Review

Chemical Composition and Nematicidal Properties of Sixteen Essential Oils—A Review

Trifone D’Addabbo (*) and Pinarosa Avato (*)

1 Institute for Sustainable Plant Protection, National Council of Research, Via Giovanni Amendola 122/D, 70126 Bari, Italy
2 Department of Pharmacy—Drug Sciences, University of Bari, Via Edoardo Orabona 4, 70125 Bari, Italy
* Correspondence: trifone.daddabbo@ipspscnr.it

Abstract: Essential oils (EOs) can be a large source of new food-safe and healthy nematicidal products, due to their strong activity on crop pathogens and pests, including phytoparasitic nematodes, as well as to their low environmental persistence. This review summarizes the results from our 10-year studies on chemical features and nematicidal properties of 16 EOs with different botanical origins and compositions, i.e., the EOs from Artemisia herba-alba Asso (Asteraceae), Cinnamomum camphora (L.) J. Presl. and C. verum J. Presl. (Lauraceae), Citrus aurantium L., C. aurantium var. amara L., Osbeck and Ruta graveolens L. (Rutaceae), Eucalyptus citriodora Hook, Eucalyptus globulus Labill. and Myrtaceae, Monarda didyma L., Monarda fistulosa L., Rosmarinus officinalis L. and Thymus zeylanicus Kosson (Lamiaceae), Pelargonium asperum Ehrh ex Wild (Geraniaceae) and Schinus molle L. (Anacardiaceae). All these EOs were chemically characterized and tested in vitro and/or in vivo for their activity against the phytoparasitic species Meloidogyne incognita Kofoid et White (Chitw.), Pratylenchus vulnus Allen et Jensen and Xiphinema index Thorne et Allen. Toxicity bioassays were conducted by exposing 2nd stage juveniles (J2) of M. incognita, mixed-age specimens of P. vulnus and adult females of X. index to 2–100 µg mL⁻¹ concentrations of EOs or EO’s major constituents for 4–96 h and checking mortality effect after a further 24–72 h permanence in water. Egg hatchability bioassays consisted in exposing (24–48 h) M. incognita egg masses to 500–1000 mg mL⁻¹ EO solutions followed by a 5-week hatching test in water. The in vivo experiments were undertaken in sandy soil strongly infested by M. incognita and treated with different doses of EOs, applied either in water solution or by fumigation. The effects of the treatments on nematode infestation on tomato and in soil were checked at the end of each experiment. Structure-activity relationships, as suggested by the different chemical compositions of tested EOs, were also highlighted. In agreement with literature data, our studies indicated that most of the tested EOs are highly suitable for the formulation of new safe nematicides, though still retarded by the lack of efficient stabilization processes and standardized EOs’ components and extraction techniques.

Keywords: aromatic plants; bionematicides; essential oils; fumigation; phytoparasitic nematodes; sustainable control; terpenes

1. Introduction

Food safety and human health preservation require severe restrictions on the use of synthetic pesticides traditionally applied for the control of crop pathogens and pests, due to their hazardous effects on soil, animals, and humans [1,2]. Phytochemicals from a large variety of plants have received an increasing interest as an alternative strategy for phytoparasitic nematode management [3–6]. Within plant-derived nematicidal compounds, a major role, as both a research topic and a source of new nematicides, has been increasingly provided to essential oils (EOs) from a wide range of aromatic and medicinal plants [7–9]. EOs’ activity has been extensively documented on root-knot nematodes of the genus...
Meloidogyne, as the phytonematode species economically most damaging and prone to worldwide spread [10–12], as well as on the pinewood nematode Bursaphelenchus xylophilus (Steiner and Buhrer) Nickle, due to the serious phytosanitary problems raised by this nematode in the pine forests of South Korea and Portugal [13–15]. Adversely, a minor attention was provided to EOs’ activity on other potentially harmful phytonematodes, such as the cyst-forming (Heterodera spp. and Globodera spp.) and root-lesion (Pratylenchus spp.) species or the stem nematode Ditylenchus dipsaci (Kühn) Filipjev [16–19]. The 10-year studies of our research group were addressed to characterize the chemical features and nematicidal properties of 16 EOs from different botanical and geographic origins, as well as their structure–activity relationship. Main findings from these studies are reviewed and commented in this work in comparison with the related literature data.

2. Essential Oils

EOs are mixtures of volatile lipophilic constituents generally produced by the specialized metabolism of aromatic and medicinal plants from a wide range of botanical families (Lamiaceae, Myrtaceae, Rutaceae, Apiaceae, and others) as responsible for their distinctive odor, flavor or scent, though also present in non-vascular plants such as some liverworts [20]. EOs are stored in plant secretory epithelial or parenchimal cells, forming structures of various kinds such as glandular trichomes or excretory idioblasts. The ecological role of EOs is still not clearly defined, though plant secretory products have been suggested to provide adaptive benefits, including plant protection against phytopathogens and parasites [21].

In general, EOs’ constituents are made up of relatively inert chemicals, consisting mainly of carbon and hydrogen, with one or more functional groups that provide alcohols, aldehydes, ketones, esters, and other chemical types contributing at different concentrations to an entire EO’s composition, with some of them present in very high amounts (up to 80%) and others only as traces.

Terpenoids are the most important group of specialized components of plant EOs and are principally represented by mono- and sesquiterpene compounds, sometimes associated with low molecular weight phenylpropanoids [22]. Plant terpenoids are synthesized via two different metabolic pathways: the mevalonate (MVA) pathway in cytosol leads to the formation of sesquiterpenoids, while the methylyerythritol phosphate (MEP) pathway occurring in chloroplasts results in the synthesis of monoterpenoids. Phenylpropanoids derive instead from the shikimate pathway mainly occurring in chloroplasts [23].

Plant EOs can be also characterized by phytochemical polymorphism, as individual plants from the same species can produce several chemotypes with different EOs’ compositional profiles, possibly resulting from diversification of EOs biosynthetic pathways under different environmental conditions [20]. This phenomenon was clearly evidenced within the Lamiaceae plants, in which several chemical types were identified in Origanum, Lippia, Mentha, Lavandula, and Ocimum species, though chemotypes were detected also within the Asteraceae, such as among Matricaria, Tagetes, and Achillea species. A summary of some of the most common components in plant essential oils is depicted in Figure 1.

Biological and pharmacological activity of EOs are often related to their main constituents, though minor components may also play a relevant role and sometimes act in a synergistic or antagonistic way with major components. Moreover, EOs’ biological and pharmacological effects are also related to their lipophilicity, which allows them to easily enter cells and interfere with membranes’ structure and fluidity by an increased permeabilization.

Products investigated in our studies were both commercial pure EOs from Eucalyptus citriodora Hook, E. globulus Labill. Citrus aurantium L., and Ruta graveolens L. (Rutaceae), Mentha piperita L. (Lamiaceae), Pelargonium asperum Ehrh ex Willd (Geraniaceae), Cinnamomum camphora (L.) J. Presl. and C. verum J. Presl. (Lauraceae), Schinus molle L. (Anacardiaceae), and Syzygium aromaticum (L.) Marry et Perry (Myrtaceae), as well as EOs directly extracted by hydrodistillation from wild Moroccan plants of Artemisia herba-alba
Asos (Asteraceae), *Citrus sinensis* L. Osbeck (Rutaceae), *Rosmarinus officinalis* L. and *Thymus satureioides* Cosson (Lamiaceae) or cultivated plants of two *Monarda* species, i.e., *M. didyma* L. and *M. fistulosa* L. (Lamiaceae) [24–27].

![Chemical structures of selected EOs' components.](image)

**Figure 1.** Chemical structures of selected EOs’ components.

The GC and GC-MS analysis of these EOs highlighted largely differentiated compositional profiles, mainly consisting of high concentrations of oxygenated monoterpenes (Figure 1). Carvacrol was present in the EOs from *M. dydima*, *M. fistulosa*, and *R. graveolens* (14, 24 and 15%, respectively), whereas its isomer thymol was among the monoterpenic components of EOs from *T. satureioides*, *M. dydima*, and *M. fistulosa* (12%, 6%, and 8%, respectively). However, EOs from *M. didyma* and *M. fistula* were also characterized by relevant amounts of γ-terpinene (22% and 25%, respectively). Large amounts of 1,8-cineole (syn eucalyptol) were found in the EOs of *R. officinalis* and *E. globulus* (47% and 92%, respectively) and in the EO of *C. camphora* (22%). Camphor was detected in the EOs of *A. herba-alba* (26%) and *R. officinalis* (12%), whereas main constituents of *P. asperum* EO were citronellol (35%) geraniol (22%) and linalool (13%).

The thujone isomers cis-thujone and trans-thujone were detected only in the *A. herba-alba* EO (25% and 16%, respectively), as well as borneol was present (29%) only in *T. satureioides* EO, α-cymene only in *M. didyma* and *M. fistulosa* EOs (13% and 11%, respectively), and menthol, menthone, and isomenthone only in the EO from *M. piperita* (55, 20 and 11%, respectively). The hydrocarbon monoterpenic limonene was almost the unique constituent of *C. australis* (95%) and *C. sinensis* (96%) EOs, though largely abundant (59%) also in *C. camphora* EO.

EOs of *S. aromaticum* and *R. graveolens* were prevalently constituted of eugenol (90%) and the aliphatic ketone 2-undecanone (83%), respectively. Analogously, citronellal prevailed in *E. citriodora* EO (84%) and the phenylpropanoid *E*-cynnamaldehyde (85%) in the EO of *C. verum*, which also included 13% of eugenol (Figure 1). In contrast, the EO of *S. molle* consisted of three main components, i.e., α-pinene, linalool, and eugenol, present at almost equal amounts: (15%, 10% and 12%, respectively).

### 3. Phytoparasitic Nematodes

Plant-parasitic nematodes are among the most serious constraints to world agriculture, globally causing damages estimated at USD 80 billion per year, most of which is due to root-knot species of the genus *Meloidogyne* [28]. Moreover, these losses are presum-
ably underestimated due to nonspecific symptoms and difficult recognition of nematode attacks [29].

Among the about 98 root-knot nematodes species included in the genus *Meloidogyne*, *M. incognita* Kofoid et White (Chitw.) is unanimously considered the most economically harmful as it is highly destructive on a wide range of herbaceous and tree crops [30] (Figure 2).

![Morphology and symptoms of the investigated nematode species](image)

Figure 2. Morphology and symptoms of the investigated nematode species: (A) juvenile, male and female of *Meloidogyne incognita*; (B) male and female of *Pratylenchus vulnus*; (C,D) whole body and tail of *Xiphinema index*; (E) tomato roots infested by *M. incognita*; (F) grapevine roots infested by *X. index*. Courtesy of Dr. Alberto Troccoli, IPSP-CNR, Bari, Italy.

A worldwide distribution on a large number of host crops is also presented by root lesion nematodes of genus *Pratylenchus*, quite rightly included among the most devastating nematode pests. In particular, *P. vulnus* Allen et Jensen is a severe parasite of fruit trees widespread in commercial orchards and nurseries of the Mediterranean region and United States [31].

The dagger nematode *Xiphinema index* Thorne et Allen is an ectoparasite species distributed throughout the world which feeds on grapevine root tips and directly causes root swelling and gall formation with a consequent reduction of plant growth. However, the economic impact of this species is mainly related to its vehiculation of dangerous grapevine viruses, such as the grapevine fanleaf virus [32].

In our studies, in vitro toxicity bioassays were conducted on 2nd stage juveniles (J2) of *M. incognita*, mixed-age specimens of *P. vulnus* and *X. index* females, which were exposed for 4–96 h intervals to 2–100 µg mL⁻¹ concentrations of EOs or their single constituents [26,27]. Egg hatchability bioassays were undertaken on *M. incognita* egg masses treated for 24–48 h with 500–1000 µg mL⁻¹ EO solutions [27]. Finally, in vivo studies on tomato (*Solanum lycopersicum* L.) were carried out in soil infested by *M. incognita* (20 eggs and J2 mL⁻¹ soil) and treated with 50–200 µg kg soil⁻¹ doses of the different EOs, applied either in water solution or by fumigation [24–27].

4. Nematicidal Activity of Experimental EOs

The EOs from *A. herba-alba* and *R. officinalis* were highly active on *M. incognita* J2 and *X. index* females, as both resulted in an almost complete mortality after a 96 h exposure to only 2 µg mL⁻¹ solutions, but were less toxic to *P. vulnus* [25]. The lesion nematode *P. vulnus* was less sensitive than *M. incognita* and *X. index* also to the EO from *T. saturejoides* and both Monarda EOs [25,26]. The two *Cinnamomum* EOs were differently active on *M. incognita* J2, as a similar 64% mortality occurred after a 24 h J2 exposure to 0.78 and 25 µg mL⁻¹ solutions of *C. verum* and *C. camphora*, respectively [27] (Figure 3).
Plants 2021, 10, x FOR PEER REVIEW 5 of 13

Figure 3. Aggregated mortality of M. incognita juveniles after a 24 h treatment with 0.78–100 μg mL−1 solutions of 10 different essential oils.

Analogously, toxicity to M. incognita J2 largely differed between the two Eucalyptus EOs, as only an 8 h exposure to a 12.5 μg mL−1 solution of E. citriodora EO was enough to cause more than 90% J2 mortality, while similar rates were reached only after a 24 h immersion in a 100 μg mL−1 solution of the E. globulus EO.

A moderate toxicity to root-knot nematode J2 was recorded for the EOs of M. piperita, S. molle, and P. asperum. Results showed more than 80% mortalities only at concentrations ≥50 μg mL−1, whereas a strong activity was provided by the EOs of R. graveolens (90% J2 mortality after a 8 h exposure to a 12 μg mL−1 solution) and S. aromaticum (30% mortality after a 24 h permanence in ≤6.25 μg mL−1 EO solutions) [27].

Both C. sinensis and C. aurantium EOs were weakly active on M. incognita, while C. sinensis EO showed a consistently higher toxicity to P. vulnus (more than 73% peak mortality) [25,27]. Adversely, solutions of both Monarda EOs were strongly toxic to M. incognita J2 but less active on P. vulnus, reaching 80–83% mortality rates after 24 h exposures to 12.5 and 100 μg mL−1 concentrations, respectively [26]. The 24 h LD50 values indicated EOs of A. herba-alba and C. verum as the most toxic to M. incognita J2, followed by the two Monarda EOs and EOs from E. citriodora, R. graveolens, and S. aromaticum, while the poorest activity was confirmed for the EOs from the two Citrus species (Table 1).

Table 1. LD50 values of tested essential oils at a 24 h exposure of M. incognita J2.

| EOs                            | LD50 Values (μg mL−1) |
|--------------------------------|----------------------|
| Artemisia herba-alba            | 0.5                  |
| Cinnamomum camphora            | 22.9                 |
| Cinnamomum verum               | 0.1                  |
| Citrus aurantium               | >> *                 |
| Citrus sinensis                | >>                   |
| Eucalyptus citriodora          | 2.4                  |
| Eucalyptus globulus            | 26.7                 |
| Mentha piperita                | 20.7                 |
| Monarda dydima                 | 1.0                  |
| Monarda fistulosa              | 1.0                  |
| Pelargonium asperum            | 13.0                 |
| Rosmarinus officinalis         | 51.8                 |
| Ruta graveolens                | 2.3                  |
| Schinus molle                  | 22.6                 |
| Syzygium aromaticum            | 2.1                  |
| Thymus satureoides             | 61.9                 |

* >> = largely above the range of tested concentrations.
In addition to their toxicity to infective J2, the tested EOs also variously affected the hatchability (Figure 4) of root-knot nematode eggs [26,27]. A 96 h exposure of M. incognita egg masses to a 500 µg mL\(^{-1}\) solution of EOs of C. verum and R. graveolens reduced the percentage of egg hatch to only 1.2% and 7.0%, respectively. Analogously, egg hatchability was strongly limited by similar treatments with M. didyma and, at least instance, M. fistulosa EOs. A lower but significant egg hatch inhibition was also caused by the two Eucalyptus EOs, as well as by the EOs of P. asperum, S. molle, and S. aromaticum. Adversely, poor or nil effects on root-knot nematode egg viability were found for C. aurantium and M. piperita EOs.

![Figure 4](https://example.com/figure4.png)

**Figure 4.** Relative hatchability of M. incognita eggs after a 48 h egg mass exposure to 500 or 1000 µg mL\(^{-1}\) solutions of 12 different essential oils.

In the experiments in soil, the strongest suppression of gall formation and nematode egg density on tomato roots (Figure 5) occurred after soil treatments with the EOs from E. citriodora, E. globulus, M. piperita, *P. asperum*, and R. graveolens, applied at 50–200 µg kg\(^{-1}\) soil doses either by fumigation or in an aqueous suspension [24,27]. Nematode infestation on tomato roots was also strongly suppressed after soil fumigation with the same range of doses of A. herba-alba, R. officinalis, and T. satureoides EOs [25], as well as by soil irrigation with 50–200 µg kg\(^{-1}\) soil doses of EOs from S. aromaticum, C. verum, and E. citriodora or M. didyma and M. fistulosa EOs [26,27] (Figure 6). Adversely, the lowest suppressive performance was provided by the soil treatments with C. aurantium and C. sinensis EOs, in good agreement with the poor or limited in vitro activity of these two EOs.

No literature data were available on the nematicidal activity of C. aurantium, S. molle, and *Monarda* EOs, while only single in vitro assays stated a limited toxicity to root-knot nematode J2 and eggs of EOs from C. sinensis and A. herba-alba and, adversely, a strong toxicity of *T. satureoides* EO [33,34].

Previous reports on the nematotoxicity of the other EOs investigated in our studies were mostly referred to in vitro assays on root-knot nematode species with EO samples not always chemically characterized, while toxicity to other phytonematode species was poorly or not at all documented. Most of these studies generally agreed with data from our experiments.

EOs from *Eucalyptus* species, also including E. citriodora and E. globulus, were always found to reduce J2 motility and viability and egg hatchability of different *Meloidogyne* species [12,35,36]. In agreement with our data, nematicidal properties of *Cinnamomum* EOs were described as consistently variable among the species, with a moderate suppressiveness of *C. camphora* EO to *M. incognita* on tomato and a strong in vitro toxicity of the EO of *C.
verum to the root-knot species M. incognita and M. graminicola Golden and Birchfield and the pine wood nematode B. xylophilus [13,14,37].

In accordance with the strong toxicity to M. incognita and P. vulnus observed in our studies, EOs of R. graveolens and S. aromaticum were described as highly active on J2 and eggs of M. incognita, M. chitwoodii Golden, O’Bannon, Santo and Finley, and M. exigua Goeldi [35,38,39], as well as on different stages of B. xylophilus [13,15]. Contrasting a greenhouse study of Meyer et al. [40] did not find any significant reduction of M. incognita population on various vegetable crops in soil treated with a S. aromaticum EO formulation.

The low activity of M. piperita EO in our experiments is also confirmed by literature data, which reported a poor in vitro toxicity of this EO to root-knot nematode J2 and eggs and its scarce effectiveness on the infestation of M. arenaria Chitwood on tomato in soil [11,12,41].

The EOs from P. asperum and R. officinalis resulted highly toxic to M. incognita in all our in vitro and in vivo experiments, but were generally documented as poorly active on root-knot nematode J2 and eggs by previous in vitro assays [10–12,33]. Contrastingly, experimental applications of R. officinalis EO to soil resulted in a strong reduction of the

Figure 5. Tomato roots from soil infested by M. incognita, non-treated and treated with EOs from E. globulus and P. asperum (100 µg Kg⁻¹ soil), or nematicide fenamiphos.

Figure 6. Relative suppression (non-treated soil = 0) of M. incognita multiplication on tomato roots after soil treatment with a 100 µg Kg⁻¹ soil dose of 16 different essential oils.
infestation of *M. incognita* on tomato [42] as well as of *M. javanica* and *P. brachyurus* (Godfrey) Filipjev and Schuurmans Stekhoven on soybean, *Glycine max* (L.) Merr. [43].

A consistent documentation is also available for the nematicidal properties of single EOs’ constituents. Carvacrol and its isomer thymol, as common components of EOs from several aromatic plants, were stated for numerous biological/pharmacological effects [44–47]. Data of Laquale et al. [26] proved a strong in vitro toxicity of carvacrol to infective stages of *M. incognita* and *P. vulnus* and its inhibitory effect on *M. incognita* egg hatch, confirming the strong in vitro toxicity of carvacrol to *M. incognita* and *M. javanica* J2 and eggs described in literature studies [11,36,48]. In addition, *M. javanica* infestation on tomato were found to be strongly reduced or even completely suppressed by soil treatments with carvacrol [11,48]. Thymol was also described by a number of reports as highly toxic, though less than carvacrol, to infective stages of root-knot nematodes [25,26,36,49–51] and to the pine nematode *B. xylophilus* [52], while a low in vitro sensitivity to thymol was observed for *P. vulnus* [26]. In agreement, greenhouse studies on thymol application to soil described a sharp decline of population densities of *M. arenaria* and of the soybean cyst nematode *Heterodera glycines* Ichinohe [53].

Eugenol, the dominant (89.6%) constituent of *S. aromaticum* EO, is a 2-alkyl(oxy)phenol sharing with carvacrol and thymol either some chemical features and a strong nematicotoxic effect. In vitro studies on *M. incognita* and *M. javanica* documented an almost complete J2 mortality and a strong reduction of egg differentiation and hatch following treatments with eugenol, either alone or in synergistic combination with other EO’s constituents [37,51,54–56]. Consistently, treatments with eugenol in soil infested by *M. incognita* or *M. arenaria* were able to suppress female and egg density and gall formation on tomato roots [41,56]. In contrast, a low activity of eugenol was observed on other phytonematodes, such as *B. xylophilus* and *P. penetrans* Filipjev and Schuurmans Stekhoven [16,57].

The main constituent of *R. graveolens* EO, 2-undecanone, was only stated for strong in vitro effects on root-knot nematode J2 and eggs [57,58], while literature data on the nematicidal efficacy of *E. cinnamaldehyde*, the major component of *Cinnamomum* EOs, are referred to its strong in vitro activity on *B. xylophilus* [14] and a high suppressiveness to *M. incognita* infestation on soybean when applied to soil [59,60].

Nematicidal performance of the major components of *P. asperum* EO, i.e., linalool, citronellol, and geraniol, varied according to the tested nematode species, as they were proved for a strong in vitro and in vivo activity on *Meloidogyne* species [11,50,55,61], but only moderately active on the soil saprophytic nematode *Caenorhabditis elegans* Maupas and the lesion nematode *P. penetrans* [16]. A synergistic activity of these three compounds was also suggested by their lower activity on *M. incognita* compared with the whole *P. asperum* EO [10].

Contrasting data are available for 1,8-cineole and limonene, the main constituents of *E. globulus* and *C. sinensis* EOs, respectively, as well as for camphor and α-pinene. In our studies, 1,8-cineole was found highly toxic to *M. incognita*, *P. vulnus*, and *X. index* [25], while it resulted poorly active in other studies on root-knot nematode J2 and eggs [36,49–51]. The poor activity of limonene on *M. incognita* J2 detected in our experiments [25] was in agreement with the total inactivity on *M. javanica* J2 reported by Santana et al. [34] but in contrast to the high toxicity of limonene to root-knot nematodes described by other reports [11,33,50]. Analogously, poor effects of camphor and α-pinene constantly observed by us on *M. incognita*, *P. vulnus*, and *X. index* [25] disagree with previous reports of a strong activity on the same root-knot species [49,50]. Regarding other EOs compounds not tested in our experiments, thujone isomers, i.e., the main constituents of the *A. herba-alba* EO, were indicated as moderately or poorly toxic to *M. incognita* and *M. javanica* J2, respectively, as well as not significantly active on other nematode species, such as *C. elegans* and emphP. penetrans [16,49]. The two main components of *M. piperita* EO, menthol and menthone, were also described for a limited in vitro toxicity to *M. incognita* and *M. javanica* [50,51,62]. Poor information was available on nematicidal activity of other EOs’ con-
5. Structure-Activity Relationship: Some Considerations

Analysis of compositional profiles and nematicidal performances of the 16 EOs as well as of structure of their major constituents allowed some considerations on structure-activity relationships. As documented by specific studies, toxicity of natural terpenoids to nematode and bacterial and microbial systems is influenced by type and position of functional groups in their molecular structure [11,24,25,27,64]. In particular, it has been shown that biocidal activity of monoterpenoids is enhanced by the presence of an oxygen-related function (aldehyde, ketone, or alcohol group) in their molecule as well as by the presence of a double bond system which would favor biological processes involving transfer of electrons, thus increasing terpenes reactivity towards nematodes [27,64]. Consistently, our in vitro assays [25,27] evidenced that EOs rich in citronellal, citronellol, linalool, geraniol, and E-cinnamaldehyde, such as those from C. verum, P. asperum, and E. citrodora, were highly active against M. incognita. In agreement, the ketone monoterpenoid thujone was also strongly toxic to root-knot nematode J2 and eggs in the in vitro experiments reported in literature [16,49]. Moreover, it has been described that acyclic monoterpenoids are more active than cyclic terpenoids with the same above functional groups [64]. This could explain the relatively lower nematicidal effect of menthol and menthane-type monoterpenoids or 1,8-cineole-containing EOs, such as those of M. piperita or E. globulus [24,27]. This was also consistent with the lower activity on M. incognita J2 of E. globulus EO compared with E. citrodora, which was characterized by E-cinnamaldehyde. On the other hand, this was somehow in contrast with results of Avato et al. [25], which described a strong time-dependent toxicity of 1,8-cineole on the three nematodes M. incognita, P. vulnus, and X. index. In agreement with the above findings on structure-activity requirements, terpenes without reactive functional groups and EOs with a high content of them did not show a relevant nematicidal activity, as found in our studies for γ-terpinene, α-pinene, limonene, and o-cymene as well as for the rich-in-limonene EOs of C. aurantium and C. sinensis [25,27].

Consistently with other studies [27,65], phenolics-containing EOs used in our investigations exerted a strong nematicidal activity, as observed for S. aromaticum EO, with a high content of the 2-alkyl(oxy) phenol eugenol, EOs of M. didyma and M. fistulosa, containing the phenolic monoterpenes carvacrol, and for T. satureioides EO, which showed a high amount of thymol. Analogously, the toxicity of T. satureioides EO to M. incognita could be at least partially related to the presence of thymol. Reactivity of phenolic molecules is related with the redox properties given by the presence of the hydroxyl group in their aromatic ring and, possibly, by the presence of a spacing group, such as, for example, the methoxyl group in the eugenol structure. As demonstrated in a targeted study on its structure-activity relationship, the bioactivity of eugenol and related molecules is also dependent on the allylic double bond which, with the phenolic proton, is an essential structural feature for the molecule interaction with cellular systems [66]. Thus, the chemical structure of phenols plays an important role in their ability to scavenge free radicals and related reactive species formed in many physiological processes and the anti-oxidant activity exerted by these compounds can also reasonably be involved in their toxic effects to phytonematodes.

6. Conclusions

Analysis of literature studies and our experimental findings clearly indicate a high potential of EOs or their pure constituents as sources of new effective nematicidal products suitable for nematode management of high-value horticultural and fruit crops. These new EO-based nematicides could have promising market prospects, joining a high nematicidal performance to environmental safety related to a low toxicity on non-target vertebrates [67].

Despite these positive features, presence on the market of EOs-derived nematicides is still poor and is limited to a few products based on mixtures of synthetic analogues of EO’s components such as thymol, geraniol, and eugenol. Success of these potential
products seems to be impeded by some unsolved key issues. Firstly, the poor knowledge of mechanisms of EOs activity and of nematode target sites. The hypotheses of an anticholinesterase activity or an alteration of cell membrane permeability suggested by literature data [11,68] have still not received confirmation from updated studies. A standardized quanti-qualitative composition of EOs raw materials, mainly achievable by using quality plant sources and appropriate extraction techniques, is also needed for ensuring homogeneity and reproducibility of nematicidal efficacy of derivative products [69]. Volatility and difficult vehiculation by irrigation water of EOs also makes the development of efficient stabilization processes necessary, such as EOs micro- or nanoencapsulation in biopolymers, to ensure slow release and water solubility of active constituents [70,71]. Finally, a simplification of the complex and expensive biopesticide registration procedures is strongly required, to encourage the development of potential EO-based nematicides by small or medium industrial companies, i.e., the most interested in biopesticide market niche.

**Author Contributions:** T.D. and P.A. equally contributed to conceptualization, methodology, visualization, writing, review, and editing. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** The data presented in this study are available on request from the corresponding author. The data are not publicly available due to journals' copyright.

**Conflicts of Interest:** The authors declare no conflict of interest.

**References**

1. Carvalho, F.P. Pesticides, environment, and food safety. *Food Energy Secur.* **2017**, *6*, 48–60. [CrossRef]
2. Tang, F.H.M.; Lenzen, M.; McBratney, A.; Maggi, F. Risk of pesticide pollution at the global scale. *Nat. Geosci.* **2021**, *14*, 206–210. [CrossRef]
3. Argentieri, M.P.; D’Addabbo, T.; Tava, A.; Agostinelli, A.; Jurzysta, M.; Avato, P. Evaluation of nematicidal properties of saponins from *Medicago* spp. *Eur. J. Plant Pathol.* **2007**, *120*, 189–197. [CrossRef]
4. Ntalί, N.G.; Caboni, P. Botanical nematicides: A review. *J. Agric. Food Chem.* **2013**, *61*, 791–802. [CrossRef]
5. D’Addabbo, T.; Laquale, S.; Lovelli, S.; Candido, V.; Avato, P. Biocide plants as a sustainable tool for the control of pests and pathogens in vegetable cropping systems. *Ital. J. Agron.* **2014**, *9*, 137–145. [CrossRef]
6. Andrés, M.F.; González-Coloma, A.; Sanz, J.; Burillo, J.; Sainz, P. Nematicidal activity of essential oils: A review. *Phytochem. Rev.* **2012**, *11*, 371–390. [CrossRef]
7. Isman, M.B. Plant essential oils for pest and disease management. *Crop Prot.* **2000**, *19*, 603–608. [CrossRef]
8. Bakkali, F.; Averbeck, S.; Averbeck, D.; Idaomar, M. Biological effects of essential oils—A review. *Food Chem. Toxicol.* **2008**, *46*, 446–475. [CrossRef] [PubMed]
9. Pandey, R.; Kalra, A.; Tandon, S.; Mehrotra, N.; Singh, H.N.; Kumar, S. EOs as potent sources of nematicidal compounds. *J. Phytopathol.* **2000**, *148*, 501–502. [CrossRef]
10. Kong, J.O.; Lee, S.M.; Moon, Y.S.; Lee, S.G.; Ahn, Y.J. Nematicidal activity of cassia and cinnamon oil compounds and related compounds toward *Bursaphelenchus xylophilus* (Nematoda: Parasitaphelenchidae). *J. Nematol.* **2007**, *39*, 31–36. [PubMed]
11. Faria, J.M.; Barbosa, P.; Bennett, R.N.; Mota, M.; Figueiredo, A.C. Bioactivity against *Bursaphelenchus xylophilus*: Nematotoxicity from essential oils, essential oils fractions and decoction waters. *Phytochemistry* **2013**, *9*, 220–228. [CrossRef]
12. Tsao, R.; Yu, Q. Nematicidal activity of monoterpenoid compounds against economically important nematodes in agriculture. *J. Essent. Oil Res.* **2000**, *12*, 350–354. [CrossRef]
17. Zouhar, M.; Douda, O.; Lhotský, D.; Pavela, R. Effect of plant essential oils on mortality of the stem nematode (*Ditylenchus dipsaci*). *Plant Prot. Sci.* 2009, 45, 66–73. [CrossRef]

18. Buda, V.; Čepulytė-Rakauskienė, R. The effect of linalool on second-stage juveniles of the potato cyst nematodes *Globodera rostochiensis* and *G. pallida*. *J. Nematol.* 2011, 43, 49–151.

19. Stavropoulou, E.; Nasiou, E.; Skia, P.; Giannakou, I.O. Effects of four terpenes on the mortality of *Ditylenchus dipsaci* (Kühn). *Filipjev. Eur. J. Plant Pathol.* 2021, 160, 137–146. [CrossRef]

20. Franz, C.; Novak, J. Sources of Essential Oils. In *Handbook of Essential Oils—Science, Technology, and Applications*; Baser, K.H.C., Buckbauer, G., Eds.; CRC Press: London, UK, 2010; pp. 39–81.

21. Lange, B.M. The evolution of plant secretory structures and emergence of terpenoid chemical diversity. *Ann. Rev. Plant Biol.* 2015, 66, 139–159. [CrossRef]

22. Baser, K.H.C.; Demirci, F. Chemistry of essential oils. In *Flavour and Fragrances—Chemistry Bioprocessing and Sustainability*; Berger, R.G., Ed.; Springer: Berlin/Heidelberg, Germany, 2007; pp. 43–86.

23. Dewick, P.M. *Medicinal Natural Products: A Biosynthetic Approach*, 3rd ed.; John Wiley & Sons LTD: Chichester, UK, 2009.

24. Laquale, S.; Candido, V.; Avato, P.; Argentieri, M.P.; D’Addabbo, T. Essential oils as soil biofumigants for the control of the root-knot nematode *Meloidogyne incognita* on tomato. *Ann. Appl. Biol.* 2015, 167, 217–224. [CrossRef]

25. Avato, P.; Laquale, S.; Argentieri, M.P.; Lamiri, A.; Radici, V.; D’Addabbo, T. Nematicidal activity of essential oils from aromatic plants of Morocco. *J. Pest Sci.* 2017, 90, 711–722. [CrossRef]

26. Laquale, S.; Avato, P.; Argentieri, M.P.; Bellardi, M.G.; D’Addabbo, T. Nematotoxic activity of essential oils from *Monarda* species. *J. Pest Sci.* 2018, 91, 1115–1125. [CrossRef]

27. D’Addabbo, T.; Argentieri, M.P.; Laquale, S.; Candido, V.; Avato, P. Relationship between chemical composition and nematicidal activity of different essential oils. *Plants* 2020, 9, 1546. [CrossRef]

28. Nicol, J.M.; Turner, S.J.; Coyne, D.L.; den Nijs, L.; Hockland, S.; Maafi, Z.T. Current nematode threats to world agriculture. In *Genomics and Molecular Genetics of Plant–Nematode Interactions*; Jones, J.T., Gheysem, G., Fenoll, C., Eds.; Springer: Heidelberg, Germany, 2011; pp. 21–44.

29. Perry, R.N.; Moens, M. *Plant Nematology*, 2nd ed.; CABI Publishing: Wallingford, UK; Boston, CT, USA, 2013; 536p.

30. Jones, J.T.; Haegeman, A.; Danchin, E.G.J.; Helder, J.; Jones, M.G.K.; Kikuchi, T.; Manzanilla-López, R.; Palomares-Rius, J.E.; Wesemael, W.M.L.; Perry, R.N. Top 10 plant-parasitic nematodes in molecular plant pathology. *Mol. Plant Pathol.* 2013, 14, 946–961. [CrossRef] [PubMed]

31. Castillo, P.; Vovlas, N. *Pratylenchus (Nematoda:Pratylenchidae): Diagnosis, Biology, Pathogenicity and Management*; Brill: Leiden, The Netherlands; Boston, MA, USA, 2007; 415p.

32. Nicol, J.M.; Stirling, G.; Rose, B.J.; May, P.; Van Heeswijk, R. Impact of nematodes on grapevine growth and productivity: Current knowledge and future directions, with special reference to Australian viticulture. *Aust. J. Grape Wine Res.* 1999, 5, 109–127. [CrossRef]

33. Ntalli, N.G.; Nasiou, E.; Menkissoglou-Spiroudi, U. Evaluation of essential oils from rosemary, orange, lavandula and false yellowhead on hatching and motility of root-knot nematode. *J. Agric. Sci. Technol. A* 2014, 139–159. [CrossRef]

34. Santana, O.; Andrade, M.F.; Sanz, J.; Errahmani, N.; Lamiri, A.; Gonzalez-Coloma, A. Valorization of essential oils from Moroccan aromatic plants. *Nat. Prod. Commun.* 2014, 8, 1109–1114. [CrossRef]

35. Salgado, S.M.; Campos, V.P. Hatching and mortality of *Meloidogyne exigua* in extracts and in natural products. *Fitopatol. Bras.* 2003, 28, 166–170. [CrossRef]

36. 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.

37. Eloho, K.; Kpebga, K.; Sasanelli, N.; Kounaglo, H.K.; Caboni, P. Nematicidal activity of some essential plant oils from tropical West Africa. *Int. J. Pest Manag.* 2020, 66, 131–141. [CrossRef]

38. Da Silva, F.G.E.; Mendes, F.R.D.S.; Assunção, J.C.D.C.; Pinheiro Santiago, G.M.; Bezerra, M.A.X.; Barbosa, E.G.; Mafezoli, J.; Rocha, R.R. Seasonal variation, larvicidal and nematicidal activities of the leaf essential oil of *Ruta graveolens* L. *Essent. Oil Res.* 2014, 26, 204–209. [CrossRef]

39. Faria, J.M.; Sena, I.; Ribeiro, B.; Rodrigues, A.M.; Maleita, C.M.N.; Abrantes, I.; Bennett, R.; Mota, M.; Figueiredo, A.C. First report on *Meloidogyne chitwoodi* hatching inhibition activity of essential oils and essential oils fractions. *J. Pest Sci.* 2016, 89, 207–217. [CrossRef]

40. Meyer, S.L.; Lakshman, D.K.; Zasada, I.A.; Vinyard, B.T.; Chitwood, D.J. Phytotoxicity of clove oil to vegetable crop seedlings and nematotoxicity to root-knot nematodes. *HortTechnology* 2008, 18, 631–638. [CrossRef]

41. Walker, J.T.; Melin, J.B. *Mentha × piperita, Mentha spicata* and effects of their essential oils on *Meloidogyne insoil*. *J. Nematol.* 1996, 28, 629–635.

42. Cetintas, R.; Yarba, M.M. Nematicidal effects of five plant essential oils on the southern root-knot nematode, *Meloidogyne incognita* Race 2b. *J. Anim. Vet. Adv.* 2010, 9, 222–225.

43. Mattei, D.; Dias-Arieira, C.R.; Biela, F.; Roldi, M.; da Silva, T.R.B.; Rampim, L.; Dadazio, T.S.; Tavarez-Silva, C.A. Essential oil of *Rosmarinus officinalis* in the control of *Meloidogyne javanica* and *Pratylenchus brachyurus* in soybean. *Biosci. J.* 2014, 30, 469–476. [CrossRef]

44. Baser, K.H.C. Biological and pharmacological activities of carvacrol and carvacrol bearing essential oils. *Curr. Pharm. Des.* 2008, 14, 3106–3119. [CrossRef] [PubMed]
Plants 2021, 10, 1368

45. Zotti, M.; Colaianna, M.; Morgese, M.G.; Tucci, P.; Schiavone, S.; Avato, P.; Trabace, L. Carvacrol: From ancient flavoring to neuromodulatory agent. *Molecules* 2013, 18, 6161–6172. [CrossRef]

46. Dheer, J.D.; Singh, D.; Kumar, G.; Karnatak, M.; Chandra, S.; Verma, V.P.; Shankar, R. Thymol chemistry: A medicinal toolbox. *Curr. Biocat. Compd.* 2019, 15, 454–474. [CrossRef]

47. Kowalczyk, A.; Prychodna, M.; Sopata, S.; Bodańska, A.; Fecka, I. Thymol and thyme essential oil—New insights into selected therapeutic applications. *Molecules* 2020, 25, 4125. [CrossRef] [PubMed]

48. Nasiou, E.; Giannakou, I.O. The potential use of carvacrol for the control of *Meloidogyne javanica*. *Eur. J. Plant Pathol.* 2017, 149, 415–424. [CrossRef]

49. Al-Banna, I.; Darwisj, R.M.; Aburjai, T. Effect of plant extracts and essential oils on root-knot nematode. *Phytopathol. Mediterr.* 2003, 42, 123–128.

50. Echeverrigaray, S.; Zacaria, J.; Beltrão, R. Nematicidal activity of monoterpenoids against the root-knot nematode *Meloidogyne incognita*. *Phytopathology* 2010, 100, 199–203. [CrossRef] [PubMed]

51. Ntalli, N.; Ferrari, F.; Giannakou, I.; Menkissoglou-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. [CrossRef]

52. Choi, I.; Kim, J.; Shin, S.; Park, I. Nematicidal activity of monoterpenoids against the pine wood nematode (*Bursaphelenchus xylophilus*). *Russ. J. Nematol.* 2007, 15, 35–40.

53. Soler-Serratosa, A.; Kokalis-Burell, 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.

54. Chatterjee, A.; Sukul, N.C.; Laskar, S.; Ghoshmajumdar, S. Nematicidal principles from two species of Lamiaceae. *J. Nematol.* 1982, 14, 118–120.

55. Sangwan, N.K.; Verma, B.S.; Verma, K.K.; Dhindsa, K.S. Nematicidal activity of some essential plant oils. *Pestic. Sci.* 1990, 28, 331–335. [CrossRef]

56. Nasiou, E.; Giannakou, I.O. The potential of eugenol as a nematicidal agent against *Meloidogyne javanica* (Treub) Chittwood. *J. Nematol.* 2020, 52, 1–10. [CrossRef]

57. Faria, J.M.; Sena, I.; Moiteiro, C.; Bennett, R.N.; Mota, M.; Figueiredo, A.C. Nematotoxic and phytotoxic activity of *Satureja montana* and *Ruta graveolens* essential oils on *Pinus pinaster* shoot cultures and *P. pinaster* with *Bursaphelenchus xylophilus* in vitro co-cultures. *Ind. Crop Prod.* 2015, 77, 59–65. [CrossRef]

58. Ntalli, N.; Menkissoglou-Spiroudi, U. Pesticides of botanical origin: A promising tool in plant protection. In *Pesticides: Formulations, Effects, Fate*; Stoytecheva, M., Ed.; INTECH Open Access Publisher: Rijeka, Croatia, 2011; pp. 3–24.

59. Jardim, I.N.; Oliveira, D.F.; Silva, G.H.; Campos, V.P.; de Souza, P.E. (E)-cinnamaldehyde from the essential oil of *Cinnamomum cassia* controls *Meloidogyne incognita* in soybean plants. *J. Pest Sci.* 2018, 110, 479–487. [CrossRef]

60. Barros, A.F.; Campos, V.P.; de Paula, L.L.; Pedrós, L.A.; Silva, F.J.; da Silva, J.C.P.; de Oliveira, D.F.; Silva, G.H. The role of *Cinnamomum zeleganicum* essential oil, (E)-cinnamaldehyde and (E)-cinnamaldehyde oxime in the control of *Meloidogyne incognita*. *J. Phytopathol.* 2021, 169, 229–238. [CrossRef]

61. Nasiou, E.; Giannakou, I.O. Effect of geraniol, a plant-based alcohol monoterpene oil, against *Meloidogyne javanica*. *Eur. J. Plant Pathol.* 2018, 152, 701–710. [CrossRef]

62. Mukherjee, A.; SinhaBabu, S.P. Potential of citral and menthol for suppression of *Meloidogyne incognita* infestation of okra plants. *J. Essent. OilBark Plants* 2014, 17, 359–365. [CrossRef]

63. Miao, J.; Wang, M.; Li, X.; Yang, F.; Liu, F. Antifungal and nematicaticidal activities of five volatile compounds against soil-borne pathogenic fungi and nematodes. *Acta Phytophyl. Sin.* 2012, 39, 561–566.

64. Perestrello, R.; Silva, C.; Fernandes, M.X.; Câmara, J.S. Prediction of terpenoid toxicity based on a quantitative structure-activity relationship model. *Foods 2019*, 8, 628. [CrossRef] [PubMed]

65. Mahizan, N.A.; Yang, S.K.; Moo, C.L.; Song, A.L.; Chong, C.M.; Chong, C.W.; Abushelabi, A.; Lim, S.H.E.; Lai, K.S. Terpene derivatives as a potential agent against antimicrobial resistance (AMR) pathogens. *Molecules* 2019, 24, 2631. [CrossRef]

66. Barbosa, J.D.; Silva, V.B.; Alves, P.B.; Guminha, G.; Santos, R.L.; Sousa, D.P.; Cavalcanti, S.C. Structure–activity relationships of eugenol derivatives against *Aedes aegypti* (Diptera: Culicidae) larvae. *Pest Manag. Sci.* 2012, 68, 1478–1483. [CrossRef]

67. Pavela, R.; Benelli, G. Essential oils as ecofriendly biopesticides? Challenges and constraints. *Trends Plant Sci.* 2016, 21, 1000–1007. [CrossRef]

68. Lee, S.E.; Lee, B.H.; Choi, W.S.; Park, B.S.; Kim, J.G.; Campbell, B.C. Fumigant toxicity of volatile natural products from Korean spices and medicinal plants towards the rice weevil, *Sitophilus oryzae* (L.). *Pest Manag. Sci.* 2001, 57, 548–553. [CrossRef] [PubMed]

69. Koul, O.; Walia, S.; Dhalival, G.S. Essential oils as green pesticides: Potential and constraints. *Biopestic. Int.* 2008, 4, 63–84.

70. Isman, M.B.; Miresmailli, S.; Machial, C. Commercial opportunities for pesticides based on plant EOs in agriculture, industry and consumer products. *Phytochem. Rev.* 2011, 10, 197–204. [CrossRef]

71. Martin, A.; Varona, S.; Navarrete, A.; Cocero, M.J. Encapsulation and co-precipitation processes with supercritical fluids: Applications with essential oils. *Open Chem. Eng. J.* 2010, 4, 31–41. [CrossRef]