−95] Saponins mainly consisting of triterpene glycosides of medicagenic acid are considered nematicidal agents,[96] and they act as membrane disruptants.[29] *Medicago sativa* L., alfalfa, is the most known plant species for its contents in saponins. In field conditions, soil amendments with 20 or 40 t/ha of a pelleted *M. sativa* meal increased tomato crop yield and reduced soil population densities and root galling of *M. incognita*.[97] *Tithonia diversifolia* (Hemsl.) A. water extract, yielding alkaloids and saponins, significantly inhibits *M. incognita* egg hatch by 98% from 2 days after incubation (DAI) and was evidenced more with 100% inhibition at 9 DAI in the in vitro studies. *M. incognita* (5000 eggs/plant) reproduction, number of eggs and juveniles, and galling were significantly suppressed by *Tithonia* residue treatment at a rate of 30 tons/ha on yam (*Discoria rotundata*) in a screen house.[98] A formulated product containing an extract from *Quillaja saponaria* (QL Agri 35 (QL)) decreased the convulsive movement of second stage juveniles of *M. incognita* after exposure for 8 days, and the most paralyzed juveniles were counted at the dose of 8 mg/L. There was also a gradual decrease in the number of juveniles emerging from egg masses of the same nematode species when the dose of *Q. saponaria* was increased from 0 to 8 mg/L.[99] Leaf and root meals from *Aster sedifolius* as well as the saponins extracted from the plant revealed nematicidal activity on *M. incognita*. Specifically, reproduction of the nematode was reduced by about 97% with 0.5 and 1 g/100 cm^3 soil of meals from leaves and roots.[100] Triterpenic saponins isolated from seeds of *Madhuca indica* and fruit pericarp from *Sapindus mukorossi* exhibited inhibitory effect against two phytoparasitic nematodes. Azadirachtin, salannin, nimbin, and desacetylnimbin were extracted from the seeds and oil of *Azadirachta indica* A. Juss. *M. indica* and *S. mukorossi* saponins were found to inhibit the movement of the preadult (J4) stage of *Rotylenchulus reniformis*, and the LC_{50} values were calculated at 68.8 and 181.9 μg/mL. Azadirachtin and the other limonoids affected the mobility of the secondary juvenile stage (J2) of *M. incognita* by 83.3 and 80.1%, respectively, at 0.5 mg/L. *M. indica* saponin (LC_{50} 220 μg/mL) exhibited a potentiating effect in the presence of azadirachtin in a 1:3 ratio (LC_{50} 120.1 μg/mL). A binary mixture (1:1) of azadirachtin and limonoids was found to show significant nematicidal activity against *M. incognita* (LC_{50} 70.9 μg/mL) and *R. reniformis* (LC_{50} 91.2 μg/mL).[82] Saponins and flavonoid rich brimstone leaf, *Morinda lucida*, was tested for its nematoxic effects on root-knot nematode in the laboratory and screen house. Brimstone leaf crude extract (50 and 100% concentrations) and brimstone leaf powder (1 and 2 t/ha) were used. Brimstone leaf significantly reduced the gall index of *Celosia argentea* compared with the control.[101] Finally, *Cestrum parqui*, a shrub used in Tunisia as an ornamental plant, contains saponins and is highly toxic to the eggs of *M. incognita* as measured in vitro.[102] Saponins also induce nematicide effects on *Xiphinema index* raising concern in the culture of *Vitis vinifera*.[103] *Medicago sativa* L., alfalfa, is the most known plant species within the *Medicago* genus. The plant has been extensively studied for its content of saponins, mainly consisting of triterpeneglycosides of medicagenic acid, possessing several biological properties including biocidal activity on different soil microorganisms. Saponins from *M. sativa* have been found effective in vitro against the virus-vector nematode *Xiphinema index*, the root-knot nematode *M. incognita*, and the potato cyst parasite *Globodera rostochiensis*. The nematicidal efficacy differed among the three assayed nematode species, *G. rostochiensis* being the most susceptible to the active compounds from alfalfa.[95]

2.6. Organic Acids. Vegetable oils contain large and heterogeneous quantities of saturated or unsaturated fatty acids, with medium to long esterified carbon chains, and esters of fatty acids with high molecular weight. In insects, they develop toxicity by inhalation and contact, suffocating by forming an impermeable film upon the cuticle. Some organic acids penetrate through the cuticle, disrupt the cellular membrane, and uncouple oxidative phosphorylation. Some fatty acids, such as oleic acid (C18), have their own insecticidal activities, whereas undecylenic (C11) acid has a lower toxicity but increases the activity of other insecticidal compounds.[8] Organic acids also act as nematicidals.[17]

Lantana camara Linn. var. *aculeata* is a poisonous plant, containing among others 11-oxo triterpenic acid. This compound was found to be active against root knot nematode *M. incognita* and showed an 85 to 90% mortality rate.[104] Seven constituents isolated from the aerial parts of *L. camara*, namely, pomolic acid, lantanolic acid, lantoic acid, camarin, lantacin, camarinin, and ursolic acid, were tested for nematicidal activity against the root-knot nematode *M. incognita*. Pomolic, lantanolic, and lantoic acids showed 100% mortality at 1 mg/mL concentration after 24 h, while camarin, lantacin, camarinin, and ursolic acid exhibited 100% mortality at this concentration after 48 h. These results are comparable to those obtained with the conventional nematicide furadan (100% mortality at 1 mg/mL concentration after 24 h).[105] Also lantanilic acid, camaric acid, and oleanolic acid isolated from the methanolic extract of the aerial parts of *L. camara* exhibited 98%, 95%, and 70% mortality, respectively, against *M. incognita* at 0.5% concentration. At this concentration, conventional nematicide furadan showed 100% mortality.[106]

Moreover, the nonessential amino acid L-3,4-dihydroxvphenylalanine (L-Dopa) was present at 6−9% in the seeds of *Mucuna* spp. When tested against the phytonematodes *M. incognita* and *H. glycines*, it exhibited nematicidal activity, and the LC_{50} values were calculated at 21 μg/mL and 0.17 μg/mL respectively.[107]

2.7. Phenolics, Flavonoids, and Quinones. According to a broad spectrum evaluation on the effects of phenylpropanoids on the behavior of *M. incognita*, repellents and motility inhibitors were found among the simple phenolic compounds. Flavonols stood out as repellent compounds, while they were, in their degraded form, also motility inhibitors. Salicylic acid was a strong attractant for *M. incognita*, but the compound was also nematicidal (LC_{50} of 46 μg/mL) and an irreversible inhibitor of hatching.[108] The nematicidal activity of phenolics has been previously reported.[1,28,80,109−112] Root leachates of a tropical weed named *L. camara*, used in combination with the plant growth-promoting rhizobacterium *Pseudomonas aeruginosa* against *M. javanica*, significantly reduced nematode population densities in roots and subsequent root-knot infection, and enhanced plant growth. Even though a high concentration of root leachate slightly reduced *P. aeruginosa* colonization in the rhizosphere and inner root tissues, the nematicidal efficacy of the bacterium was unaffected. The root leachate of *L. camara* was found to contain phenolic compounds, including *p*-hydroxybenzoic acid, vanillic acid, caffeic acid, ferulic acid, and a quercetinglycoside, 7-glucoside.[113] The ethyl acetate fraction of the crude methanolic extract of *Viola betonicifolia*, rich in flavonoid and phenolic contents, was found to be highly effective against *M. incognita* and *M. javanica*.[114] In vitro investigation of *Tagetes patula* L. flower polar extract against *Heterodera zeae* revealed activity based on the phenolic contents. In the nonpolar extract, a few fatty acids, their methyl esters, and thiophenes (including α-terthienyl) were detected. In studies of compounds obtained commercially, α-terthienyl and gallic and linoleic acids showed 100% mortality at concentrations of 0.125% after 24 h. Assessment of structure−activity relationships revealed that an increase in the number of hydroxyl groups in phenolic acids increased the activity; with fatty acids, activity depended on chain length and the number and position of double bonds.[115] Ethyl acetate extract of the branches of *Magnolia tripetala* exhibited nematicidal activity against *Bursaphelenchus xylophilus*, *Panagrellus redivivus*, and *Caenorhabditis elegans*. Two nematicidal phenolic compounds magnolol and honokiol were isolated from the extract based on bioassay-guided fractionation. The median lethal concentrations (LC_{50}) of the isolated compounds were 149.3 and 63.7 mg/L, respectively, against *B. xylophilus*, 74.5 and 75.9 mg/L, respectively, against *P. redivivus*, and 64.7 and 57.8 mg/L, respectively, against *C. elegans* at 48 h.[116] *Chromolaena odorata* is a widespread weed found in humid the tropical south, Southeast Asia, and West Africa, exhibiting nematicidal properties due to its phenolics, alkaloid, and amino acids contents.[117] Ether-soluble phenolics from the chicory rhizome exhibited nematicidal activity.[118] In a greenhouse experiment, thymol, a phenolic monoterpene added in soil at 0, 50, 100, and 150 mg/kg, showed synergistic effects in suppressing initial and final soil populations of *M. arenaria* in combination with 100 mg/kg benzaldehyde, an aromatic aldehyde present in nature as a moiety of plant cyanogenic glucosides. Significant reductions in root galling and cyst formation on soybean were attributable to thymol at ≥50 mg/kg.[32] The crude extract of *Arisana erubescens* exhibited significant nematicidal activity against *M. incognita* with a LC_{50} value of 258.11 μg/mL, while the LC_{50} values of the phenolic compounds schaftoside and isoschaftoside contained in extracts were 114.66 μg/mL and 323.09 μg/mL, respectively.[119] *Caernohabditis elegans* and *C. brissage* treatment with flavones induced embryonic and larval lethality that was pronounced in early larval stages. Specifically, flavone (2-phenyl chromone) LD_{50} values were calculated at 100 μM for both nematode species.[120] *Acacia gummifera* and *T. patula* aqueous extracts, rich in flavonoids, suppressed *Meloidogyne* spp., at 84% and 82%, while the extract of *Ononis natrix* and *Ceratonia siliqua* had a nematicidal effect against *Meloidogyne* spp., with 67% and 71% of mortality, respectively.[24] The internal aerial tissues of *Polygonum senegalense* containing common flavonoids such as quercetin, kaempferol, luteolin, and their glycosides as well as the stomach ache medicine *Psiadia punctulata* (Compositae) from which novel methylated flavonoids, kaurene, and trachyloban diterpenes have been found exhibit nematicidal activities.[121] *Nothofagus alessandri* and *N. pumilio* exhibit nematicidal activity against *Caenorhabditis elegans*. The discovery of the phytoalexin, pinosylvin, in the leaves, raises the possibility that *Nothofagus* in general and *N. alessandri* in particular may have induced chemical defense mechanisms.[122] Nonetheless, a negative efficacy result was obtained when fractionation of the methanolic extract from *Gochnatia barrosii* Cabrera (Asteraceae) leaves resulted in the isolation of the flavonol glycoside *trans*-tiliroside kaempferol 3-*O*-β-D-(6″-*O*-*E*-*p*-coumaroyl)-glucopyranoside that lacked activity at 500 μg/mL against *M. exigua* Goeldi larvae.[123] The Myrsinaceae are well established ethno-anthelmintics, harbingers of long alkyl side chain benzoquinones. The main component of the subfamily Myrsinodae is embelin, while for the Maesodae it is maesaquinone together with its 5-acetyl derivative; the distribution of these benzoquinones by their alkyl side chain length or the presence/absence of a 6-methyl group is in accordance with morphological subfamily delimitation. The benzoquinones show nematicidal activity. Also, plants belonging to the Polygonaceae family are widely used as ethno-anthelmintics, and the common anthelmintic anthraquinones are obtained from various *Rumex* species while the naphthalenic acetogenin derivative, nepodin is more selectively distributed.[121]

2.8. Piperamides. The PSMs produced by many species in the genus *Piper* are called piperamides among which capsaicin is obtained from the genus *Capsicum*, such as chili peppers (*Capsicum frutescens*, Mill.), and is characterized by nematicidal properties.[124,125]

Piperamides evoke contact toxicity and repellent and antifeedant activities, and at a biochemical level, they act as neurotoxins, and they photodegrade.[126] As an emerging biocide, very little data are available on the environmental fate of capsaicin, but initial assessment suggests that it will bind to sediments.[127]

2.9. Polyacetylenes and Polythienyls. *Tagetes* species, commonly called marigolds, of the botanical family Asteraceae, contain polyacetylenes and polythienyls exhibiting nematicidal properties.[1,128] Incorporating marigolds in *M. incognita*-infected cowpea or soybean fields has the potential to suppress nematode populations and reduce damage on the yields of the associated leguminous crops.[129] Interestingly, the variation of marigold nematicidal efficacy has been attributed to the differences in the way marigolds are used (e.g., intercrop/cover crop/soil amendment, seeding rate, and time between marigold and cash crop), the marigold cultivar, the species or races of target nematodes, the temperature, or the age of marigold plant.[130] Marigold suppressed *M. incognita* efficiently when planted immediately following a *M. incognita*-susceptible crop but did not enhance beneficial soil mesofauna including free-living nematodes and soil mesoarthropods.[131] Vermicomposts of African marigold effectively reduced *M. incognita* infection in tomato.[132] Aqueous marigold root extracts applied in root-knot nematode infested tomato seedlings resulted in increased plant height and plant leaf and fruit yield over the control treatment.[133] The response of the marigold species *T. patula* L. against 4 populations of *M. arenaria*, 13 of *M. hapla*, 3 of *M. javanica*, and 46 of *M. incognita* from Spain and Uruguay was studied in order to determine the races and virulence groups of each *Meloidogyne* species and the resistance of marigold characterized. Although no differences in response to marigold were observed among the virulence groups of *M. incognita*, differential behavior of populations among and within races A and B of *M. hapla* was observed showing that effective agronomic decisions should rely on the screening of the *M. hapla* population against which *T. patula* is going to be used.[134] The antagonistic effect of the nematode suppressive crops is carried over to reduce the infestation of plant-parasitic nematodes in the following crop. In fact, rotating marigold with other ornamental plants or rotating nematode-suppressive cover crops, such as sunn hemp, with field or cash crops may strongly suppress plant-parasitic nematode populations and benefit the following crop.[135]

2.10. Terpenes. Essential oils (EOs) are volatile, natural compounds with a strong odor, formed as PSMs by aromatic plants, exhibiting many biological activities. They are obtained by hydrodistillation, and they comprise heterogeneous mixtures of terpenes and terpenoids as well as other aromatic and aliphatic constituents, the biological actions of which are a very complicated concert of synergistic or antagonistic activities. Terpenes are formed structurally by coupling different numbers of isoprene units (5-carbon-base; C_5), and they may or may not contain oxygen (terpenoids and terpenes). The main terpenoid classes are monoterpenes (C_{10}), sesquiterpenes (C_{15}), hemiterpenes (C_5), diterpenes (C_{20}), triterpenes (C_{30}), and tetraterpenes (C_{40}).[136] Several factors can affect the chemical composition, toxicity, and bioactivity of the extracts such as the phenological age of the plant, percent humidity of the harvested material, and the method of extraction.[137] The broad spectrum of EO activities, ranging from insecticidal, antifeedant, repellent, oviposition deterrent, growth regulatory, and antivector activities, along with their wide availability from the flavor and fragrance industries, can make possible the commercialization of essential oil-based pesticides, particularly for organic food production.[138] Because of the great number of constituents, EOs affect several targets at the same time, decreasing the target organisms' resistance or adaptation, while the interspecific toxicity of individual oils and compounds is highly idiosyncratic. Phenols and alcohols induce cytotoxicity, damage the cellular and organelle membranes, act as prooxidants on proteins and DNA, and produce reactive oxygen species (ROS). Furocoumarins exposed to activating light, penetrate the cell without damaging the membranes, proteins, and DNA, and then produce radical reactions and an oxygen singlet. In some cases, essential oils and their components have demonstrated nuclear and cytoplasmic mutagenicity, acting on mitochondria and the respiratory system.[139] In general, EOs have favorable mammalian toxicity and are nonpersistant in the environment, for which reason they are exempted from the usual data requirements for registration in the USA.[140] Essential oils have been mostly studied for their activities against agricultural pests like insects and fungi,[140] while concerning their nematicidal potency[141] the focus of the international literature to a much lesser extent is briefly reviewed hereafter. Essential oils of *Carum carvi*, *Foeniculum vulgare*, *Mentha rotundifolia*, and *Mentha spicata* showed nematicidal activity against *Meloidogyne javanica* at a concentration of 1,000 μL/L. These EOs and those from *Origanum vulgare*, *O. syriacum*, and *Coridothymus capitatus* mixed in sandy soil at concentrations of 100 and 200 mg/kg reduced the root galling of cucumber seedlings in pot experiments.[142] EOs of *Eucalyptus citriodora*, *Eucalyptus hybrida*, and *Ocimum basilicum* followed by *Pelargonium graveolens*, *Cymbopogon martinii*, *Mentha arvensis*, *Mentha piperita*, and *Mentha spicata* oils were found nematicidal against *Meloidogyne incognita*. The eucalyptus (*E. citriodora* and *E. hybrida*) and Indian basil (*O. basilicum*) oils were highly toxic even at concentrations as low as 500 and 250 mg/L.[143] The EO of *Kadsura heteroclite*, containg as main components α-eudesmol (17.56%) and 4-terpineol (9.74%), is nematicidal against *M. incognita* with an LC_{50} value of 122.94 μg/mL.[144] The EOs of *A. triphylla*, *L. juneliana*, and *L. turbinate*, paralyze more than 80% of *Meloidogyne* sp. juveniles at 667 μL/L.[145] The clove oil concentration that reduced egg hatching by 50% (EC_{50}) is 0.097% (v/v), while the EC_{50} for second-stage juvenile (J2) paralysis was 0.145%. Volatiles from 5.0% clove oil reduce nematode egg hatching in water by 30% and decrease the viability of hatched J2 by as much as 100. In soil trials, the EC_{50} value is calculated at 0.192% clove oil.[146] *Chrysanthemum coronarium* EO concentrations of 2, 4, 8, and 16 μL/mL, significantly reduced the hatching, J2 survival, and reproduction rate of *Meloidogyne artiellia* in vitro.[147] Thyme and garlic EO applied at 150 μL/plant reduce root galling significantly (2.82 ± 0.47%) (5.53 ± 1.68%) and yield the lowest egg masses 2.46 ± 0.17 and 2.50 ± 0.22, respectively.[148] The mixture of *Haplophyllum* and *Plectranthus* EOs (1:1) was found to be highly toxic against *M. javanica* in vitro and similarly toxic to carbofuran, as it killed all nematode juveniles and inhibited the hatching of eggs at 12.5 μg/mL after 24 h of exposure time.[149] The EC_{50} values calculated for the EOs of *Origanum vulgare*, *Origanum dictamnus*, *Mentha pulegium*, *Melissa officinalis*, *Foeniculum vulgare*, *Pimpinela anisum*, *Eucalyptus meliodora*, and *Pistacia terebinthus* against *M. incognita* were 1.55, 1.72, 3.15, 6.15, 231, 269, 807, and 1116 μL/mL, respectively.[11,13] The EO of *Ruta chalepensis* L. paralyzes *M. incognita* and *M. javanica* ($EC_{50/1d}$ = 77.5 and 107.3 mg/L).[17] Interestingly, the residues of aromatic plants also seem to be nematicidal when used as soil amendments against root-knot nematodes. Specifically, residues from herb crop production can serve as organic amendments for the control of *M. javanica*, particularly tarragon, spearmint, and wild rocket, result in high mortality of the tested pathogens.[150] In pot trials with chickpea cv. PV 61, *Chrysanthemum coronarium* EO concentrations of 10−40 μL per 500 cm^3 soil, applied on sterile cotton pellets, also significantly reduced the nematode's reproduction rate.[147] Tomatoes grown in soil treated with a combination of *Haplophyllum* and *Plectranthus* EOs (1:1) developed fewer root galls than those grown in soil treated with higher doses of either oil.[149] Interestingly, growing peppermint (*Mentha piperita*) and spearmint (*M. spicata*) accessions for 8 or 12 weeks in *M. arenaria*-infested soil before tomatoes resulted in 90% reduction of root galls compared with tomato plants followed by tomato plants; whereas geraniol, eugenol, linalool, and peppermint oils at 1,500 mg oil/kg soil reduced the number of galls caused by *M. arenaria* without inducing any decrease in galling caused by *M. incognita*. Geraniol, linalool, and peppermint oil at 1,000 and 1,500 mg/L were phytotoxic to tomato.[151] When essential oils components are used individually, they also exhibit high nematicidal activity. *Ruta chalepensis* L. EO, a first-ranking volatile, namely, 2-undecanone, exhibits an activity of EC_{50} = 20.6 and 22.5 mg/L for *M. incognita* and *M. javanica*, respectively.[17] In our previous studies, we have demonstrated that the oxygenated compounds (alcohols and ketones) are generally more active than hydrocarbons and the activity against *M. incognita* decreases in the order of L-carvone, pulegone, *trans*-anethole, geraniol, eugenol, carvacrol, thymol, terpinen-4-ol, estragole, and γ-eudesmol.[13,15] Also, others report on the high nematicidal potency of compounds with hydroxyl and carbonyl groups such as borneol, carveol, citral, geraniol, and α-terpineol showing high nematicidal activity against *M. incognita* at a concentration of 250 mg/L. These monoterpenoids, at 100 and 250 mg/kg concentrations, diminished root galling of tomato plants in pot experiments.[152] Ascaridole, the predominant constituent (33.9−17.0%) of the nematicidal EO of *Croton regelianus*[153] and *Chenopodium ambrosioides* (27.27%), exhibits strong nematicidal activity against *M. incognita* with LC_{50} values of 49.55 μg/mL and 32.79 μg/mL, respectively.[154] Geraniol, thymol, and camphor are most effective against *M. javanica* J2s, with 91, 60, and 56% mortality, respectively, after 72 h of exposure, contrary to cineole, menthol, and pinene not showing any activity against this nematode species. Carvacrol, thymol, and geraniol were most effective against *M. incognita* J2s inducing mortalities of 100, 90, and 74%, respectively, after 72 h of exposure. Cineole was the least effective against *M. incognita*.[155] Also, according to Oka et al., carvacrol, *t*-anethole, thymol, and (+)-carvone are characterized by strong nematicidal potential against *M. javanica*, immobilizing the juveniles and inhibiting egg hatching at >125 μL/L in vitro, while mixed in sandy soil at concentrations of 75 and 150 mg/kg, it significantly reduced the root galling of cucumber seedlings. In pot experiments, nematicidal activity of the EOs and their components was confirmed at 200 and 150 mg/kg, respectively.[142] Low concentrations (1, 2, and 4 mg/L) of carvacrol, thymol, and linalool completely inhibited the hatching of *Meloidogyne incognita*.[156] In a field application, when thymol was applied as preplant fumigation through drip irrigation lines under polyethylene mulch at a rate of 73 kg/ha in combination with acibenzolar-*S*-methyl, applied primarily as a foliar spray at a concentration of 25 mg/L, it provided the greatest reduction in root galling on tomato (*Lycopersicon esculentum*).[157] The contribution of each terpene ingredient compound to the overall activity of an EO seems to be a rather complicated pattern of interactions[137,158] since they may act together synergistically or antagonistically. Notably, inactive constituents have at times some synergic effect on the active constituents, and although not active individually, their presence is necessary to achieve full toxicity. Some terpene pairs exhibiting high binary action (synergism) on *M. incognita* paralysis in decreasing order were *trans*-anethole/geraniol, *trans*-anethole/eugenol, carvacrol/eugenol, and geraniol/carvacrol.[15] It is therefore very important to understand the synergy and antagonism interactions among individual constituents of a nematicidal EO, as well as the responsible underlying biological mechanisms. Additionally, further investigation is required in order to evaluate interaction effects between nematicidal and nonnematicidal terpenes.

2.11. Conclusions. Overall, the approaches to integrated pest management have changed dramatically. While the botanical nematicides can be promising tools in *Meloidogyne* sp. control, the delineation of the targets or the mechanisms of action together with the practical application in the field are the challenges still to be overcome.[159] New knowledge is required for the production of novel nematicidal compounds, and plant secondary metabolites can play a major role in finding leading compounds for chemical synthesis. A plant metabolomic approach that allows one to study plant metabolites as end products of cellular processes can be a potent tool for this scope.

The biochemical understanding of the interaction between semiochemicals and root-knot nematodes, as well as the host−parasite interactions, is crucial in developing new and environmentally benign nematode control strategies.

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Notes

The authors declare no competing financial interest.

REFERENCES

(1) Chitwood, D. J. Phytochemical based strategies for nematode control (Review). *Annu. Rev. Phytopathol.* **2002**, *40*, 221−249.

(2) Qui, S. J.; Can, J. Y.; Liu, W. P.; Becker, J. O. Degradation and absorption of fosthiazate in soil. *J. Agric. Food Chem.* **2004**, *52*, 6239−6242.

(3) Karpouzas, D. G.; Karanasios, E.; Menkissoglu-Spiroudi, U. Enhanced microbial degradation of cadusafos in soils from potato monoculture: demonstration and characterization. *Chemosphere* **2004**, *56*, 549−559.

(4) Arbeli, Z.; Fuentes, C. L. Accelerated biodegradation of pesticides: An overview of the phenomenon, its basis and possible solutions; and a discussion on the tropical dimension. *Crop Prot.* **2007**, *26*, 1733−1746.

(5) Meher, H. C.; Gajbhiye, V. T.; Chawla, G.; Singh, G. Virulence development and genetic polymorphism in *Meloidogyne incognita* (Kofoid & White) Chitwood after prolonged exposure to sublethal concentrations of nematicides and continuous growing of resistant tomato cultivars. *Pest Manag. Sci.* **2009**, *65*, 1201−1207.

(6) Isman, M. B. Botanical insecticides, deterrents, and repellents in modern agriculture and an increasingly regulated world. *Annu. Rev. Entomol.* **2006**, *51*, 45−66.

(7) Isman, M. B. Botanical insecticides: for richer, for poorer. *Pest Manag. Sci.* **2008**, *64*, 8−11.

(8) Regnault-Roger, C.; Philogène, B. J. R. Past and current prospects for the use of botanicals and plant allelochemicals in integrated pest management. *Pharmaceut. Biol.* **2008**, *46*, 41−52.

(9) Al-Banna, L.; Darwish, R. M.; Aburjai, T. Effect of plant extracts and essential oils on root-knot nematode. *Phytopathol. Mediterr.* **2003**, *42*, 123−128.

(10) Ntalli, N. G.; Vargiu, S.; Menkissoglu-Spiroudi, U.; Caboni, P. Nematicidal carboxylic acids and aldehydes from *Melia azedarach* fruits. *J. Agric. Food Chem.* **2010**, *58*, 11390−11394.

(11) Ntalli, N. G.; Menkissoglu-Spiroudi, U.; Giannakou, I. O. Nematicidal activity of powder and extracts of *Melia azedarach* fruits against *Meloidogyne incognita*. *Ann. Appl. Biol.* **2010**, *156*, 309−317.

(12) Rodriges-Kabana, R.; Kloepper, J. W.; Weaver, C. F.; Robertson, D. G. Control of plant parasitic nematodes with furfural-a naturally occurring fumigant. *Nematropica* **1993**, *23*, 63−73.

(13) Ntalli, N. G.; Ferrari, F.; Giannakou, I. O.; Menkissoglu-Spiroudi, U. Phytochemistry and nematicidal activity of the essential oils from 8 Greek Lamiaceae aromatic plants and 13 terpene components. *J. Agric. Food Chem.* **2010**, *58*, 7856−7863.

(14) Oka, Y. Nematicidal activity of essential oil components against the root-knot nematode *Meloidogyne javanica*. *Nematology* **2001**, *3*, 159−164.

(15) Ntalli, N. G.; Ferrari, F.; Giannakou, I. O.; Menkissoglu-Spiroudi, U. Synergistic and antagonistic interactions of terpenes against *Meloidogyne incognita* and nematicidal activity of essential oils from 7 plants indigenous in Greece. *Pest Manag. Sci.* **2011**, *67*, 341−51.

(16) Caboni, P.; Ntalli, N. G.; Aissani, N.; Cavoski, I.; Angioni, A. Nematicidal activity of (E,E)-2,4-decadienal and (E)-2-decenal from *Ailanthus altissima* against *Meloidogyne javanica*. *J. Agric. Food Chem.* **2012**, *60*, 1146−51.

(17) Ntalli, N. G.; Manconi, F.; Leonti, M.; Maxia, A.; Caboni, P. Aliphatic ketones from *Ruta chalepensis* (Rutaceae) induce paralysis on root knot nematodes. *J. Agric. Food. Chem.* **2011**, *59*, 7098−7103.

(18) Soler-Serratosa, A.; Kokalis-Burelle, N.; Rodríguez-Kábana, R.; Weaver, C. F.; King, P. S. Allelochemicals for control of plant-parasitic nematodes. 1. In vivo nematicidal efficacy of thymol and thymol/benzaldehyde combinations. *Nematropica* **1996**, *26*, 57−71.

(19) Chitwood, D. J. Research on plant-parasitic nematode biology conducted by the United States Department of Agriculture-Agricultural Research Service. *Pest Manag. Sci.* **2003**, *59*, 748−53.

(20) Odeyemi, I. S.; Adewale, K. A. Phythonematoxic properties and nematicidal potential of *Tithonia diversifolia* extract and residue on *Meloidogyne incognita* infecting yam (*Discoria rotundata*). *Arch. Phytopathol. Plant Prot.* **2011**, *44*, 1745−1753.

(21) Thoden, T. C.; Boppré, M. Plants producing pyrrolizidine alkaloids: Sustainable tools for nematode management. *Nematology* **2010**, *12*, 1−24.

(22) Thoden, T. C.; Boppré, M.; Hallmann, J. Effects of pyrrolizidine alkaloids on the performance of plant-parasitic and free-living nematodes. *Pest Manag. Sci.* **2009**, *65*, 823−830.

(23) Olabiyi, T. I.; Oyedunmade, E. E. A.; Ibikunle, G. J. Phytochemical screening and nematoxic effect of brimstone, *Morinda lucida*, on nematode pests of amaranth, *Celosia argentea*. *Biol. Agric. Hortic.* **2008**, *26*, 131−137.

(24) El Allagui, N.; Tahrouch, S.; Bourijate, M.; Hatimi, A. Action of plant extracts on rot-knot nematods (*Meloidogyne* asp.) mortality 503. [Action de différents extraits végétaux sur la mortalité des nématodes à galles du genre Meloidogyne ssp.]. *Acta Bot. Gallica* **2007**, *154*, 503−509.

(25) Zagrobelny, M.; Bak, S.; Rasmussen, A. V.; Jørgensen, B.; Naumann, C. M.; Møller, B. L. Cyanogenic glucosides and plant-insect interactions. *Phytochemistry* **2004**, *65*, 293−306.

(26) Morant, A. V.; Jørgensen, K.; Jørgensen, B.; Dam, W.; Olsen, C. E.; Møller, L. B.; Bak, S. Lessons learned from metabolic engineering of cyanogenic glucosides. *Metabolomics* **2007**, *3*, 383−398.

(27) Bjarnholt, N.; Laegdsmand, M.; Hansen, H. C. B.; Jacobsend, O. H.; Møller, B. L. Leaching of cyanogenic glucosides and cyanide from white clover green manure. *Chemosphere* **2008**, *72*, 897−904.

(28) Carlsen, S. C. K.; Fomsgaard, I. S. Biologically active secondary metabolites in white clover (*Trifolium repens* L.): a review focusing on contents in the plant, plant−pest interactions and transformation. *Chemoecology* **2008**, *18*, 129−170.

(29) Majak, W. Mammalian metabolism of toxic glycosides from plants. *J. Toxicol. Toxin Rev.* **1992**, *11*, 1−40.

(30) Widmer, T. L.; Abawi, G. S. Relationship between levels of cyanide in sudangrass hybrids incorporated into soil and suppression of *Meloidogyne hapla*. *J. Nematol.* **2002**, *34*, 16−22.

(31) Magalhães, C. P.; Xavier-Filho, J.; Campos, F. A. P. Biochemical basis of the toxicity of manipueira (liquid extract of cassava roots) to nematodes and insects. *Phytochem. Anal.* **2000**, *11*, 57−60.

(32) Soler-Serratosa, A.; Kokalis-Burelle, N.; Rodríguez-Kábana, R.; Weaver, C. F.; King, P. S. Allelochemicals for control of plant-parasitic nematodes. 1. In vivo nematicidalefficacy of thymol and thymol/benzaldehyde combinations. *Nematropica* **1996**, *26*, 57−71.

(33) Zinovieva, S. V.; Udalova, Z. V.; Vasiljeva, I. S.; Paseschnichenko, V. A. Action of sterol glycosides on *Meloidogyne incognita* infecting tomato and cucumber roots. *Russ. J. Nematol.* **1997**, *5*, 77−80.

(34) Vasil'eva, I. S.; Udalova, Z. V.; Zinov'eva, S. V.; Paseshnichenko, V. A. Steroid furostanol glycosides: A new class of natural adaptogenes (review). *Appl. Biochem. Microbiol.* **2009**, *45*, 463−472.

(35) Udalova, Zh. V.; Zinov'eva, S. V.; Vasil'eva, I. S.; Paseshnichenko, V. A. Correlation between the structure of plant steroids and their effects on phytoparasitic nematodes. *Appl. Biochem. Microbiol.* **2004**, *40*, 93−97.

(36) Du, S. S.; Zhang, H. M.; Bai, C. Q.; Wang, C. F.; Liu, Q. Z.; Liu, Z. L.; Wang, Y. Y.; Deng, Z. W. Nematocidal flavone-C-glycosides against the root-knot nematode (*Meloidogyne incognita*) from *Arisaema erubescens* tubers. *Molecules* **2011**, *16*, 5079−5086.

(37) Mari, M.; Leoni, O.; Bernardi, R.; Neri, F.; Palmieri, S. Control of brown rot on stonefruit by synthetic and and glucosinolate-derived isothiocyanates. *Postharvest Biol. Technol.* **2008**, *47*, 61−67.

(38) Vig, A. P.; Rampal, G.; Thind, T. S.; Arora, S. Bio-protective effects of glucosinolates − A review. *LWT Food Sci. Technol.* **2009**, *42*, 1561−1572.

(39) Schlaeppi, K.; Abou-Mansour, E.; Buchala, A.; Mauch, F. Disease resistance of Arabidopsis to *Phytophthora brassicae* is established by the sequential action of indole glucosinolates and camalexin. *Plant J.* **2010**, *62*, 840−851.

(40) Gimsing, A. L.; Kirkegaard, J. A. Glucosinolates and biofumigation: fate of glucosinolates and their hydrolysis products in soil. *Phytochem. Rev.* **2009**, *8*, 299−310.

(41) Cao, A. C.; Zhang, W. J.; Liu, J. H. Progress in the alternatives to methyl bromide in soil disinfestation. *Plant Prot.* **2007**, *33*, 15−18.

(42) Pietro, D. P.; Gamliel., A.; Austerweil, M.; Steiner, B.; Beniches, M.; Peretz Alon, I.; Katan, J.. Accelerated degradation of metam-sodium and dazomet in soil: characterization and consequences for pathogen control. *Crop Prot.* **2003**, *22*, 635−646.

(43) Ben, W.; John, N. M.; Margaret, M. The soil organisms responsible for the enhanced biodegradation of metham sodium. *Biol. Fertil. Soils* **2001**, *34*, 264−269.

(44) Ahuja, I.; Rohloff, J.; Bones, A. M. Defence mechanisms of Brassicaceae: implications for plant-insect interactions and potential for integrated pest management. A review. *Agron. Sustainable Dev.* **2010**, *30*, 311−348.

(45) Monfort, A. S.; Csinos, J.; Desaeger, K.; Seebold, T. M.; Webster, J. C. Diaz-Perez. Evaluating Brassica species as an alternative control measure for rootknot nematode (*M. incognita*) in Georgia vegetable plasticulture. *Crop Prot.* **2007**, *26*, 1359−1368.

(46) Kissen, R.; Rossiter, J. T.; Bones, A. M. The 'mustard oil bomb': not so easy to assemble! Localization, expression and distribution of the components of the myrosinase enzyme system. *Phytochem. Rev.* **2009**, *8*, 69−86.

(47) Agerbirk, N.; De Vos, M.; Kim, J. H.; Jander, G. Indole glucosinolate breakdown and its biological effects. *Phytochem. Rev.* **2009**, *8*, 101−120.

(48) Zasada, I. A.; Meyer, S. L. F.; Morra, M. J. Brassicaceous seed meals as soil amendments to suppress the plant-parasitic nematodes *Pratylenchus penetrans* and *Meloidogyne incognita*. *J. Nematol.* **2009**, *41*, 221−227.

(49) Zasada, I. A.; Weiland, J. E.; Reed, R. L.; Stevens, J. F. Activity of meadowfoam (*Limnanthes alba*) seed meal glucolimnanthin degradation products against soilborne pathogens. *J. Agric. Food Chem.* **2012**, *60*, 339−345.

(50) Lazzeri, L.; Curto, G.; Dallavalle, E.; D'Avino, L.; Malaguti, L.; Santi, R.; Patalano, G. Nematicidal efficacy of biofumigation by defatted brassicaceae meal for control of *Meloidogyne incognita* (Kofoid et White) Chitw. on a full field zucchini crop. *J. Sustainable Agric.* **2009**, *33*, 349−358.

(51) López-Pérez, J. A.; Roubtsova, T.; De Cara García, M.; Ploeg, A. The potential of five winter-grown crops to reduce root-knot nematode damage and increase yield of tomato. *J. Nematol.* **2010**, *42*, 120−127.

(52) Lazzeri, L.; Curto, G.; Leoni, O.; Dallavalle, E. Effects of glucosinolates and their enzymatic hydrolysis products via myrosinase on the root-knot nematode *Meloidogyne incognita* (Kofoid et White) Chitw. *J. Agric. Food. Chem* **2004**, *52*, 6703−6707.

(53) Wu, H.; Wang, C. J.; Bian, X. W.; Zeng, S. Y.; Lin, K. C.; Wu, B.; Zhang, G. A.; Zhang, X. Nematicidal efficacy of isothiocyanates against root-knot nematode *Meloidogyne javanica* in cucumber. *Crop Prot.* **2011**, *30*, 33−37.

(54) Henderson, D. R.; Riga, E.; Ramirez, R. A.; Wilson, J.; Snyder, W. E. Mustard biofumigation disrupts biological control by *Steinernema* spp. nematodes in the soil. *Biol. Control* **2009**, *48*, 316−322.

(55) Manners, G. D. Citrus limonoids: analysis, bioactivity and biomedical prospects. *J. Agric. Food Chem.* **2007**, *55*, 8285−8294.

(56) Roy, A.; Saraf, S. Limonoids: Overview of significant bioactive triterpenes distributed in plants kingdom. *Biol. Pharm. Bull.* **2006**, *29*, 191−201.

(57) Connolly, J. D.; Hill, R. A. Triterpenoids. *Nat. Prod. Rep.* **2008**, *25*, 794−830.

(58) Akhtar, Y.; Yeoung, Y. R.; Isman, M. B. Comparative bioactivity of selected extracts from Meliaceae and some commercial botanical insecticides against two noctuid caterpillars, *Trichoplusia ni* and *Pseudaletia unipuncta*. *Phytochem. Rev.* **2008**, *7*, 77−88.

(59) Akhtar, M. Nematicidal potential of the neem tree *Azadirachta indica* (A. Juss). *Integ. Pest Manag. Rev.* **2000**, *5*, 57−66.

(60) Oka, Y.; Tkachi, N.; Shuker, S.; Yerumiyahu, U. Enhanced nematicidal activity of organic and inorganic ammonia-releasing amendments by *Azadirachta indica* extracts. *J. Nematol.* **2007**, *39*, 9−16.

(61) Schmutterer, H. Properties and potential of natural pesticides from the neem tree. *Azadirachta indica. Annu. Rev. Entomol.* **1990**, *35*, 271−97.

(62) El-Din, H. K. M.; Allam, A.; Tag, B. A. Nematicidal activity of some biopesticide agents and microorganisms against root-knot nematode on tomato plants under greenhouse conditions. *J. Plant Prot. Res.* **2012**, *52*, 47−52.

(63) Javed, N.; Gowen, S. R.; Inam-ul-Haq, M.; Abdullah, K.; Shahina, F. Systemic and persistent effect of neem (*Azadirachta indica*) formulations against root-knot nematodes, *Meloidogyne javanica* and their storage life. *Crop Prot.* **2007**, *26*, 911−916.

(64) Charleston, D. S.; Kfir, R.; Dicke, M.; Vet, L. E. M. Impact of botanical pesticides derived from *Melia azedarach* and *Azadirachta indica* on the biology of two parasitoid species of the diamondback moth. *Biol. Control* **2005**, *33*, 131−142.

(65) Sengottayan, S. N.; Sehoon, K. Effects of *Melia azedarach* L. extract on the teak defoliator *Hyblaea puera* Cramer (Lepidoptera: Hyblaeidae). *Crop Prot.* **2006**, *25*, 287−291.

(66) Morgan, E. D. Azadirachtin, a scientific gold mine. *Bioorg. Med. Chem.* **2009**, *17*, 4096−4105.

(67) Caboni, P.; Sarais, G.; Angioni, A.; Garcia, A. J.; Lai, F.; Dedola, F.; Cabras, P. Residues and persistence of neem formulations on strawberry after field treatment. *J. Agric. Food Chem.* **2006**, *54*, 10026−10032.

(68) Caboni, P.; Sarais, G.; Angioni, A.; Lai, F.; Dedola, F.; Cabras, P. Fate of azadirachtin A and related azadirachtoids on tomatoes after greenhouse treatment. *J. Environ. Sci. Health, Part B* **2009**, *44*, 598−605.

(69) Isman, M. B. Neem and other botanical insecticides: barriers to commercialization. *Phytoparasitica* **1997**, *25*, 339−344.

(70) Veitch, G. E.; Boyer, A.; Ley, S. V. The azadirachtin story. *Angew. Chem., Int. Ed.* **2008**, *47*, 9402−9429.

(71) Mordue (Luntz), A. J.; Blackwell, A. Azadirachtin: an update. *J. Insect Physiol.* **1993**, *39*, 903−924.

(72) Aldhous, P. Neem chemical: the pieces fall in to place. *Science* **1992**, *258*, 893.

(73) Salehzadeh, A.; Akhkha, A.; Cushley, W.; Adams, R. L. P.; Kusel, J. R.; Strang, R. H. C. The antimitotic effect of the neem terpenoid azadirachtin on cultured insect cells. *Insect Biochem. Mol. Biol.* **2003**, *33*, 681−689.

(74) Tiyagi, S. A.; Mahmood, I.; Khan, Z.; Ahmad, H. Biological control of soil-pathogenic nematodes infecting mungbean using *Pseudomonas fluorescens*. *Arch. Phytopathol. Plant Prot.* **2011**, *44*, 1770−1778.

(75) Hadian, S.; Rahnama, K.; Jamali, S.; Eskandari, A. Comparing neem extract with chemical control on *Fusarium oxysporum* and *Meloidogyne* incognita complex of tomato. *Adv. Environ. Biol.* **2011**, *5*, 2052−2057.

(76) Abo-Elyousr, K. A.; Khan, Z.; El-Morsi Award, M.; Abedel-Moneim, M. F. Evaluation of plant extracts and *Pseudomonas* spp. for control of root-knot nematode, *Meloidogyne incognita* on tomato. *Nematropica* **2010**, *40*, 289−299.

(77) Ashraf, M. S.; Khan, T. A. Integrated approach for the management of *Meloidogyne javanica* on eggplant using oil cakes and biocontrol agents. *Arch. Phytopathol. Plant Prot.* **2010**, *43*, 609−614.

(78) Haseeb, A.; Sharma, A.; Shukla, P. K. Studies on the management of root-knot nematode, *Meloidogyne incognita*-wilt fungus, *Fusarium oxysporum* disease complex of green gram, *Vigna radiata* cv ML-1108. *J. Zhejiang Univ. Sci.* **2005**, *6*, 736−742.

(79) Lynn, O. M.; Song, W. G.; Shim, J. K.; Kim, J. E.; Lee, K. Y. Effects of azadirachtin and neem-based formulations for the control of sweetpotato whitefly and root-knot nematode. *J. Appl. Biol. Chem.* **2010**, *53*, 598−604.

(80) Ntalli, N. G.; Menksissoglu-Spiroudi, U.; Giannakou, I. O.; Prophetou-Athanasiadou, D. A. Efficacy evaluation of a neem (*Azadirachta indica* A. Juss) formulation against root-knot nematodes *Meloidogyne incognita*. *Crop Prot.* **2009**, *28*, 489−494.

(81) Ntalli, N. G.; Cottiglia, F.; Bueno, C. A.; Alché, L. E.; Leonti, M.; Vargiu., S.; Menkissoglu-Spiroudi, U.; Caboni, P. Cytotoxic tirucullane triterpenoids from *Melia azedarach* fruits. *Molecules* **2010**, *15*, 5866−5877.

(82) Saha, S.; Walia, S.; Kumar, J.; Parmer, B. S.; Prasad, D. Synergistic/potentiation interaction between nematostatic constituents from *Azadirachta indica*, *Madhuca indica* and *Sapindus mukorossi*. *Arch. Phytopathol. Plant Prot.* **2010**, *43*, 357−367.

(83) Sarais, G.; Cossu, M.; Vargiu, S.; Cabras, P.; Caboni, P. Liquid chromatography electrospray ionization tandem mass spectrometric determination of quassin and neoquassin in fruits and vegetables. *J. Agric. Food Chem.* **2010**, *58*, 2807−2811.

(84) Kuriyama, T.; Ju, X. L.; Fusazaki, S.; Hishinuma, H.; Satou, T.; Koike, K.; Nikaido, T.; Ozoe, Y. Nematocidal quassinoids and bicyclophosphorothionates: A possible common mode of action on the GABA receptor. *Pest. Biochem. Physiol.* **2005**, *81*, 176−187.

(85) Prot, J. C.; Kornprob, J. M. Effects of quassinoids extracted from *Hannoa undulata* seed on the penetration and reproduction of *Meloidogyne javanica* on tomato. *Revue Nématol.* **1985**, *8*, 383−389.

(86) Watanabe, I.; Koike, K.; Satou, T.; Nikaido, T. Nematocidal activity of quassinoids against a species of Diplogastridae. *Biol. Pharmaceut. Bull.* **2000**, *23*, 723−726.

(87) Koul, O. Phytochemicals and insect control: An antifeedant approach. *Crit. Rev. Plant Sci.* **2008**, *27*, 1−24.

(88) Duke, S. O.; Baerson, S. R.; Dayan, F. E.; Rimando, A. M.; Scheffler, B. E.; Tellez, M. R.; Wedge, D. E.; Schrader, K. K.; Akey, D. H.; Arthur, F. H.; De Lucca, A. J.; Gibson, D. M.; Harrison, H. F., Jr.; Peterson, J. K.; Gealy, D. R.; Tworkoski, T.; Wilson, C. L.; Brad, M. United States Department of Agriculture-Agricultural Research Service research on natural products for pest management. *Pest Manag. Sci.* **2003**, *59*, 708−717.

(89) D'Addabbo, T.; Curto, G.; Santi, R.; Carella, A. Control of root-knot nematode *Meloidogyne incognita* by *Quillaja saponaria* extracts. *Atti delle Giornate Fitopatologiche* **2006**, *1*, 239−242.

(90) D'Addabbo, T.; Carbonara, T.; Leonetti, P.; Radicci, V.; Tava, A.; Avato, P. Control of plant parasitic nematodes with active saponins and biomass from *Medicago sativa*. *Phytochem. Rev.* **2010**, *10*, 503−519.

(91) Ribera, A.; Cotoras, M.; Zúñiga, G. E. Effect of extracts from in vitro-grown shoots of *Quillaja saponaria* Mol. on *Botrytis cinerea* Pers. *World J. Microbiol. Biotechnol.* **2008**, *24*, 1803−1811.

(92) Martín, R. S.; Magunacelaya, J. C. Control of plant-parasitic nematodes with extracts of Quillaja saponaria. *Nematology* **2005**, *7*, 577−585.

(93) Powell, G.; Hardie, J.; Pickett, J. A. The effects of antifeedant compounds and mineral oil on stylet penetration and transmission of potato virus Y by *Myzus persicae* (Sulz.) (Hom., Aphididae). *J. App. Entomol.* **1998**, *122*, 331−333.

(94) Leskinen, V.; Polonsky, J.; Bhatnagar, S. Antifeedant activity of quassinoids. *J. Chem. Ecol.* **1984**, *10*, 1497−1507.

(95) Lin, L. J.; Peiser, G.; Ying, B. P.; Mathias, K.; Karasina, F.; Wang, Z.; Itatani, J.; Green, L.; Hwang, Y. S. Identification of plant growth inhibitory principles in *Ailanthus altissima* and *Castela tortuosa*. *J. Agric. Food Chem.* **1995**, *43*, 1708−1711.

(96) D'Addabbo, T.; Carbonara, T.; Leonetti, P.; Radicci, V.; Tava, A.; Avato, P. Control of plant parasitic nematodes with active saponins and biomass from *Medicago sativa*. *Phytochem. Rev.* **2011**, *10*, 503−519.

(97) Leonetti, P.; D'Addabbo, T.; Avato, P.; Tava, A. Control of root-knot nematodes with biomasses from alfalfa (*Medicago sativa* L.) and their bioactive saponins. *Acta Hort.* **2011**, *914*, 225−228.

(98) Odeyemi, I. S.; Adewale, K. A. Phythonematoxic properties and nematicidal potential of Tithonia diversifolia extract and residue on *Meloidogyne incognita* infecting yam (*Discoria rotundata*). *Arch. Phytopathol. Plant Prot.* **2011**, *44*, 1745−1753.

(99) Giannakou, I. O. Efficacy of a formulated product containing *Quillaja saponaria* plant extracts for the control of root-knot nematodes. *Eur. J. Plant Pathol.* **2011**, *130*, 587−596.

(100) Di Vito, M.; Catalano, F.; Pecchia, P.; Cammareri, M.; Conicella, C. Effects of meal and saponins of aster caucasicus and of *A. sedifolius* on the control of nematodes. *Acta Hortic.* **2010**, *883*, 361−368.

(101) Olabiyi, T. I.; Oyedunmade, E. E. A.; Ibikunle, G. J. Phytochemical screening and nematoxic effect of brimstone, *Morinda lucida*, on nematode pests of amaranth, *Celosia argentea*. *Biol. Agric. Hortic.* **2008**, *26*, 131−137.

(102) Ikbal, C.; Monia, B. H. K.; Mounir, T.; Wassila, H.; Najet, R.; Dorsaf, B. A.; Mejda, D.; Habib, B. H. M. *Pesticidal potentialities of Cestrum parqui* saponins. *J. Agric. Res.* **2007**, *2*, 275−281.

(103) Fischer, M. J. C.; Pensec, F.; Demangeat, G.; Farine, S.; Chong, J.; Ramírez-Suero, M.; Mazet, F.; Bertsch, C. Impact of *Quillaja saponaria* saponins on grapevine ecosystem organisms. *Antonie Van Leeuwenhoek* **2011**, *100*, 197−206.

(104) Srivastava, M.; Kapoor, A.; Sharma, S.; Siddiqi, N. U.; Aslam, M. Microbial active triterpene from *Lantana camara*. *Biosci. Biotechnol. Res. Asia* **2006**, *3*, 505−507.

(105) Begum, S.; Zehra, S. Q.; Siddiqui, B. S.; Fayyaz, S.; Ramzan, M. Pentacyclic triterpenoids from the aerial parts of *Lantana camara* and their nematicidal activity. *Chem. Biodiversity* **2008**, *5*, 1856−1866.

(106) Qamar, F.; Begum, S.; Raza, S. M.; Wahab, A.; Siddiqui, B. S. Nematicidal natural products from the aerial parts of *Lantana camara* Linn. *Nat. Prod. Res.* **2005**, *19*, 609−613.

(107) Barbarosa, L. C. A.; Barcelos, F. F.; Demuner, A. J.; Santos, M. A. Chemical constituents from *Mucuna aterrima* with activity against *Meloidogyne incognita* and *Heterodera glycines*. *Nematropica* **1999**, *29*, 81−88.

(108) Wuyts, N.; Swennen, R.; De Waele, D. Effects of plant phenylpropanoid pathway products and selected terpenoids and alkaloids on the behaviour of the plant-parasitic nematodes *Radopholus similis*, *Pratylenchus penetrans* and *Meloidogyne incognita*. *Nematology* **2006**, *8*, 89−101.

(109) Simmonds, M. S. J.; Stevenson, P. C. Effects of isoflavonoids from *Cicer* on larvae of *Heliocoverpa armigera*. *J. Chem. Ecol.* **2001**, *27*, 965−977.

(110) Popa, V. I.; Dumitru, M.; Volf, I.; Anghel, N. Review. Lignin and polyphenols as allelochemicals. *Ind. Crop. Prod.* **2008**, *27*, 144−149.

(111) Wu, H. J.; Pratley, D. L.; Haig, T. Allelopathy in wheat (*Triticum aestivum*). *Ann. Appl. Biol.* **2001**, *139*, 1−9.

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

(113) Shazaukat, S. S.; Siddiqui, I. A.; Ali, N. I.; Ali, S. A.; Khan, G. H. Nematicidal and allelopathic responses of *Lantana camara* root extract. *Phytopathol. Mediterr.* **2003**, *42*, 71−78.

(114) Muhammad, N.; Saeed, M. Biological screening of *Viola betonicifolia* Smith whole plant. *Afr. J. Pharm. Pharmacol.* **2011**, *5*, 2323−2329.

(115) Faizi, S.; Fayyaz, S.; Bano, S.; Yawar Iqbal, E.; Lubna, L.; Siddiqi, H.; Naz, A. Isolation of nematicidal compounds from *Tagetes patula* L. yellow flowers: Structure-activity relationship studies against cyst nematode heterodera zeae infective stage larvae. *J. Agric. Food. Chem.* **2011**, *59*, 9080−9093.

(116) Li, G. H.; Dang, L. Z.; Hong, L. J.; Zheng, L. J.; Liu, F. F.; Li, L.; Liu, Y. J.; Zhang, K. Q. Nematicidal activity of honokiol and magnolol isolated from magnolia tripetala. *J. Phytopathol.* **2009**, *157*, 390−392.

(117) Ambika, S. R. Allelopathic Plants. 5. *Chromolaena odorata* (L) King and Robinson. *Allelopathol. J.* **2002**, *9*, 35−41.

(118) Nishimura, H.; Kondo, Y.; Nagasaka, T.; Satoh., A. Allelochemicals in chicory and utilization in processed foods. *J. Chem. Ecol.* **2000**, *26*, 2233−2241.

(119) Du, S. S.; Zhang, H. M.; Bai, C. Q.; Wang, C. F.; Liu, Q. Z.; Liu, Z. L.; Wang, Y. Y.; Deng, Z. W. Nematocidal flavone-C-glycosides against the root-knot nematode (*Meloidogyne incognita*) from *Arisaema erubescens* tubers. *Molecules* **2011**, *20*, 5079−86.

(120) Lee, Y. U.; Kawasaki, I.; Lim, Y.; Oh, W. S.; Paik, Y. K.; Shim, Y. H. Inhibition of developmental processes by flavone in *Caenorhabditis elegans* and its application to the pinewood nematode, *Bursaphelenchus xylophilus*. *Mol. Cells* **2008**, *26*, 171−174.

(121) Midiwo, J. O.; Yenesew, A.; Juma, B. F.; Derese, S.; Ayoo, J. A.; Aluoch, A. O.; Guchu, S. Bioactive compounds from some Kenyan ethnomedicinal plants: Myrsinaceae, Polygonaceae and *Psiadia punctulata* (Conference Paper). *Phytochem. Rev.* **2002**, *1*, 311−323.

(122) Russell, G. B.; Bowers, W. S.; Keesing, V.; Niemeyer, H. M.; Sevenet, T.; Vasanthaverni, S.; Wratten., S. D. Patterns of bioactivity and herbivory on nothofagus species from chile and new zealand. *J. Chem. Ecol.* **2000**, *26*, 41−56.

(123) dos Santos, H. M., Jr.; Tirelli, A. A.; Carvalho, H. W. P.; Oliveira, D. F.; do Prado, N. R. T.; Campos, V. P. Purification of the flavonoid trans-tiliroside from the methanolic extract of *Gochnatia barrosii* cabrera (Asteraceae) leaves and evaluation of the nematicidal activity. [Purificação do flavonóide trans-tilirosídeo do extrato metanólico das folhas de *Gochnatia barrosiicabrera* (Asteraceae) e avaliação da suaatividade nematicida]. *Cienc Agrotecnol.* **2010**, *34*, 1224−1231.

(124) Neves, W. S.; de Freitas, L. G.; Coutinho, M. M.; Dallemole-Giaretta, R.; Fabry, C. F. S.; Dhingra, O. D.; Ferraz, S. Nematicidal activity of extracts of red hot chilli pepper, mustard and garlic on *Meloidogyne javanica* in green house. *Summa Phytopathol.* **2009**, *35*, 255−261.

(125) Djian-Caporalino, C.; Fazari, A.; Arguel, M. J.; Vernie, T.; VandeCasteele, C.; Faure, I.; Brunoud, G.; Pijarowski, L.; Palloix, A.; Lefebvre, V.; Abad, P. Root-knot nematode (*Meloidogyne* spp.) Me resistance genes in pepper (*Capsicum annuum* L.) are clustered on the P9 chromosome. *Theor. Appl. Genet.* **2007**, *114*, 473−86.

(126) Scott, I. M.; Jensen, H. R.; PHilogene, B. J. R.; Arnason, J. T. A review of *Piper* spp. (Piperaceae) phytochemistry and insecticidal activity and mode of action. *Phytochem. Rev.* **2008**, *1*, 65−75.

(127) Thomas, K. V.; Brooks, S. The environmental fate and effects of antifouling paint biocides. *Biofouling* **2010**, *26*, 73−88.

(128) Wat, C. K.; Prasad, S. K.; Graham, E. A.; Partington, S.; Arnason, T.; Towers, G. H. N.; Lam, J. Photosensitization of invertebrates by natural polyacetylenes. *Biochem. Syst. Ecol* **1981**, *9*, 59−62.

(129) Adekunle, O. K. Amendment of soil with African marigold and sunn hemp for management of *Meloidogyne incognita* in selected legumes. *Crop Prot.* **2011**, *30*, 1392−1395.

(130) Hooks, C. R. R.; Wang, K. H.; Ploeg, A.; McSorley, R. Using marigold (*Tagetes* spp.) as a cover crop to protect crops from plant-parasitic nematodes. *Appl. Soil Ecol.* **2010**, *46*, 307−320.

(131) Marahatta, S. P.; Wang, K. H.; Sipes, B. S.; Hooks, C. R. R. Strip-tilled cover cropping for managing nematodes, soil mesoarthropods, and weeds in a bitter melon agroecosystem. *J. Nematol.* **2010**, *42*, 111−119.

(132) Pandey, R.; Kalra, A. Inhibitory effects of vermicompost produced from agro-waste of medicinal and aromatic plants on egg hatching in *Meloidogyne incognita* (Kofoid and White) Chitwood. *Curr. Sci.* **2010**, *98*, 833−835.

(133) Olabiyi, T. I. Pathogenicity study and nematoxic properties of some plant extracts on the root-knot nematode pest of tomato, *Lycopersicon esculentum* (L.) Mill. *Plant Pathol.* **2008**, *7*, 45−49.

(134) Piedra Buena, A.; Díez-Rojo, M. A.; López-Pérez, J. A.; Robertson, L.; Escuer, M.; Bello, A. Screening of *Tagetes patula* L. on different populations of *Meloidogyne*. *Crop Prot.* **2008**, *27*, 96−100.

(135) Wang, Q.; Li, Y.; Handoo, Z.; Klassen, W. Influence of cover crops on populations of soil nematodes. *Nematropica* **2007**, *37*, 79−92.

(136) Aharoni, A.; Jongsma, M. A.; Bouwmeester, H. J. Volatile science? Metabolic engineering of terpenoids in plants. *Trends Plant Sci.* **2005**, *10*, 594−602.

(137) Lahlou, M. Methods to study the phytochemistry and bioactivity of essential oils. *Phytother. Res.* **2004**, *18*, 435−448.

(138) Mohan, M.; Haider, S. Z.; Andola, H. C.; Purohit, V. K. Essential oils as green pesticides: For sustainable agriculture (Review). *Res. J. Pharm. Biol. Chem. Sci.* **2011**, *2*, 100−106.

(139) Bakkali, F.; Averbeck, S.; Averbeck, D.; Idaomar, M. Biological effects of essential oils-A review. *Food Chem. Toxicol.* **2008**, *46*, 446−475.

(140) Isman, M. B. Plant essential oils for pest and disease management. *Crop Prot.* **2000**, *19*, 603−608.

(141) Oka, Y.; Koltai, H.; Bar-Eyal, M.; Mor, M.; Sharon, E.; Chet, I.; Spiegel, Y. New strategies for the control of plant-parasitic nematodes. *Pest Manag. Sci.* **2000**, *56*, 983−988.

(142) Oka, Y.; Nacar, S.; Putievsky, E.; Ravid, U.; Yaniv, Z.; Spiegel, Y.. Nematicidal activity of essential oils and their components against the root-knot nematode. *Phytopathol.* **2000**, *90*, 710−715.

(143) Pandey, R.; Kalra, A.; Tandon, S.; Mehrotra, N.; Singh, H. N.; Kumar, S. Essential oils as potent sources of nematicidal compounds. *J. Phytopathol.* **2000**, *148*, 501−502.

(144) Li, H. Q.; Bai, C. Q.; Chu, S. S.; Zhou, L.; Du, S. S.; Liu, Z. L.; Liu, Q. Z. Chemical composition and toxicities of the essential oil derived from *Kadsura heteroclita* stems against Sitophilus zeamais and *Meloidogyne incognita*. *J. Med. Plants Res.* **2011**, *5*, 4943−4948.

(145) Duschatzky, C. B.; Martinez, A. N.; Almeida, N. V.; Bonivardo, S. L. Nematicidal activity of the essential oils of several Argentina plants against the root-knot nematode. *J. Essent. Oil Res.* **2004**, *16*, 626−628.

(146) Meyer, S. L. F.; Lakshman, D.,K.; Zasada, I.,A.; Vinyard, B. T.; Chitwood, D. J. Dose-response effects of clove oil from *Syzygium aromaticum* on the root-knot nematode *Meloidogyne incognita*. *Pest Manag Sci.* **2008**, *64*, 223−229.

(147) Pérez, M. P.; Navas-Cortés, J. A.; Pascual-Villalobos, M. J.; Castillo, P. Nematicidal activity of essential oils and organic amendments from Asteraceae against root-knot nematodes. *Plant Pathol.* **2003**, *52*, 395−401.

(148) Cetintas, R.; Yarba, M. M. Nematicidal effects of five plant essential oils on the southern root-knot. Nematode, *Meloidogyne incognita* Race 2. *J. Anim. Vet. Adv.* **2010**, *9*, 222−225.

(149) Onifade, A. K.; Fatope, M. O.; Deadman, M. L.; Al-Kindy, S. M. Z. Nematicidal activity of *Haplophyllum tuberculatum* and *Plectranthus cylindraceus* oils against *Meloidogyne javanica*. *Biochem. Syst. Ecol.* **2008**, *36*, 679−683.

(150) Klein, E.; Katan, J.; Gamliel, A. Combining residues of herb crops with soil heating for control of soilborne pathogens in a controlled laboratory system. *Crop Prot.* **2011**, *30*, 368−374.

(151) Walker, J. T.; Melin, J. B. *Mentha piperita*, *Mentha spicata* and effects of their essential oils on *Meloidogyne* in soils. *J. Nematol.* **1996**, *28*, 629−635.

(152) Echeverrigaray, S.; Zacaria, J.; Beltrão, R. Nematicidal activity of monoterpenoids against the root-knot nematode *Meloidogyne incognita*. *Phytopathology* **2010**, *100*, 199−203.

(153) Torres, M. C. M.; Assunção, J. C.; Santiago, G. M. P.; Andrade-Neto, M.; Silveira, E. R.; Costa-Lotufo, L. V.; Bezerra, D. P.; Filho, J. D. B. M.; Viana, F. A.; Pessoa, O. D. L. Larvicidal and nematicidal activities of the leaf essential oil of *Croton regelianus*. *Chem. Biodiversity* **2008**, *5*, 2724−2728.

(154) Chuan, Q. B.; Zhi, L. L.; Qi, Z. L. Nematicidal constituents from the essential oil of *Chenopodium Ambrosioides* aerial parts. *Eur. J. Chem.* **2011**, *8*, 143−148.

(155) Al-Banna, L.; Darwish, R. M.; Aburjai, T. Effect of plant extracts and essential oils on root-knot nematode. *Phytopathol. Mediterr.* **2003**, *42*, 123−128.

(156) Ibrahim, S. K.; Traboulsi, A. F.; El-Haj, S. Effect of essential oils and plant extracts on hatching, migration and mortality of *Meloidogyne incognita*. *Phytopathol. Mediterr.* **2006**, *45*, 238−246.

(157) Ji, P.; Momol, M. T.; Rich, J. R.; Olson, S. M.; Jones, J. B. Development of an integrated approach for managing bacterial wilt and root-knot on tomato under field conditions. *Plant Dis.* **2007**, *91*, 1321−1326.

(158) Jiang, Z.; Akhtar, Y.; Bradbury, R.; Zhang, X.; Isman, M. B. Comparative toxicity of essential oils of *Litsea pungens* and *Litsea cubeba* and blends of their major constituents against the cabbage looper, *Trichoplusia ni*. *J. Agric. Food Chem.* **2009**, *57*, 4833−4837.

(159) Agrios, G. N. Plant Diseases Caused by Nematodes. In *Plant Pathology*; Agrios, G. N., Ed.; Elsevier Academic Press Ltd.: London, 2005; pp 717.