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Essential Oils for Myiasis Control: Potentialities for Ecofriendly Insecticides

Amanda Chaaban[1,2*], Erik Nunes Gomes[3], Vera Maria Carvalho Silva Santos[2], Cícero Deschamps[3] and Marcelo Beltrão Molento[1,4]

[1]Laboratory of Parasitic Diseases, Federal University of Paraná (UFPR), Curitiba, PR, Brazil.
[2]Department of Veterinary Medicine, Catarinense Federal Institute (IFC), Araquari, SC, Brazil.
[3]Department of Plant Sciences, Federal University of Paraná (UFPR), Curitiba, PR, Brazil.
[4]National Institute of Science and Technology, INCT-Livestock, Belo Horizonte, MG, Brazil.

Authors' contributions

This work was carried out in collaboration between all authors. Authors AC and ENG designed the study, performed the literature analysis, and wrote the first draft of the manuscript. Authors VMCSS, CD and MBM managed the analyses of the study. Authors AC, ENG, VMCSS, CD and MBM managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Flies that cause myiasis are considered one of the main ectoparasites affecting livestock. This pathology may produce a reduction in body development, compromises animal welfare, and in severe cases, can lead to death. Although the control of this pathology relies on the use of synthetic insecticides, drug failure has been reported worldwide. Essential oils (EO) are an alternative to control infecting flies, with reports showing 100% efficacy. Studies on the chemical structure of EO compounds linked to their specific bioactivity can shed light for efficient myiasis control. Thus, we need to explore new possibilities of EO, including the identification of their chemical composition for the development of an ecofriendly control of myiasis.

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*Corresponding author: E-mail: amanda.chaaban@ifc.edu.br

Aims: The aim of the present article is to provide a detailed review about the Brazilian native and adapted plants and their potential biological activity.

Keywords: Brazilian plants; biopesticides; Lucilia cuprina; Cochliomyia macellaria; Cochliomyia hominivorax.

1. MYIASIS: CLASSIFICATION, CONTROL AND ECONOMIC IMPORTANCE

Infections of live tissue by dipterous larvae have been described since the first missionaries arrived in 1587 in Latin America [1,2]. The infestation of living tissues by blowfly larvae is considered one of the main ectoparasites affecting farm animals, as this pathology exerts a reduction in development capacity, generating stress, and in severe cases, can lead to the animal's death [3]. Gabriel Soares de Souza described one of the first cases of myiasis caused by *Cochliomyia* [1,4], as well as, the first reports of the use of natural products in the control of this pathology in Brazil.

In Brazil, true flies of the order Diptera from Calliphoridae and Cuterebridae families have received attention due to human and animal infestation, inducing primary, secondary or facultative myiasis [5]. Mandatory, or primary myiasis are those in which the larvae develop exclusively in living tissue, being subdivided according to the predilection of the tissue on the host. Facultative myiasis, or secondary develop in cadavers, necrotic tissues or decomposing organic matter, and may occasionally parasitize living organisms previously infected [5]. Cutaneous furuncular myiasis type, for example, is characterized by ulcerative lesions that damage subcutaneous tissues in the hosts. *Dermatobia hominis* L. popularly known as "bot fly", belongs to the Cuterebrinae subfamily and is capable of promoting cutaneous furuncular myiasis. It can parasitize humans, domestic and wild animals but bovine species is the most affected. Its pathology is considered endemic in neotropical regions [5,6], and their presence is associated with regions that have moderately high temperatures during the day and relatively cold nights, medium to heavy precipitation, and the proximity of dense vegetation [6]. Likewise, *Lucilia cuprina* W. has great medico-sanitary and veterinary importance due to the larval forms ability to develop in decaying organic matter, and optionally parasitize vertebrates [7]. *L. cuprina* is the main cause of primary myiasis in sheep in Australia and New Zealand, and is responsible for millions of dollars of losses annually to the wool and meat industries [8,9]. In Brazil, this species is associated to secondary myiasis in sheep although primary myiasis has been shown to be possible in experimental infection [10]. *Cochliomyia macellaria* F. is another species involved in secondary myiasis exacerbating the primary myiasis symptoms [4]. Moreover, both *Cochliomyia* and *Lucilia* genus can be potential vectors of various human enteropathogenic diseases, and foretic egg vectors of furuncular myiasis caused by *D. hominis* [5]. Economic losses caused by diptera live tissue infestation was estimated at US$ 383.4 million/year, due to *D. hominis* and US$ 336.6 million/year caused by *Cochliomyia hominivorax* affecting cattle in Brazil [11]. Data obtained by the National Union of the Animal Health Products Industry showed that 53.9% of the sector's sales were directed to ruminants, and 49% of this figure were the sales of parasiticides [12]. In Brazil, avermectins represent the most used chemical group in ruminants. Nowadays, there is a growing concern for food safety and residue detection of avermectins in meat and milk products [13]. Conventional control of myiasis, currently depends almost exclusively on synthetic insecticides [6,14]. However, Lopes et al. [15] evaluated the efficacy of ivermectin and abamectin administered in different routes (subcutaneous, intramuscular and pour-on) and doses (200 and 500 mcg kg^{-1}) against *C. hominivorax* in the scrotal sac of cattle after castration. The results evidenced the inefficacy in preventing scrotal myiasis in bulls, irrespectively of the route of administration and dose used. Resistance to various classes of chemical insecticides used for *L. cuprina* control, including organochlorines, organophosphates, the benzoyl-phenyl urea diflubenzuron and the triazine cyromazine have been reported [16,17]. Although, the macrocyclic lactone, ivermectin and cyanopyrimidine dicyclanil remain effective with no resistance yet reported [18]. Some studies have clarified the genetic mechanism of resistance. Carvalho et al. [20] characterized the *C. hominivorax* genome and identified putative genes involved in insecticide resistance. The presence of mutations in the acetylcholinesterase (target site) and carboxylesterase E3 genes was investigated and all of the resistant flies presented the E3 mutation. Resistance to organophosphates is another concern of livestock in areas affected by

C. hominivorax. Bergamo et al. [20] have associated the Gly137Asp and Trp251Leu mutations in the active site of carboxylesterase E3 to the resistance to diethyl and dimethyl-organophosphates insecticides. In this sense, synthetic insecticides toxicity and the negative effects on human health and the environment, together with the development of insecticide resistance led to a resurgence of interest in botanical pesticides [21].

2. CLINICAL SIGNS OF MYIASIS AND ANIMAL WELFARE

Myiasis condition can quickly compromise animal welfare. Broom [22] conceptualize animal welfare as an individual state, regarding its attempt to adapt to the local environment. However, an important idea behind the concept of animal welfare is to look for an understanding of the animal's life quality from the animal perspective and taking appropriate action according to such understanding [23]. So, in order to provide a good degree of welfare, it is important to recognize the animals' requirements. At the host skin surface, the fly eggs hatch after 12 to 24 h, the larvae molts (L1 → L2) after another 12–18 h and again the second molt (L2 → L3) about 30 h later [8]. Hence, they feed for a total of 3 - 4 days before leaving the skin, to fall to the soil to pupate. Generally, myiasis diagnosis is made when the animal already has a secretion and a specific odor is produced by the pathology, attracting other gravid female, having multiple oviposition in the same host [8]. Myiasis infections are highly likely to predispose the host to further infestation resulting in a rapid clinical disease [24]. In this sense, it is worth to note the relationship of the pathogeny and animal welfare commitment, either directly by pain and discomfort caused by infestation or indirectly due to mutilating practices, as in the case of mulesing in Australia [9,25-26]. Therefore, when detecting myiasis, the intervention must be immediate, otherwise animal welfare will be severely compromised.

3. PROPERTIES OF ESSENTIAL OILS (EO)

EO are produced by various aromatic plants and can be synthesized by all plant organs (i.e. buds, flowers, leaves, stems, twigs, seeds, fruits, roots, wood or bark). Secretory and storage activities occur in canals, epidermic cells or glandular trichomes [27]. The compounds can be isolated from the plants by hydrodistillation, steam distillation, dry distillation, or cold pressing. They may be liquid, volatile, limpid and rarely colored, lipid soluble and soluble in organic solvents with a generally lower density than water [28]. Characterized by a complex mixture of phytochemicals, whose constituents belong mainly to terpenoids or, to a lesser extent, phenylpropanoids, EO are formed by secondary metabolites of aromatic plants. Plants secondary metabolism is genetically dependent and the physiological expression follows on the plant interaction with biotic and abiotic factors. The production of EO in plants differs not only in quantity, but especially in composition, according to the type of extraction, climate (temperature, photoperiod, humidity), soil composition, plant organ, age and vegetative cycle stage, circadian rhythm and herbivorous attack [27,29-30]. In this sense, agricultural management of aromatic plants can also influence the chemical profile of EO. The knowledge about specific practices is a key factor to achieve a desired compound synthesis or the production of EO with an adequate composition for biopesticide use. Several reports have been made about this topic under Brazilian conditions of cultivation. Deschamps et al. [31] reported lower amounts ($p<0,05$) of menthol and neomenthol in *Mentha* x *piperita* L. when fertilized with 40 kg ha^{-1} of urea in comparison with the same doses of ammonium sulphate. In chamomile cultivation Amaral et al. [32] reported a seedling rate of 4 kg/hec reducing the amount of α-pinene, a compound with potential insecticide use. In *Ocimum basilicum* L. (basil), the application of elicitors chitosan and methyl jasmonate provided an increase of 25 and 48% of methylchavicol, respectively [33]. For the same species, elicitation with *Methyl jasmonate* resulted in increase of β-caryophyllene, 1,8-cinelole, and limonene [34], which are important compounds with potential for myiasis control. The period of harvest and post-harvest have a great influence over the production of volatile compounds in aromatic plants. Santos et al. [35] reported higher levels of menthol and lower levels of menthone in *Mentha canadensis* L. harvested 60 days after regrowth when compared to harvesting 95 days after planting in Southern Brazil. For the *Lavandula dentata* L. grown in southern Brazil, harvest of senescent flowers in April resulted in a high level of 1,8-cineol whereas camphor levels increased in the pre-anthesis/anthesis and senescence stages in January [36]. Both compounds have been reported in compositions for insects control uses [37,38]. For *Piper hispidinervum* C.D.C., drying leaves at 40°C for 12 days reduced the amount of EO components, but increased the content of safrole [39]. Dabague et al. [40] showed that *Zingiber officinale* Roscoe rhizomes presented higher geranial and neral (important as insecticides and repellents) levels, after longer periods of drying.

4. POTENTIAL USE OF ESSENTIAL OILS IN MYIASIS CONTROL

The biodiversity of Brazilian plants and the adapted exotic plants have stimulated the interest on investigating their chemical composition and biological activity, especially concerning the possibility of future ecofriendly insecticides. Table 1 presents the main individual compounds with insecticidal, anti-inflammatory, antibacterial and other activities of native and exotic plants cultivated in Brazil. Likewise, it also shows important compound activities, that could be selected as candidates for myiasis control.

Different chemical compounds can be found on EO, mostly terpenes, and it is necessary to investigate the contribution of the major components to better determine their mechanism of action [53]. It is well known, for example, that the effect of EO from basil and clove act as insecticides, and is largely attributed to eugenol that works by blocking insects octopamine receptors and/or by potentially working through the tyramine receptor cascades, similarly to the effects of thymol, present in thyme EO [222-224]. In *Cinnamomum camphora* L. Presl the terpene linalool was found to be a significant contributor to the insecticidal and repellent activities [38]. Some studies support that the hydrocarbon skeleton, a common structural feature of terpenoids, confers hydrophobicity, which is associated with protein deactivation and enzyme inhibition. Thus, the toxicity of several terpenoids such as linalool, camphor, pulegone, 1,8 cineole (eucalyptol) is commonly related to their reversible competitive inhibition of acetylcholinesterase, by occupying the hydrophobic site of the enzyme's active center [225,226]. In *Piper gaudichaudianum* Kunth, a common plant used in Brazil, the larvicidal activity was attributed to the oxygenated sesquiterpene (E)-nerolidol. The activity of this compound was associated to the generation of reactive oxygen species (ROS) that caused oxidative damage in the DNA of cells, promoting cytotoxicity [110]. Regarding the EO of some plants of Brazil, Simas et al. [227] highlight that the larvicidal activities may be attributed mainly to the compounds (E)-nerolidol, (E,E)-farnesol, eugenol, safrole, antethole and β-pinene. The related compound, β-pinene and its enantiomer α-pinene, present in EO of several species, are largely associated to larvicidal and insecticidal activities [46,62,65]. Concerning these compounds, it is important to emphasize their isolated biological activities as enantioselectivity. Evaluating α and β-pinenes from *Citrus* spp. EO, Michaelakis et al. [53] have shown that (−)-β enantiomer was the more toxic among pinenes. According to Simas et al. [227] the enantioselectivity of β-pinene may be related to its exocyclic double bond that appeared to be more important than the α-pinene endocyclic double bond to insecticidal activities. The enantioselectivity was also observed on menthone, showing higher toxicity for *Culex pipiens* larvae than its enantiomer isomenthone [228]. Lima et al. [229] similarly related stronger larvicidal of (+)-carvone epoxide when compared to (−)-carvone epoxide. These findings draw attention to the importance of knowing the EO composition and the chemical structure of its components, which may be strongly related to their biological properties. In general, it is well known that the level of lipophilicity of EO plays a significant role in larval activity. Simas et al. [227] reported that lipophilic sesquiterpenes exhibited higher larvicidal activities than monoterpenes. Santos et al. [230] also showed that the presence of lipophilic groups in the aromatic rings, observed in thymol and carvacrol, increased its larvicidal potency. Removal of the hydroxyl group from carvacrol or thymol molecules, resulted in p-cymene, significantly ($p \le 0,05$) increase its larvicidal potency. Similarly, replacing the ortho hydroxyl group of catechol by a lipophilic group, resulting in eugenol, led to more than 3.5-fold increase of its larvicidal activity in *Aedes aegypti* L3 larvae [230]. This is the reason that makes molecules with the presence of hydroxyl in aromatic rings or other cyclic structures to have a low toxicity over larvae. Hydroxyl group increases compounds' hydrophobicity and consequently reduces their capacity of penetration in the larvae cuticle of several species [93,230,231]. Another study reported that the lipophilicity of the compounds with hydroxyl, carbonyl and methoxyl groups proved to be less active than molecules lacking these structures [227]. Although some compounds may have more larvicidal potential than others, synergism may also play a role on this activity, considering that substances such as terpenoids can increase the transmembrane absorption of both lipophilic and hydrophilic drugs [227,232].

Table 1. Main compounds with insecticidal, anti-inflammatory, antibacterial and other myiasis control related activities

Compounds	**Biological activity/ Properties**	**Main uses (Patents)**	**Examples of native, naturalized and/or cultivated plants in Brazil that contain the compounds in the essential oil composition**	**Ref.**
β-Pinene	Antimicrobial; Insecticidal; insect repellent	Synergistic pest-control compositions; insect pest control agent; essential oil compositions for killing or repelling ectoparasites and pests; antimicrobial compositions; gel for topical application of clove essential oil with broad spectrum anti-inflammatory action	*Rosmarinus officinalis* L.; *Citrus* spp.; *Achillea millefolium* L.; *Melissa officinalis* L.; *Mentha x piperita* L.; *Artemisia absinthium* L.; *Salvia officinalis* L.; *Tanacetum vulgare* L; *Laurus nobilis* L*;* *Eucalyptus camaldulensis* Dehn.; *Eucalyptus grandis* Hill ex Maiden.; *Zingiber officinale* Roscoe; *Schinus terebinthifolius* Raddi.; *Origanum vulgare* L.; *Nectandra angustifolia* (Schrad.) Nees; *Cyperus rotundus* L.; *Myrrhinium atropurpureum* Schott.	[41-64]
α-Pinene	Antimicrobial; insecticidal; insect repellent	Insecticidal compositions; synergistic pest-control compositions; pesticidal compositions; gel for topical application of clove essential oil with broad spectrum anti-inflammatory action; antimicrobial compositions	*Schinus terebinthifolius* Raddi; *Rosmarinus officinalis* L.; *Varronia curassavica* Jacq.; *Calendula officinalis* L.; *Citrus sinensis* L.; *Eucalyptus globulus* Labill.; *Origanum vulgare* L.; *Achillea millefolium* L.; *Foeniculum vulgare* Mill.; *Nectandra angustifolia* (Schrad.) Nees; *Salvia officinalis* L.; *Cyperus rotundus* L.; *Daucus carota* L. *Eucalyptus camaldulensis* Dehn.; *Tanacetum vulgare* L.; *Laurus nobilis* L.; *Eucalyptus grandis* Hill ex Maiden.; *Myrrhinium atropurpureum* Schott.; *Plectranthus barbatus* Andr.	[41-43, 45,48-51,57, 60-62, 65-80]
Limonene	Antibacterial; anti-inflammatory; insecticidal; insect repellent;	Pesticidal compositions; synergistic pest-control compositions; long-lasting insect repellant, pesticide and antifeedant compositions; pest	*Citrus limon* Burm. f.; *Citrus bergamia* Risso; *Citrus aurantium* L.; *Citrus sinensis* (L.) Osbeck *Mentha spicata* (Linn.); *Eucalyptus*	[43,54, 66,72,81-102]

Compounds	Biological activity/ Properties	Main uses (Patents)	Examples of native, naturalized and/or cultivated plants in Brazil that contain the compounds in the essential oil composition	Ref.
	anti-oxidant	control using natural pest control agent blends; antimicrobial and antiviral compositions	*globulus* Labill.; *Nasturtium officinale* R. Br.; *Lippia alba* (Mill.) N. E. Br.; Tagetes patula L.; *Conyza bonariensis* L.; *Valeriana officinalis* L.; *Ocimum basilicum.* L.; *Lantana camara* L.; *Mentha viridis* L.; *Mentha x piperita* L.	
Nerolidol	Anti-inflamatory; antibacterial; anti-oxidant; insecticidal; insect repellent	Pesticidal compositions; repellent compositions for insects and other arthropods; insecticidal compounds	*Zornia brasiliensis* Vogel; *Baccharis dracunculifolia* DC; *Piper gaudichaudianum* Kunth.	[43,103-112]
β-caryophyllene	Anti-inflammatory; insect repellent	Methods for repelling insects using sesquiterpene hydrocarbons and their derivatives; Composition for treating pain and/or inflammation comprising eugenol and beta-caryophyllene	*Spiranthera odoratissima* A. St. Hil; *Origanum vulgare* L.; *Artemisia annua* L.; *Rosmarinus officinalis* L.; *Varronia curassavica* Jacq.; *Eugenia caryophyllata Thunb.; Curcuma longa L.; Lantana camara L.; Mentha x piperita L.; Plectranthus barbatus Andr.*	[54,65, 97,113-123]
α-Phellandrene	Insecticidal	Synergistic pest-control compositions; pesticidal compositions; compositions for controlling insects; anti-microbial compositions	*Schinus terebinthifolius* Raddi; *Foeniculum vulgare* Mill.; *Lantana camara* L.; *Thymus vulgaris* L.; *Curcuma longa* L.; *Moringa oleifera* Lam.; *Zingiber officinale* Roscoe.	[77,102,124,125,127-132,137-149]
1,8-Cineole (eucalyptol)	Insecticidal; anti-inflammatory; anti-oxidant; antimicrobial; insect repellent	Combination of biological pesticides; natural pesticides composition; insect repellent compositions; botanical insecticides; antioxidant compositions for treatment of inflammation or oxidative damage;	*Rosmarinus officinalis* L.; *Salvia officinalis* L.; *Eucalyptus* spp.; *Thymus vulgaris* L.; *Origanum vulgare* L.; *Laurus nobilis* L.; *Lippia sidoides* Cham.; *Ocimum basilicum.* L.; *Lippia alba* (Mill.) N. E. Br.; *Callistemon lanceolatus* (Sm.); *Ocimum selloi* Benth.; *Lantana camara* L.; *Myrrhinium*	[37,48, 51,52, 54,55, 90,97, 101,117,134-154]

Compounds	Biological activity/ Properties	Main uses (Patents)	Examples of native, naturalized and/or cultivated plants in Brazil that contain the compounds in the essential oil composition	Ref.
		topical anti-inflammatory compositions; volatile organic compound formulations having antimicrobial activity	*atropurpureum* Schott.; *Artemisia annua* L.; *Zingiber officinale* Roscoe; *Ocimum gratissimum* L.; *Mentha spicata* L.; *Mentha suaveolens* Ehrh.; *Mentha viridis* L.; *Mentha longifólia* (L.) Huds.; *Mentha x piperita* L.; *Artemisia absinthium* L.; *Tanacetum vulgare* L; *Melaleuca alternifolia* Cheel.	
Dillapiole	Anti-inflammatory; insecticidal	Insecticidal composition	*Piper gaudichaudianum* Kunth; *Ocimum basilicum* L.; *Piper aduncum* L.	[155-159]
Thymol	insecticidal; anti-inflammatory; antimicrobial; anti-oxidant	Pesticidal compositions; agricultural pesticide compositions; insect repellent compositions; natural insecticide compositions; antimicrobial compositions comprising essential oil combinations; antimicrobial compositions; antioxidant compositions for treatment of inflammation or oxidative damage	*Thymus vulgaris* L.; *Origanum vulgare* L.; *Ocimum gratissimum* L.; *Mentha viridis* L.; *Origanum majorana* L.; *Rosmarinus officinalis* L.; *Lippia sidoides* Cham.	[101,115,133,134,160-174]
Carvacrol	Insecticidal; antimicrobial; anti-inflammatory; anti-oxidant	Pesticidal compositions; repellent compositions for insects and other arthropods; natural insecticide composition; topical anti-inflammatory compositions; Antimicrobial compositions	*Origanum vulgare* L.; *Urtica dioica* L.; *Thymus vulgaris* L.; *Laurus nobilis* L.; *Lippia sidoides* Cham.	[103,115,140,146,160,162,165,169-173,175-179]
Eugenol	Insecticidal; insect repellent; antimicrobial; anti-inflammatory;	Pesticidal compositions; insect repellent compositions; antimicrobial compositions comprising essential oil	*Ocimum basilicum* L.; *Ocimum selloi* Benth.; *Ocimum gratissimum* L.; *Cinnamomum* spp.; *Plectranthus barbatus* Andr.; *Syzygium aromaticum* (L.) Merr. &	[64,106, 134,151,163,164,171,175, 178,180-189]

Compounds	**Biological activity/ Properties**	**Main uses (Patents)**	**Examples of native, naturalized and/or cultivated plants in Brazil that contain the compounds in the essential oil composition**	**Ref.**
	anti-oxidant	combinations; antimicrobial compositions; analgesic and anti-inflammatory compositions	L. M. Perry; *Pogostemon cablin* Benth; *Piper divaricatum* G. Mey.	
Camphor	Insecticidal; anti-inflammatory; antibacterial	Pesticidal compositions; repellent compositions for insects and other arthropods; insecticidal compounds; antimicrobial compositions; treatment of inflammatory disorders in non-human mammals	*Cinnamomum camphora L.; Salvia officinalis* L.; *Artemisia annua* L.; *Mentha viridis* L.; *Rosmarinus officinalis* L.; *Lavandula × intermedia* Emeric ex Loiseleur	[38,101, 103,116,142,143,175,190-196]
Citronellal	Insect repellent; anti-oxidant; anti-inflammatory	Natural pesticide compositions; formulations containing insect repellent compounds; insect pest control agent; antimicrobial compositions	*Eucalyptus citriodora* Hook; *Cymbopogon nardus* L.; *Cymbopogon winterianus* Jowitt; *Melissa officinalis* L.	[44,137, 163,181,197-203]
Citral (Geranial + Neral)	Insect repellent; insecticidal; anti-oxidant; antimicrobial; anti-inflammatory	Pesticidal compositions; insect repellent compositions; insect pest control agent; antimicrobial compositions	*Lippia alba* (Mill.) N. E. Br.; *Callistemon lanceolatus* (Sm.); *Zingiber officinale* Roscoe; *Melissa officinalis* L.; *Ocimum basilicum* L.; *Cymbopogon flexuosus* Stapf.; *Citrus sinensis* (L.) OSBECK; *Cymbopogon citratus* (DC); *Elionurus muticus* (Spreng.) Kuntze.	[42,44, 108,133,148,150,181,202,204-211]
Terpinen-4-ol	Insect repellent; insecticidal; anti-inflammatory	Pesticidal compositions; insect and disease control; essential oil compositions for killing or repelling ectoparasites and pests; antimicrobial compositions; inhibitor of inflammatory conditions	*Curcuma zedoaria* (Berg.) Roscoe; *Melaleuca alternifolia* Cheel; *Origanum majorana* L.; *Thymus vulgaris* L.; *Origanum vulgare* L.	[55,64,65,123,126,153,174,212-218]
Carvone	Insect repellent	Insecticidal compositions	*Mentha viridis* L.; *Urtica dioica* L.; *Lippia alba* (Mill.)N. E. Br.;	[101,177,208,219-221]

Table 2. Plant, part used and major constituents of essential oil EO considered active against dipteran muscoids

Plant	Part used	Major constituents of Essential oil	Target organism	Insect stage	Application	LC 50 (unit)	Ref.
Pogostemon cablin	Leaves	Patchouli alcohol (42.70%), α - Bulnesene (16.20%)	*Musca domestica*	A	Topical application	3µg/fly	[235]
Mentha pulegium	Leaves	Pulegone (83.3%), Piperitenone (8.6%)	*Musca domestica*	A	Fumigation	4.7 µg/cm^2	[235]
Origanum compactum	Herb	Carvacrol (58.3%), Thymol (12.6%)	*Musca domestica*	A	Topical application	13 µg/fly	[235]
Trigonella foenum-graecum	NAA	NAA	*Lucilia sericata*	TIL	Ingestion assays	2.81%	[236]
Apium graveolens	NAA	NAA	*Lucilia sericata*	TIL	Ingestion assays	4.60%	[236]
Raphanus sativus	NAA	NAA	*Lucilia sericata*	TIL	Ingestion assays	6.93%	[236]
Brassica compestris	NAA	NAA	*Lucilia sericata*	TIL	Ingestion assays	7.92%	[236]
Minthostachys verticillata	Leaves	(R)(+)-pulegone (69.70%), menthone (12.17%)	*Musca domestica*	A	Fumigation	0.5 mg/dm^3	[237]
Hedeoma multiflora	Leaves	(R)(+)-pulegone (52.80%), Menthone (24.33%)	*Musca domestica*	A	Fumigation	1.3 mg/dm^3	[237]
Artemisia annua	Leaves	Artemisia ketone (22.36%), 1,8-cineole (16.67%)	*Musca domestica*	A	Fumigation	6.5 mg/dm^3	[237]
Citrus sinensis	Fruit peel	Linalool (63.53%), δ-Terpinene (6.55%)	*Musca domestica*	A	Fumigation	3.9 mg/dm^3	[238]
Citrus aurantium	Fruit peel	Limonene (94.07%),	*Musca domestica*	A	Fumigation	4.8 mg/dm^3	[238]
Eucalyptus ocinerea	Leaves	1,8-Cineol (56.86%), α-Pinene (6.42%)	*Musca domestica*	A	Fumigation	5.5 mg/dm^3	[238]
Eucalyptus globulus	NAA	1,8-cineole (33.6%), α-pinene (14.2%)	*Musca domestica*	SIL	Contact	0.60 µl/cm^2	[72]
Melaleuca alternifolia	NAA	*Terpinen-4-ol (43.0%), λ-Terpinene (20.9%)*	*Lucilia cuprina*	SIL and TIL	Feeding assays	2.5%	[213]
Minthostachys verticillata	Leaves	(4R)(+)-pulegone (67.5%),	*Musca domestica*	A	Fumigant assay	0.5 mg/dm^3	[239]

Plant	Part used	Major constituents of Essential oil	Target organism	Insect stage	Application	LC 50 (unit)	Ref.
		menthone (22.3%)					
Mentha piperita	Leaves	NAA	*Musca domestica*	TIL	Immersion	104 ppm	[240]
Citrus sinensis	Fruit peel	(4R)(+)-limonene (95.1%)	*Musca domestica*	A	Fumigant assay	3.9 mg/dm^3	[241]
Mentha piperita	NAA	NAA	*Musca domestica*	SIL	Contact	2.5%	[242]
Melaleuca alternifolia	Aerial parts	4-terpineol, (35.10%), ϒ-terpinene (17.40%)	*Ceratitis capitata*	TIL	Contact	0.117 µL oil/cm^2	[243]
Cucurbita maxima	NAA	NAA	*Cephalopina titillator*	TIL	Immersion	0.48%	[244]
Eucalyptus cinerea	Leaves	1,8-cineole (88.5%), alfa-terpineol (9%)	*Musca domestica*	A	Fumigant assay	5.5 mg/dm^3	[245]
Cymbopogon citratus	Leaves	E – citral (53.2), Z – citral (36.37%)	*Musca domestica*	FIL	Feeding assays	4.25%	[246]
Cymbopogon citratus	Leaves	NAA	*Chrysomya putoria*	FILA	Feeding assays	85.48%	[247]
NAA	NAA	Menthone	*Musca domestica*	SIL	Contact	0.023 µL oil/cm^2	[248]
Commiphora molmol	NAA	NAA	*Lucilia sericata*	TIL	Feeding assays	6.55 mg/ml	[249]
Tagetes minuta	Aerial parts	Dihydrotagetone (67.64%), Trans-beta-ocimene (16.23%)	*Cochliomyia macellaria*	TIL	Contact	0.58µL oil/cm^2	[250]
Baccharis dracunculifolia	Aerial parts	β-pinene (9.94%), D-limonene (9.59%), β-nerolidol (7.93%), caryophyllene (7.69%), spathulenol (6.69)	*Cochliomyia macellaria*	TIL	Contact	2.47 µL oil/cm^2	[251]
Piper gaudichaudianum	Leaves	germacrene B (21.5%), δ-cadinene (9.3%), γ-elemene (6.1%), (Z)-cariophyllene (5.2%), α-copaene (4.3%), (E)-cariophyllene (3.7%)	*Lucilia cuprina*	TIL	Contact	2.19 µL oil/cm^2	[252]

Note: NAA; Not assessed in article; A: Adult; TIL: Third instar larvae (L3); SIL: Second instar larvae (L2); FIL: First instar larvae (L1); FILA: First instar larvae to adult.

5. USE OF ESSENTIAL OILS AS BIOPESTICIDES AGAINST FLIES CAUSING MYIASIS

The research and use of EO in the control of veterinary ectoparasites have increased considerably (Table 2) due to their popularity with organic farmers and environmentally sensible consumers [21,233]. Since the 80s, EO were categorized as botanical pesticides and research investigation of their constituents, different biological activities and insect control potential have been growing considerably [234].

Compounds from EO can exert their activities on insects through neurotoxic effects involving several mechanisms notably through inhibition of P450, GABA receptors, inhibition of acetylcholinesterase (AchE) and modulation of octopaminergic system [21,224]. Furthermore, some studies have demonstrated that mixtures of different isolated compound may have synergistic actions [232,253,254]. Mechanisms causing synergistic interaction were suggested by Wagner and Ulrich-Merzenich [255] as: (1) having multi-target effects; (2) bioavailability effects based on solubility and absorption rate; (3) interactions of components with resistance mechanisms; an (4) respective elimination of adverse effects [254,255]. Bassolé and Juliani [256] related that phenolic monoterpenes like thymol and carvacrol, and phenylpropanoids such as eugenol, have a tendency to enhance the activity of other natural substances when used in mixtures. In this sense, the use of synergistic combinations may reduce the concentration of each isolated substance, increasing its biological activity against the target organism and possibly contributing for future standardization of biopesticides [254,257]. Sustainable use of certain spontaneous species considered weeds may also be an interesting possibility. *Cyperus rotundus* (Cyperaceae), for example is a cosmopolitan herb belonging to the Cyperaceae family. *C. rotundus* is encountered in tropical, subtropical and temperate regions and presents constituents with insecticide activity such as α-pinene, 1,8 cineole and carvone [258]. *Lantana camara* (Verbenaceae) is another example of a native and aromatic plant of tropical America with spontaneous growth, and ornamental use. When ingested in large amounts, it causes intoxication in livestock and may induce hepatotoxic photosensitization [259]. EO of *L. camara* presents β-caryophyllene, 1,8 cineole, α-phellandrene, α-pinene and limonene, with potential for myiasis control [260,261]. Therefore, the use of these plants can be a viable and integrated alternative; i.e, it is possible to remove the weed from the field, avoid animals' intoxication and take advantage of its insecticide activity.

6. FUTURE CHALLENGES AND RESEARCH PRIORITIES

Different forms of application of EO (contact, immersion, fumigation, ingestion) and different insect phases (adult, first, second and third stage larvae) have been investigated in recent years (Table 2). However, it is important to note that several authors evidence that mature larvae represent the greatest resistance phase of the myiasis fly [213,249-252,262]. Therefore, the biological assays testing insecticidal activity against myiasis flies should be directed mainly to the parasitic phase of higher resistance, so as to the approach in field conditions. Aiming to produce quality raw material for biopesticides, the standardization of cultivation practices is one of the most important factors to be observed, as significant changes in the chemical profile can occur. Adequate fertilization, plant spacing, harvesting times, drying and extraction methods are some of the main factors that also deserve attention. It is necessary to study the best practices in order to produce high vegetative growth, high EO yields, with reasonable contents of the compounds of interest. Some challenges must be considered in order to move towards ecofriendly insecticide products:

1. Test the use of new technologies such as nanoemulsion and microencapsulation formulations;
2. Determine the proper EO carriers to improve bioavailability;
3. Work with EO standardization (major compounds, dosages);
4. Determine toxicity levels in non-target organisms;
5. Evaluate the antioxidant and cytotoxicity activity in mammalian host cells;
6. Determine sub-lethal doses responsible for residual effects;
7. Determine *in vivo* evaluations in field conditions.

7. CONCLUDING REMARKS AND FUTURE PERSPECTIVES

Considering that differences in plant secondary metabolism are a function of genetic factors and environmental conditions, the more applied research in this area, the closer we will get from finding optimal conditions to develop the correct product. Further studies concerning the activity of EO candidates, as biopesticides in myiasis control, are still needed that should focus on the sub-lethal concentration effects on fly reproduction and longevity. Another area of great promise is the information on the mechanism of action with research of morphological biomarkers of structure damage assessment for investigate intoxication of target cells, enzymatic biomarkers as well as synergistic interactions between individual compounds. These data would support the use on blend compounds, not only increasing insecticide activity but reducing the products' volume.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Papavero N, Couri MC. Essays on the history of Brazilian dipterology. I. The first notices about Brazilian Diptera (16th century). Rev Bras Entomol. 2012a; 56(1):1-6.
2. Papavero N, Couri MC. Essays on the history of Brazilian dipterology. III. Three remarkable notices from the 18 th century, mainly related to myiasis-producing flies (*Cochliomyia* and *Dermatobia*). Rev Bras Entomol. 2012b;56(4):393-398.
3. Guimarães JH, Prado AP, Linhares AX. Three newly introduced blowfly species in souther Brasil (Diptera: *Calliphoridae*). Rev Bras Entomol. 1978;22(1):53-60.
4. Guimarães JHN, Prado AP. As miíases na região neotropical (identificação, biologia, bibliografia). Rev Bras Zool. 1982;1:239-416.
5. Guimarães JH, Papavero N. Myiasis and animals in the Neotropical region: bibliographic database. São Paulo, Ed. Plêidade, FAPESP. 1999;308.
6. Moya-Borja GE. Erradicação ou manejo integrado das miíases neotropicais das Américas. Pesq Vet Bras. 2003; 23(32):131-138.
7. D' Almeida. Sinantropia em dípteros caliptratos na área metropolitana do Rio de Janeiro. Doctoral thesis, Universidade Federal Rural do Rio de Janeiro, Brazil. 1983;193.
8. Wall R. Ovine cutaneous myiasis: Effects on production and control. Vet Par. 2012;189(1):44-51.
9. Windsor PA, Lomax S. Addressing welfare concerns in control of ovine cutaneous myiosis in sheep in Australia. Small Rum Res. 2013;110(2):165-169.
10. Moreira-Lima MA, Moya-Borja GE. Estudo comparativo de miíases produzidas por *Cochliomyia hominivorax* (Coquerel, 1858) e *Lucilia cuprina* (Wiedemann, 1830) (Diptera: Calliphoridae) em ovinos artificialmente infestados. Rev Bras Med Vet. 1997;19(5):200-205.
11. Grisi L, Leite RC, Martins JRS, Barros TM, Andreotti R, Cançado PHD, Léon AP, Pereira JB, Villela HS. Ressessment of the potential economic impact of cattle parasites in Brazil. Braz J Vet Parasitol. 2014;23(2):150-156.
12. Sindicato nacional da indústria de produtos para saúde animal (SINDAN). 2015. Acessado em 10/06/2017. Available:http://www.sindan.org.br/sd/base.aspx?controle=8
13. Brasil. Instrução Normativa n. 13, de 29 de maio de 2014. Dispõe sobre a proibição da fabricação, manipulação, fracionamento, comercialização, importação e uso de produtos antiparasitários de longa ação que contenham como princípios ativos as lactonas macrocíclicas.
14. Qin Y, Jatamunua F, Zhang J, Li Y, Han Y, Zou N, Shan J, Jiang Y, Pan C. Analysis of sulfonamides. Tilmicosin and Avermectins Residues in Typical Animal Matrices with multi-Plug Filtration Cleanup by Liquid Chromatography–Tandem Mass Spectrometry Detection. J Chromat B. 2017;1053:27-33.
15. Lopes WDZ, Teixeira WFP, Felippelli G, Cruz BC, Maciel WG, Matos LVS, Pereira JCM, Buzzulini C, Soares VE, Santos TR, Oliveira GP, Costa AJ. Ivermectina e abamectina em diferentes doses e vias de aplicação contra larvas de *Cochliomyia hominivorax* em bolsas escrotais de

bovinos recém-castrados, provenientes da região sudeste do Brasil. Ciênc. Rural. 2013; 43(12):2195-2201.

16. Levot GW. Cyromazine resistance detected in Australian sheep blowfly. Aust Vet J. 2012;90(11):433-437.
17. Sandeman RM, Levot GW, Heath AC, James PJ, Greeff JC, Scott MJ, Batterham P, Bowles VM. Control of the sheep blowfly in Australia and New Zealandeare we there yet? Int J Parasitol. 2014;44:879-891.
18. Bagnall NH, Hines BM, Lucke AJ, Gupta PK, Reid RC, Fairlie DP, Kotze AC. Insecticidal activities of histone deactylase inhibitors against a dipteran parasite of sheep, *Lucilia cuprina*. Int J Parasitol Drugs Drug Resis. 2017;7:51-60.
19. Carvalho RA, Azeredo-Espin AML,Torres TT. Deep sequencing of New World screw-worm transcripts to discover genes involved in insecticide resistance. BMC Genomics. 2010;11(1):695.
20. Bergamo LW, Fresia P, Azeredo-Espin AML. Incongruent nuclear and mitochondrial genetic structure of New World screwworm fly populations due to positive selection of mutations associated with dimethyl-and diethyl-organophosphates resistance. PloS One. 2015;10(6):e0128441.
21. Pavela R, Benelli G. Essential oils as ecofriendly biopesticides? Challenges and Constraints. Trends Plant Sc. 2016; 21(12):1000-1007.
22. Broom DM. Indicators of poor welfare. British Vet J. 1986;142(6):524-526.
23. Molento CFM. Public health and animal welfare. In: Dilemmas in Animal Welfare. CABI International, Boston. 2014;102-123.
24. Wall R. Ectoparasites: Future challenges in a changing world. Vet Par. 2007;62-74.
25. Fisher AD. Addressing pain caused by mulesing in sheep. Appl Anim Behav Sci. 2011;135(3):232-240.
26. Lomax S, Sheil M, Windsor PA. Duration of action of a topical anaesthetic formulation for pain management of mulesing in sheep. Austr Vet J. 2013; 91(4):160-167.
27. Bakkali F, Averbeck S, Averbeck D, Idaomar M. Biological effects of essencial oils - A review. Food Chem Tox. 2008;46:446-475.
28. Stratakos AC, Koidis A. Methods for extracting essential oils. In: Essential oils in food preservation, flavor and safety. Academic Press, San Diego, CA. 2016;10:31-38.
29. Gobbo-Neto L, Lopes NP. Plantas medicinais: Fatores de influência no conteúdo de metabólitos secundários. Quím Nova. 2007;30(2):374-381.
30. Lewinsohn E, Gijzen M. Phytochemical diversity: The sounds of silent metabolism. Plant Sci. 2009;176(2):161-169.
31. Deschamps C, Monteiro R, Machado MP, Bizzo H, Biasi, LA. Produção de biomassa, teor e composição do óleo essencial de *Mentha* x *piperita* L. em resposta a fontes e doses de nitrogênio. Rev Bras Plantas Med. 2012;14(1):12-17.
32. Amaral W, Deschamps C, Machado MP, Koehler HS, Scheer AP, Cocco L, Yamamoto C. Avaliação de germoplasma de camomila e densidade de semeadura na produção e composição do óleo essencial. Hort Bras. 2012;30(2):195-200.
33. Deschamps C, Raskin I, Simon JE. Regulation of essential oil accumulation in basil (*Ocimum basilicum* L.) in response to elicitation. Int J Plant Sci. 2008;169(8):981-986.
34. Deschamps C, Simon JE. Terpenoid essential oil metabolism in basil (*Ocimum basilicum* L.) following elicitation. J Essent Oil Res. 2006;18(6):618-621.
35. Santos VMCS, Schneider TR, Bizzo HR, Deschamps C. Alternativas de propagação na produção de óleo essencial de *Mentha canadensis* L. no Litoral Norte Catarinense. Rev Bras Plantas Med. 2012; 14(1):97-102.
36. Masetto MAM, Deschamps C, Mógor AF, Bizzo HR. Teor e composição do óleo essencial de inflorescências e folhas de *Lavandula dentata* L. em diferentes estádios de desenvolvimento floral e épocas de colheita. Rev Bras Plantas Med. 2011;13(4):413-421.
37. Lucia A, Juan LW, Zerba EN, Harrand L, Marcó M, Masuh HM. Validation of models to estimate the fumigant and larvicidal activity of Eucalyptus essential oils against *Aedes aegypti* (Diptera: Culicidae). Parasitol Res. 2012;110(5):1675-1686.
38. Jiang H, Wang J, Song L, Cao X, Yao X, Tang F, Yue Y. GC× GC-TOFMS analysis of essential oils composition from leaves, twigs and seeds of *Cinnamomum camphora* L. Presl and their insecticidal and repellent activities. Molecules. 2016;21(4):423-435.

39. Machado MP, Bergo CL, Deschamps C, Bizzo HR, Biasi LA. Effect of the natural and artificial drying of leaf biomass *Piper hispidinervum* on the chemical composition of the essential oil. 2013;Semin: Cien Agrar 34(1):265-270.
40. Dabague ICM, Deschamps C, Mógor AF, Scheer AP, Côcco L. Teor e composição de óleo essencial de rizomas de gengibre (*Zingiber officinale* Roscoe) após diferentes períodos de secagem. Bras Plantas Med. 2011;13(1):79-84.
41. Cavallaro A. Gel for topical application of clove essential oil with broad spectrum anti-inflammatory action and method of preparing same. US Patent No. 9,095,607; 2015.
42. Malast M. Antimicrobial compositions and methods of use. U.S. Patent Application No. 14/448,452; 2014.
43. Enan E. Pest control compositions and methods. U.S. Patent Application No. 14/290,892; 2014.
44. Atarashi M, Matsubara A, Abe R. Insect pest control agent. U.S. Patent Application No. 14/406,292; 2013.
45. Silva ACRD, Lopes PM, Azevedo MMBD, Costa DCM, Alviano CS, Alviano DS. Biological activities of a-pinene and β-pinene enantiomers. Molecules. 2012; 17(6):6305-6316.
46. Wang W, Li N, Luo M, Zu Y, Efferth T. Antibacterial activity and anticancer activity of *Rosmarinus officinalis* L. essential oil compared to that of its main components. Molecules. 2012;17(3):2704-2713.
47. Phillips CA, Gkatzionis K, Laird K, Score J, Kant A, Fielder MD. Identification and quantification of the antimicrobial components of a citrus essential oil vapor. Nat Prod Commun. 2012;7(1):103-107.
48. Verma RS, Padalia RC, Chauhan A. Volatile constituents of *Origanum vulgare* L., 'thymol'chemotype: Variability in North India during plant ontogeny. Nat Prod Res. 2012;26(14):1358-1362.
49. Santana JS, Sartorelli P, Guadagnin RC, Matsuo AL, Figueiredo CR, Soares MG, Lago JHG. Essential oils from *Schinus terebinthifolius* leaves-chemical composition and *in vitro* cytotoxicity evaluation. Pharm Biol. 2012;50(10):1248-1253.
50. Falconieri D, Piras A, Porcedda S, Marongiu B, Gonçalves MJ, Cabral C, Salgueiro L. Chemical composition and biological activity of the volatile extracts of *Achillea millefolium*. Nat Prod Commun. 2011;6(10):1527-1530.
51. Victorio CP, Moreira CB, Souza MC, Sato A, Arruda RC. Secretory cavities and volatiles of *Myrrhinium atropurpureum* Schott var. atropurpureum (Myrtaceae): An endemic species collected in the restingas of Rio de Janeiro, Brazil. Nat Prod Commun. 2011;6(7):1045-1050.
52. Koliopoulos G, Pitarokili D, Kioulos E, Michaelakis A, Tzakou, O. Chemical composition and larvicidal evaluation of *Mentha, Salvia*, and *Melissa* essential oils against the West Nile virus mosquito *Culex pipiens*. Parasitol Res. 2010;107(2):327-335.
53. Michaelakis A, Papachristos D, Kimbaris A, Koliopoulos G, Giatropoulos A, Polissiou MG. Citrus essential oils and four enantiomeric pinenesagainst *Culex pipiens* (Diptera: *Culicidae*). Parasitol Res. 2009; 105(3):769-773.
54. Schmidt E, Bail S, Buchbauer G, Stoilova I, Atanasova T, Stoyanova A, Jirovetz, L. Chemical composition, olfactory evaluation and antioxidant effects of essential oil from *Mentha* x *piperita*. Nat Prod Commun 2009;4(8):1107-1112.
55. Judzentiene A, Tomi F, Casanova J. Analysis of essential oils of *Artemisia absinthium* L. from Lithuania by CC, GC (RI), GC-MS and 13C NMR. Nat Prod Commun. 2009;4(8):1113-1118.
56. Wang JL, Li Y, Lei CL. Evaluation of monoterpenes for the control of *Tribolium castaneum* (Herbst) and *Sitophilus zeamaise* Motschulsky. Nat Prod Res. 2009;23(12):1080-1088.
57. Lawal OA, Oyedeji AO. Chemical composition of the essential oils of *Cyperus rotundus* L. from South Africa. Molecules. 2009;14(8):2909-2917.
58. Chanthaphon S, Chanthachum S, Hongpattarakere T. Antimicrobial activities of essential oils and crude extracts from tropical *Citrus* spp. against food-related microorganisms. Songklanakarin J Sci Technol. 2008;30(1):125-131.
59. Hayouni EA, Chraief I, Abedrabba M, Bouix M, Leveau JY, Mohammed H, Hamdi M. Tunisian *Salvia officinalis* L. and *Schinus molle* L. essential oils: Their chemical compositions and their preservative effects against Salmonella

inoculated in minced beef meat. Int J Food Microbiol. 2008;125(3):242-251.

60. Pålsson K, Jaenson TG, Bæckström P, Borg-Karlson AK. Tick repellent substances in the essential oil of *Tanacetum vulgare*. J Med Entomol. 2008; 45(1):88-93.
61. Yalçin H, Anik M, Şanda MA, Çakir A. Gas chromatography/mass spectrometry analysis of *Laurus nobilis* essential oil composition of northern Cyprus. J Med Food. 2007;10(4):715-719.
62. Lucia A, Gonzalez Audino PAOLA, Seccacini E, Licastro S, Zerba E, Masuh H. Larvicidal effect of *Eucalyptus grandis* essential oil and turpentine and their major components on *Aedes aegypti* larvae. J Am Mosq Control Assoc. 2007;23(3):299-303.
63. Riyazi A, Hensel A, Bauer K, Geissler N, Schaaf S, Verspohl EJ. The effect of the volatile oil from ginger rhizomes (*Zingiber officinale*), its fractions and isolated compounds on the 5-HT3 receptor complex and the serotoninergic system of the rat ileum. Planta Med. 2007;73(04):355-362.
64. Wolff R. Essential oil compositions for killing or repelling ectoparasites and pests and methods for use thereof. U.S. Patent Application No. 11/674,882, February 14; 2007.
65. Govindarajan M, Rajeswary M, Hoti SL, Bhattacharyya A, Benelli G. Eugenol, α-pinene and β-caryophyllene from *Plectranthus barbatus* essential oil as eco-friendly larvicides against malaria, dengue and Japanese encephalitis mosquito vectors. Parasitol Res. 2016b;115(2):807-815.
66. Jones A. Pesticidal compositions and methods of use thereof. U.S. Patent No. 8,834,908, September 16; 2014.
67. Rather MA, Dar BA, Dar MY, Wani BA, Shah WA, Bhat BA, Qurishi MA. Chemical composition, antioxidant and antibacterial activities of the leaf essential oil of *Juglans regia* L. and its constituents. Phytomedicine. 2012;19(13):1185-1190.
68. Hieu TT, Kim SI, Ahn YJ. Toxicity of *Zanthoxylum piperitum* and *Zanthoxylum armatum* oil constituents and related compounds to Stomoxys calcitrans (Diptera: *Muscidae*). J Med Entomol. 2012;49(5):1084-1091.
69. Lakušić DV, Ristić MS, Slavkovska VN, Šinžar-Sekulić JB, Lakušić BS. Environment-Related Variations of the Composition of the Essential Oils of Rosemary (*Rosmarinus officinalis* L.) in the Balkan Penninsula. Chem Biodivers. 2012;9(7):1286-1302.
70. Rodrigues FF, Oliveira LG, Rodrigues FF, Saraiva ME, Almeida SC, Cabral ME, Costa JGM. Chemical composition, antibacterial and antifungal activities of essential oil from *Cordia verbenacea* DC leaves. Pharmacognosy Res. 2012; 4(3):161-165.
71. Mishra AK, Mishra A, Verma A, Chattopadhyay P. Effects of Calendula essential oil-based cream on biochemical parameters of skin of albino rats against ultraviolet B radiation. Sci Pharm. 2012;80(3):669-684.
72. Kumar P, Mishra S, Malik A, Satya S. Compositional analysis and insecticidal activity of *Eucalyptus globulus* (family: *Myrtaceae*) essential oil against housefly (*Musca domestica*). Acta Trop. 2012A; 122(2):212-218.
73. Kumar P, Mishra S, Malik A, Satya S. Insecticidal evaluation of essential oils of *Citrus sinensis* L. (Myrtales: *Myrtaceae*) against housefly, *Musca domestica* L.(Diptera: *Muscidae*). Parasitol Res. 2012b;110(5):1929-1936.
74. Chung IM, Ro HM, Moon HI. Major essential oils composition and immunotoxicity activity from leaves of *Foeniculum vulgare* against *Aedes aegypti* L. Immunopharmacol Immunotoxicol. 2011; 33(3):450-453.
75. Alzogaray RA, Lucia A, Zerba EN, Masuh HM. Insecticidal activity of essential oils from eleven *Eucalyptus* spp. and two hybrids: lethal and sublethal effects of their major components on *Blattella germanica*. J Econ Entomol. 2011;104(2):595-600.
76. Miguel G, Cruz C, Faleiro ML, Simoes MTF, Figueiredo AC, Barroso JG, Pedro LG. *Salvia officinalis* L. essential oils: effect of hydrodistillation time on the chemical composition, antioxidant and antimicrobial activities. Nat Prod Res. 2011;25(5):526-541.
77. Freitas FP, Freitas SP, Lemos G, Vieira IJ, Gravina GA, Lemos FJ. Comparative larvicidal activity of essential oils from three medicinal plants against *Aedes*

aegypti L. Chem Biodivers. 2010; 7(11):2801-2807.

78. Maxia A, Marongiu B, Piras A, Porcedda S, Tuveri E, Gonçalves MJ, Salgueiro L. Chemical characterization and biological activity of essential oils from *Daucus carota* L. subsp. carota growing wild on the Mediterranean coast and on the Atlantic coast. Fitoterapia. 2009;80(1): 57-61.
79. Navarro MC, Noguera MA, Romero MC, Montilla MP, De Selgas JG, Valero, A. *Anisakis simplex* sl: Larvicidal activity of various monoterpenic derivatives of natural origin against L3 larvae *in vitro* and *in vivo*. Exp Parasitol. 2008;120I(4):295-299.
80. Ozel MZ, Gogus F, Lewis AC. Composition of *Eucalyptus camaldulensis* volatiles using direct thermal desorption coupled with comprehensive two-dimensional gas chromatography-time-of-flight-mass spectrometry. J Chromatogr Sci. 2008; 46(2):157-161.
81. Enan E. Pest control using natural pest control agent blends. U.S. Patent No. 9,492,490, November 15; 2016.
82. Steward VB, Fasano S, Huchet GR. Insecticidal compositions with disinfectant. U.S. Patent No. 8,741,874, June 3; 2014.
83. Friend LE, Nelson Jr EC. Long-lasting insect repellant, pesticide and antifeedant compositions. U.S. Patent No. 8,758,787. June 24.
84. Furneri PM, Mondello L, Mandalari G, Paolino D, Dugo P, Garozzo A, Bisignano G. *In vitro* antimycoplasmal activity of *Citrus bergamia* essential oil and its major components. Eur J Med Chem. 2012; 52(1):66-69.
85. Govindarajan M, Sivakumar R, Rajeswari M, Yogalakshmi K. Chemical composition and larvicidal activity of essential oil from *Mentha spicata* (Linn.) against three mosquito species. Parasitol Res. 2012; 110(5):2023-2032.
86. Hirota R, Nakamura H, Bhatti AS, Ngatu NR, Muzembo BA, Dumavibhat N, Suganuma N. Limonene inhalation reduces allergic airway inflammation in Dermatophagoides farinae-treated mice. Inhal Toxicol. 2012;24(6):373-381.
87. Amiri H. Volatile constituents and antioxidant activity of flowers, stems and leaves of *Nasturtium officinale* R. Br. Nat Prod Res. 2012;26(2):109-115.
88. Sonboli A, Gholipour A, Yousefzadi M. Antibacterial activity of the essential oil and main components of two *Dracocephalum* species from Iran. Nat Prod Res. 2012;26(22):2121-2125.
89. Zhang JS, Zhao NN, Liu QZ, Liu ZL, Du SS, Zhou L, Deng ZW. Repellent constituents of essential oil of *Cymbopogon distans* aerial parts against two stored-product insects. J Agric Food Chem. 2011;59(18):9910-9915.
90. Al-Maskri AY, Hanif MA, Al-Maskari MY, Abraham AS, Al-Sabahi JN, Al-Mantheri O. Essential oil from *Ocimum basilicum* (Omani Basil): A desert crop. Nat Prod Commun. 2011;6(10):1487-1490.
91. Villafañe E, Tolosa D, Bardon A, Neske A. Toxic effects of *Citrus aurantium* and *C. limon* essential oils on *Spodoptera frugiperda* (Lepidoptera: Noctuidae). Nat Prod Commun. 2011;6(9):1389-1392.
92. López MA, Stashenko EE, Fuentes JL. Chemical composition and antigenotoxic properties of *Lippia alba* essential oils. Genet Mol Biol. 2011;34(3):479-488.
93. Santos SR, Melo MA, Cardoso AV, Santos R L, Sousa DP, Cavalcanti SC. Structure–activity relationships of larvicidal monoterpenes and derivatives against *Aedes aegypti* Linn. Chemosphere. 2011;84(1): 150-153.
94. Marques MM, Morais SM, Vieira ÍG, Vieira MG, Silva ARA, De Almeida RR, Guedes MIF. Larvicidal activity of *Tagetes erecta* against *Aedes aegypti*. J Am Mosq Control Assoc. 2011;27(2):156-158.
95. Park HM, Kim J, Chang KS, Kim BS, Yang YJ, Kim GH, Park IK. Larvicidal activity of Myrtaceae essential oils and their components against *Aedes aegypti*, acute toxicity on *Daphnia magna*, and aqueous residue. J Med Entomol. 2011;48(2):405-410.
96. Mabrouk S, Elaissi A, Ben Jannet H, Harzallah-Skhiri F. Chemical composition of essential oils from leaves, stems, flower heads and roots of *Conyza bonariensis* L. from Tunisia. Nat Prod Res. 2011; 25(1):77-84.
97. Tesch NR, Mora F, Rojas L, Díaz T, Velasco J, Yánez C, Pasquale S. Chemical composition and antibacterial activity of the essential oil of *Lantana camara* var. moritziana. Nat Prod Commun. 2011;6(7):1031-1034.

98. Samaneh ET, Tayebeh R, Hassan E, Vahid N. Composition of essential oils in subterranean organs of three species of *Valeriana* L. Nat Prod Res. 2010; 24(19):1834-1842.
99. Singh P, Shukla R, Prakash B, Kumar A, Singh S, Mishra PK, Dubey NK. Chemical profile, antifungal, antiaflatoxigenic and antioxidant activity of *Citrus maxima* Burm. and *Citrus sinensis* (L.) Osbeck essential oils and their cyclic monoterpene, DL-limonene. Food Chem Toxicol. 2010; 48(6):1734-1740.
100. Roberto D, Micucci P, Sebastian T, Graciela F, Anesini C. Antioxidant activity of limonene on normal murine lymphocytes: Relation to H2O2 modulation and cell proliferation. Basic Clin Pharmacol Toxicol. 2010;106(1):38-44.
101. Mkaddem M, Bouajila J, Ennajar M, Lebrihi A, Mathieu F, Romdhane M. Chemical composition and antimicrobial and antioxidant activities of *Mentha* (*longifolia* L. and *viridis*) essential oils. J Food Sci. 2009;74(7):M358-M363.
102. Willimann JA, Chandler W. Antimicrobial and antiviral composition. U.S. Patent Application No. 11/906,640, October 3; 2007.
103. Saini R, Hassanali A. Repellent Compositions for Insects and Other Arthropods. U.S. Patent Application No. 15/016,303, February 5; 2016.
104. Costa EV, Menezes LR, Rocha SL, Baliza IR, Dias RB, Rocha CA, Bezerra DP. Antitumor properties of the leaf essential oil of *Zornia brasiliensis*. Planta Med. 2015; 81(7):563-567.
105. Assis Lage TC, Montanari RM, Fernandes AS, Oliveira Monteiro CM, Senra TDOS, Zeringota V, Daemon E. Chemical composition and acaricidal activity of the essential oil of *Baccharis dracunculifolia* De Candole (1836) and its constituents nerolidol and limonene on larvae and engorged females of *Rhipicephalus microplus* (Acari: Ixodidae). Exp Parasitol. 2015;148(1):24-29.
106. Lee K, Lee JH, Kim SI, Cho MH, Lee J. Anti-biofilm, anti-hemolysis, and anti-virulence activities of black pepper, cananga, myrrh oils, and nerolidol against *Staphylococcus aureus*. Appl Microbiol Biotechnol. 2014;98(22):9447-9457.
107. Schaetzer JH, Benfatti F, Pabba J, Rendler S, Crossthwaite A. Insecticidal compounds. U.S. Patent Application No. 14/916,017, August 20; 2014.
108. Abrey AJ, Brooks KW, Gill ABN, Newitt CR. Pesticidal composition. U.S. Patent Application No. 15/037,187, November 21; 2013.
109. Neto JDN, Almeida AAC, Silva Oliveira J, Santos OS, Sousa DP, Freitas RM. Antioxidant effects of nerolidol in mice hippocampus after open field test. Neurochem Res. 2013;38(9):1861-1870.
110. Sperotto ARM, Moura DJ, Péres VF, Damasceno FC, Caramão EB, Henriques JAP, Saffi J. Cytotoxic mechanism of *Piper gaudichaudianum* Kunth essential oil and its major compound nerolidol. Food Chem Toxicol. 2013;57:57-68.
111. Di Campli E, Di Bartolomeo S, Pizzi PD, Di Giulio M, Grande R, Nostro A, Cellini L. Activity of tea tree oil and nerolidol alone or in combination against *Pediculus capitis* (head lice) and its eggs. Parasitol Res. 2012;111(5):1985-1992.
112. Navarro-Moll MC, Romero MC, Montilla MP, Valero A. In vitro and in vivo activity of three sesquiterpenes against L 3 larvae of Anisakis type I. Exp Parasitol. 2011; 127(2):405-408.
113. Evans D, Evans S. Composition for treating pain and/or inflammation comprising eugenol and beta-caryophyllene. U.S. Patent Application No. 2014/000545, July 5; 2013.
114. Galdino PM, Nascimento MVM, Florentino IF, Lino RC, Fajemiroye JO, Chaibub BA, Costa EA. The anxiolytic-like effect of an essential oil derived from *Spiranthera odoratissima* A. St. Hil. leaves and its major component, β-caryophyllene, in male mice. Prog Neuropsychopharmacol Biol Psychiatry. 2012;38(2):276-284.
115. Pande C, Tewari G, Singh S, Singh C. Chemical markers in *Origanum vulgare* L. from Kumaon Himalayas: A chemosystematic study. Nat Prod Res. 2012;26(2):140-145.
116. Padalia RC, Verma RS, Chauhan A, Chanotiya CS, Yadav A. Variation in the volatile constituents of *Artemisia annua* var. CIM-Arogya during plant ontogeny. Nat Prod Commun. 2011;6(2):239-242.
117. Birkett MA, Hassanali A, Hoglund S, Pettersson J, Pickett JA. Repellent activity of catmint, *Nepeta cataria* and iridoid nepetalactone isomers against Afro-tropical mosquitoes, ixodid ticks and red

poultry mites. Phytochemistry. 2011; 72(1):109-114.

118. Bernardes WA, Lucarini R, Tozatti MG, Bocalon Flauzino LG, Souza MG, Turatti IC, CunhamWR. Antibacterial activity of the essential oil from *Rosmarinus officinalis* and its major components against oral pathogens. Z Naturforsch C Bio. 2010;65(10):588-593.
119. Zhang Q, Margaryan A, Schneidmiller RG. Methods for repelling insects using sesquiterpene hydrocarbons and their derivatives. U.S. Patent Application No. 12/346,082, December 30; 2008.
120. Fernandes ES, Passos GF, Medeiros R, Cunha FM, Ferreira J, Campos MM, Calixto JB. Anti-inflammatory effects of compounds alpha-humulene and (−)-trans-caryophyllene isolated from the essential oil of *Cordia verbenacea*. Eur J Pharmacol. 2007;569(3):228-236.
121. Fichi G, Flamini G, Giovanelli F, Otranto D, Perrucci S. Efficacy of an essential oil of *Eugenia caryophyllata* against *Psoroptes cuniculi*. Exp Parasitol. 2007;115(2):168-172.
122. Qin NY, Yang FQ, Wang YT, Li SP. Quantitative determination of eight components in rhizome (Jianghuang) and tuberous root (Yujin) of *Curcuma longa* using pressurized liquid extraction and gas chromatography–mass spectrometry. J Pharm Biomed Anal. 2007;43(2):486-492.
123. Blain EJ, Duance VC, Ali AY, Bowen ID. Inhibitor of inflammatory conditions. U.S. Patent No. 9,439,936, September 13; 2016.
124. Enan E. Synergistic pest-control compositions. U.S. Patent No. 8,734,869, May 27; 2014b.
125. Enan, E. Compositions for controlling insects. U.S. Patent No. 8,507,013, August 13; 2013.
126. Sims SR. Pesticidal compositions. U.S. Patent n. 13/562,073, July 3; 2012.
127. Nascimento AF, Camara CA, De Moraes MM, Ramos CS. Essential oil composition and acaricidal activity of *Schinus terebinthifolius* from Atlantic Forest of Pernambuco, Brazil against *Tetranychus urticae*. Nat Prod Commun. 2012;7(1):129-132.
128. El-Nekeety AA, Mohamed SR, Hathout AS, Hassan NS, Aly SE, Abdel-Wahhab MA. Antioxidant properties of *Thymus vulgaris* oil against aflatoxin-induce oxidative stress in male rats. Toxicon. 2011;57(7):984-991.
129. Sindhu S, Chempakam B, Leela NK, Bhai RS. Hemoprevention by essential oil of turmeric leaves (*Curcuma longa* L.) on the growth of *Aspergillus flavus* and aflatoxin production. Food Chem Toxicol. 2011; 49(5):1188-1192.
130. Ogunbinu AO, Flamini G, Cioni PL, Adebayo MA, Ogunwande IA. Constituents of *Cajanus cajan* (L.) Millsp., *Moringa oleifera* Lam., *Heliotropium indicum* L. and *Bidens pilosa* L. from Nigeria. Nat Prod Commun. 2009;4(4):573-578.
131. Riyazi A, Hensel A, Bauer K, Geissler N, Schaaf S, Verspohl EJ. The effect of the volatile oil from ginger rhizomes (*Zingiber officinale*), its fractions and isolated compounds on the 5-HT3 receptor complex and the serotoninergic system of the rat ileum. Planta Med. 2007;73(04): 355-362.
132. Rosenbloom RA. Anti-microbial compositions and methods of using same. U.S. Patent No. 7,396,546, July 8; 2008.
133. Jack N, Busch J. Insect repellent compositions. U.S. Patent No. 9,326,524, May 3; 2016.
134. Zielinski J, Moon TR, Allen EP. Antioxidant compositions for treatment of inflammation or oxidative damage. U.S. Patent No. 9,421,180, August 23; 2016.
135. Morais SR, Oliveira TLS, De Oliveira LP, Tresvenzol LMF, Da Conceição EC, Rezende MH, Paula JR. Essential oil composition, antimicrobial and pharmacological activities of *Lippia sidoides* cham.(verbenaceae) from São Gonçalo do Abaeté, Minas Gerais, Brazil. Pharmacogn Mag. 2016;12(48):262-270.
136. Zhong T. Botanical insecticides. U.S. Patent No. 14/611613, Februry 2; 2015.
137. Bailey-Jackson S. Natural pesticide composition and method of producing. U.S. Patent No. 9,198,435, December 1; 2015.
138. Strobel GA, Blatt B. Volatile organic compound formulations having antimicrobial activity. U.S. Patent Application n. 14/322,757, July 2; 2014.
139. Benavides P, Gongora C. Combination of biological pesticides. U.S. Patent Application No. 14/762,213, November 29; 2013.
140. Mcwherter JF, Reiss U. Topical anti-inflammatory compositions and uses

thereof. U.S. Patent Application No. 14/054,578, October 15; 2013.

141. Sánchez Chopa C, Deschamps LR. Composition and biological activity of essential oils against *Metopolophium dirhodum* (Hemiptera: Aphididae) cereal crop pest. Pest Manag Sci. 2012; 68(11):1492-1500.

142. Liu ZL, Zhao NN, Liu CM, Zhou L, Du SS. Identification of insecticidal constituents of the essential oil of *Curcuma wenyujin* rhizomes active *against Liposcelis bostrychophila* Badonnel. Molecules. 2012b;17(10):12049-12060.

143. Jug-Dujaković M, Ristić M, Pljevljakušić D, Dajić-Stevanović Z, Liber Z, Hančević K, Šatović Z. High diversity of indigenous populations of dalmatian sage (*Salvia officinalis* L.) in essential-oil composition. Chem Biodivers. 2012;9(10):2309-2323.

144. Sousa JP, Araújo Torres R, Azerêdo GA, Figueiredo RCBQ, Silva Vasconcelos MA, Souza EL. Carvacrol and 1, 8-cineole alone or in combination at sublethal concentrations induce changes in the cell morphology and membrane permeability of *Pseudomonas fluorescen*s in a vegetable-based broth. Int J Food Microbiol. 2012; 158(1):9-13.

145. Elaissi A, Rouis Z, Mabrouk S, Salah KBH, Aouni M, Khouja ML, Harzallah-Skhiri F. Correlation between chemical composition and antibacterial activity of essential oils from fifteen Eucalyptus species growing in the Korbous and Jbel Abderrahman Arboreta (North East Tunisia). Molecules. 2012;17(3):3044-3057.

146. Abu-Darwish MS, Alu'datt MH, Al-Tawaha AR, Ereifej K, Almajwal A, Odat N, Al Khateeb W. Seasonal variation in essential oil yield and composition from *Thymus vulgaris* L. during different growth stages in the south of Jordan. Nat Prod Res. 2012; 26(14):1310-1317.

147. Saab AM, Tundis R, Loizzo MR, Lampronti I, Borgatti M, Gambari R, Menichini F. Antioxidant and antiproliferative activity of *Laurus nobilis* L.(Lauraceae) leaves and seeds essential oils against K562 human chronic myelogenous leukaemia cells. Nat Prod Res. 2012;26(18):1741-1745.

148. Shukla R, Singh P, Prakash B, Kumar A, Mishra PK, Dubey NK. Efficacy of essential oils of *Lippia alba* (Mill.) NE Brown and *Callistemon lanceolatus* (Sm.) Sweet and their major constituents on mortality, oviposition and feeding behaviour of pulse beetle, *Callosobruchus chinensis* L. Journal Sci Food Agr. 2011;91(12):2277-2283.

149. Nascimento AF, Camara CA, De Moraes MM, Ramos CS. Essential oil composition and acaricidal activity of *Schinus terebinthifolius* from Atlantic Forest of Pernambuco, Brazil against *Tetranychus urticae*. Nat Prod Commun. 2012;7(1):129-132.

150. Gupta S, Pandotra P, Ram G, Anand R, Gupta AP, Husain K, Mallavarapu GR. Composition of a monoterpenoid-rich essential oil from the rhizome of *Zingiber officinale* from north western Himalayas. Nat Prod Commun. 2011;6(1):93-96.

151. Galindo LA, De Moraes Pultrini A, Costa M. Biological effects of *Ocimum gratissimum* L. are due to synergic action among multiple compounds present in essential oil. J Nat Med. 2010;64(4):436-441.

152. Formisano C, Senatore F, Bruno M, Rosselli S, Bellone G, Spadaro V. Essential oil composition of *Tanacetum vulgare* subsp. siculum (Guss.) Raimondo et Spadaro (Asteraceae) from Sicily. Nat Prod Commun. 2009;4(4):567-570.

153. Terzi V, Morcia C, Faccioli P, Vale G, Tacconi G, Malnati M. *In vitro* antifungal activity of the tea tree (*Melaleuca alternifolia*) essential oil and its major components against plant pathogens. Lett Appl Microbiol. 2007;44(6):613-618.

154. Gaia AM, Yamaguchi LF, Jeffrey CS, Kato MJ. Age-dependent changes from allylphenol to prenylated benzoic acid production in *Piper gaudichaudianum* Kunth. Phytochemistry. 2014;106(1):86-93.

155. Liu SQ, Scott IM, Pelletier Y, Kramp K, Durst T, Sims SR, Arnason JT. Dillapiol: A pyrethrum synergist for control of the Colorado potato beetle. J Econ Entomol. 2014;107(2):797-805.

156. Shah SA, Horsler CW. Insecticidal composition. U.S. Patent No. 8,137,715, March 20; 2012.

157. Parise-Filho R, Pastrello M, Pereira Camerlingo CE, Silva GJ, Agostinho LA, De Souza T, Polli MC. The anti-inflammatory activity of dillapiole and some semisynthetic analogues. Pharm Biol. 2011; 49(11):1173-1179.

158. Silva WC, De Souza Martins JR, De Souza HEM, Heinzen H, Cesio MV, Mato M, De

Barros NM. Toxicity of *Piper aduncum* L.(Piperales: Piperaceae) from the Amazon forest for the cattle tick *Rhipicephalus (Boophilus) microplus* (Acari: Ixodidae). Vet Parasitol. 2009;164(2): 267-274.

159. Chalchat JC, Özcan MM. Comparative essential oil composition of flowers, leavesand stems of basil (*Ocimum basilicum* L.) used as herb. Food Chem. 2008;110(2):501-503.

160. Gallucci MN, Carezzano ME, Oliva MM, Demo MS, Pizzolitto RP, Zunino MP, Dambolena JS. *In vitro* activity of natural phenolic compounds against fluconazole-resistant Candida species: A quantitative structure–activity relationship analysis. J Appl Microbiol. 2014;116(4): 795-804.

161. Goyal R, Shanmuga K, Wilson SL. Agricultural pesticide compositions. U.S. Patent Application No. 14/585,440, December 30; 2014.

162. Kellar S, Kellar C. Natural insecticide composition. U.S. Patent Application No. 14/514,513, October 15; 2014.

163. Pesaro M, Hölscher B, Schmaus G, Köhler A. Antimicrobial Compositions. U.S. Patent Application No. 14/773,071, March 6; 2014.

164. Prencipe M, Potnis S, Fisher S, Lewis N, Tambs G. Antimicrobial compositions comprising essential oil combinations. U.S. Patent Application No. 14/783,077, June 18; 2013.

165. Farias-Junior PA, Rios MC, Moura TA, Almeida RP, Alves PB, Blank AF, Scher R. Leishmanicidal activity of carvacrol-rich essential oil from *Lippia sidoides* Cham. Biol Res. 2012;45(4):399-402.

166. Kpoviessi K, Bénédicta GH, Ladekan EY, Kpoviessi DS, Gbaguidi F, Yehouenou B, Accrombessi GC. Chemical variation of essential oil constituents of *Ocimum gratissimum* L. from Benin, and Impact on Antimicrobial Properties and Toxicity against *Artemia salina* Leach. Chem Biodivers. 2012;9(1):139-150.

167. Nowak A, Kalemba D, Krala L, Piotrowska M, Czyzowska A. The effects of thyme (*Thymus vulgaris*) and rosemary (*Rosmarinus officinalis*) essential oils on *Brochothrix thermosphacta* and on the shelf life of beef packaged in high-oxygen modified atmosphere. Food Microbiol. 2012;32(1):212-216.

168. Riella KR, Marinho RR, Santos JS, Pereira-Filho RN, Cardoso JC, Albuquerque-Junior RLC, Thomazzi SM. Anti-inflammatory and cicatrizing activities of thymol, a monoterpene of the essential oil from *Lippia gracilis*, in rodents. J Ethnopharmacol. 2012;143(2):656-663.

169. Aazza S, Lyoussi B, Miguel MG. Antioxidant and antiacetylcholinesterase activities of some commercial essential oils and their major compounds. Molecules. 2011;16(9):7672-7690.

170. Abrey AJ, Brooks KW, Gill ABN, Newitt CR. Pesticidal Composition. U.S. Patent Application No. 15/037,187, November 21; 2013.

171. García-García R, López-Malo A, Palou E. Bactericidal action of binary and ternary mixtures of carvacrol, thymol and eugenol against *Listeria innocua*. J Food Sci. 2011;76(2):95-100.

172. Guarda A, Rubilar JF, Miltz J, Galotto MJ. The antimicrobial activity of microencapsulated thymol and carvacrol. Int J Food Microbiol. 2011; 146(2):144-150.

173. Pavela R. Insecticidal properties of phenols on *Culex quinquefasciatus* Say and *Musca domestica* L. Parasitol Res. 2011;109(6):1547-1553.

174. Soliman FM, Yousif MF, Zaghloul SS, Okba MM. Seasonal variation in the essential oil composition of *Origanum majorana* L. cultivated in Egypt. Z Naturforsch C Bio. 2009;64(10):611-614.

175. Zhang Y, Kubota A, Niyaz NM, Barton T, Trullinger TK, Lowe CT, Hunter R. Pesticidal compositions and related methods. U.S. Patent No. 9,523,100, December 30; 2016.

176. Birtic S, Heudre MMPP, Pierre FXH, Mesnier XPF, Passemard A, Bily AC, Roller M. Antimicrobial compositions. U.S. Patent Application No. 14/615,527, February 6; 2015.

177. Gül S, Demirci B, Başer KHC, Akpulat HA, Aksu P. Chemical composition and *in vitro* cytotoxic, genotoxic effects of essential oil from *Urtica dioica* L. Bull Environ Contam Toxicol. 2012;88(5):666-671.

178. Liu Y, Song M, Che TM, Bravo D, Pettigrew JE. Anti-inflammatory effects of several plant extracts on porcine alveolar macrophages *in vitro.* J Anim Sci. 2012a;90(8):2774-2783.

179. Ramos C, Teixeira B, Batista I, Matos O, Serrano C, Neng NR, Marques A.

Antioxidant and antibacterial activity of essential oil and extracts of bay laurel *Laurus nobilis* Linnaeus (Lauraceae) from Portugal. Nat Prod Res. 2012;26(6): 518-529.

180. Jordán MJ, Quílez M, Luna MC, Bekhradi F, Sotomayor JA, Sánchez-Gómez P, Gil MI. Influence of water stress and storage time on preservation of the fresh volatile profile of three basil genotypes. Food Chem. 2017;221(1):169-177.
181. Reis SL, Mantello AG, Macedo JM, Gelfuso EA, Da Silva CP, Fachin AL, Beleboni RO. Typical monoterpenes as insecticides and repellents against stored grain pests. Molecules. 2016;21(3):258-268.
182. Sharma UK, Sharma AK, Pandey AK. Medicinal attributes of major phenylpropanoids present in cinnamon. BMC Complement Altern Med. 2016; 156(16):1-11.
183. Budri PE, Silva NCC, Bonsaglia ECR, Fernandes A, Araújo JP, Doyama JT, Rall VLM. Effect of essential oils of *Syzygium aromaticum* and *Cinnamomum zeylanicum* and their major components on biofilm production in *Staphylococcus aureus* strains isolated from milk of cows with mastitis. J Dairy Sci. 2015;98(9):5899-5904.
184. Swamy MK, Sinniah UR. A comprehensive review on the phytochemical constituents and pharmacological activities of *Pogostemon cablin* Benth.: An aromatic medicinal plant of industrial importance. Molecules. 2015;20(5):8521-8547.
185. Silva JKR, Silva JRA, Nascimento SB, Da Luz SF, Meireles EM, Alves CN, Maia JGS. Antifungal activity and computational study of constituents from *Piper divaricatum* essential oil against *Fusarium* infection in black pepper. Molecules. 2014; 19(11):17926-17942.
186. Takken W, Van Loon JJA, Zwiebel LJ, Pask GM, Mukabana WR. Insect repellent compositions and methods of use. U.S. Patent Application No. 15/033,884, October 30; 2014.
187. Edwards JD, Palermo J. Analgesic and anti-inflammatory composition. U.S. Patent No. 8,617,893, December 31; 2013.
188. Gülçin I. Antioxidant activity of eugenol: A structure–activity relationship study. J Med Food. 2011;14(9):975-985.
189. Nascimento JC, Barbosa LC, Paula VF, David JM, Fontana R, Silva LA, França RS. Chemical composition and antimicrobial activity of essential oils of *Ocimum canum* Sims. and *Ocimum selloi* Benth. An Acad Bras Ciênc. 2011; 83(3):787-800.
190. Bertrand H, Kyriazis M. Topical formulation for pain relief. U.S. Patent Application No. 15/141,872, April 29; 2016.
191. Carrasco A, Martinez-Gutierrez R, Tomas V, Tudela J. Lavandin (*Lavandula*× *intermedia* Emeric ex Loiseleur) essential oil from Spain: Determination of aromatic profile by gas chromatography–mass spectrometry, antioxidant and lipoxygenase inhibitory bioactivities. Nat Prod Res. 2016;30(10):1123-1130.
192. Stoller A, Edmunds A, Pitterna T, Hueter OF, Jung PJM. Insecticidal compounds. U.S. Patent No. 9,402,395, August 2; 2016.
193. Tak JH, Isman MB. Enhanced cuticular penetration as the mechanism for synergy of insecticidal constituents of rosemary essential oil in *Trichoplusiani.* Sci Rep. 2015;5(1):1-10.
194. Fraňková A, Marounek M, Mozrová V, Weber J, Klouček P, Lukešová D. Antibacterial activities of plant-derived compounds and essential oils toward *Cronobacter sakazakii* and *Cronobacter malonaticus*. Foodborne Pathog Dis. 2014; 11(10):795-797.
195. Liebowitz S, Traistaru NC. Antimicrobial compositions. U.S. Patent Application No. 15/031,036, October 22; 2014.
196. Guedes AGP, Hammock BD, Morisseau C. Treatment of Inflammatory Disorders in Non-Human Mammals. U.S. Patent Application No. 14/384,910, March 5; 2013.
197. Batubara I, Suparto IH, Sa'diah S, Matsuoka R, Mitsunaga T. Effects of Inhaled Citronella Oil and Related Compounds on Rat Body Weight and Brown Adipose Tissue Sympathetic Nerve. Nutrients. 2015;7(3):1859-1870.
198. Tolba H, Moghrani H, Benelmouffok A, Kellou D, Maachi R. Essential oil of algerian *Eucalyptus citriodora*: Chemical composition, antifungal activity. J Mycol Med. 2015;25(4):e128-e133.
199. Mello V, De Azevedo Prata MC, Da Silva MR, Daemon E, Da Silva LS, Del Gaudio Guimarães F, Cabral LM. Acaricidal

properties of the formulations based on essential oils from *Cymbopogon winterianus* and *Syzygium aromaticum* plants. Parasitol Res. 2014;113(12):4431-4437.

200. Scialdone MA. Formulations containing insect repellent compounds. U.S. Patent No. 8,748,477, June 10; 2014.
201. Victoria FN, Anversa R, Penteado F, Castro M, Lenardão EJ, Savegnago L. Antioxidant and antidepressant-like activities of semi-synthetic α-phenylseleno citronellal. Eur J Pharmacol. 2014;742(1): 131-138.
202. Taherpour A, Maroofi H, Rafie Z, Larijani K. Chemical composition analysis of the essential oil of *Melissa officinalis* L. from Kurdistan, Iran by HS/SPME method and calculation of the biophysicochemical coefficients of the components. Natural Prod Res. 2012;26(2):152-160.
203. Melo MS, Guimarães AG, Santana MF, Siqueira RS, De Lima ADCB, Dias AS, Almeida JR. Anti-inflammatory and redox-protective activities of citronellal. Biol Res. 2011;44(4):363-368.
204. Adukwu EC, Bowles M, Edwards-Jones V, Bone H. Antimicrobial activity, cytotoxicity and chemical analysis of lemongrass essential oil (*Cymbopogon flexuosus*) and pure citral. Appl Microbiol Biotechnol. 2016;100(22):9619-9627.
205. Ajayi EO, Sadimenko AP, Afolayan AJ. GC–MS evaluation of *Cymbopogon citratus* (DC) Stapf oil obtained using modified hydrodistillation and microwave extraction methods. Food Chem. 2016; 209(1):262-266.
206. Federman C, Ma C, Biswas D. Major components of orange oil inhibit *Staphylococcus aureus* growth and biofilm formation, and alter its virulence factors. J Med Microbiol. 2016;65(7):688-695.
207. Keramati S, Pirdashti H, Babaeizad V, Dehestani A. Essential oil composition of sweet basil (*Ocimum basilicum* L.) in symbiotic relationship with *Piriformospora indica* and paclobutrazol application under salt stress. Acta Biol Hung. 2016; 67(4):412-423.
208. Peixoto MG, Costa-Júnior LM, Blank AF, Da Silva Lima A, Menezes TSA, De Alexandria Santos D, Arrigoni-Blank MF. Acaricidal activity of essential oils *from Lippia alba* genotypes and its major components carvone, limonene, and citral against *Rhipicephalus microplus*. Vet Parasitol. 2015;210(1):118-122.
209. Füller TN, Bertrand C, Simon A, De Barros IBI, Neto JFB. *Elionurus muticus* as an Alternative Source of Citral from Pampa biome. Brazil. J Oleo Sci. 2014; 63(11):1109-1116.
210. Kumar P, Mishra S, Malik A, Satya S. Housefly (*Musca domestica* L.) control potential of *Cymbopogon citratus* Stapf. (Poales: Poaceae) essential oil and monoterpenes (citral and 1, 8-cineole). Parasitol Res. 2013;112(1):69-76.
211. Ortiz MI, González-García MP, Ponce-Monter HÁ, Castañeda-Hernández G, Aguilar-Robles P. Synergistic effect of the interaction between naproxen and citral on inflammation in rats. Phytomedicine. 2010;18(1):74-79.
212. Grando TH, De Sá MF, Baldissera MD, Oliveira CB, De Souza ME, Raffin RP, Monteiro SG. *In vitro* activity of essential oils of free and nanostructured *Melaleuca alternifolia* and of terpinen-4-ol on eggs and larvae of *Haemonchus contortus*. J Helminthol. 2016;90(3):377-382.
213. Callander JT, James PJ. Insecticidal and repellent effects of tea tree (*Melaleuca alternifolia*) oil against *Lucilia cuprina*. Vet Par. 2012;184: 271-278.
214. Tumbers N. Insect and disease control. U.S. Patent No. 9,066,522, June 30; 2015.
215. Zhang WJ, Yang K, You CX, Wang Y, Wang CF, Wu Y, Deng ZW. Bioactivity of essential oil from *Artemisia stolonifera* (Maxim.) Komar. and its main compounds against two stored-product insects. J Oleo Sci. 2015;64(3):299-307.
216. Harcourt NR. Antimicrobial composition and its method of use. U.S. Patent Application No. 13/920,485, June 18; 2013.
217. Ninomiya K, Hayama K, Ishijima SA, Maruyama N, Irie H, Kurihara J, Abe S. Suppression of inflammatory reactions by terpinen-4-ol, a main constituent of tea tree oil, in a murine model of oral candidiasis and its suppressive activity to cytokine production of macrophages *in vitro*. Biol Pharm Bull. 2013;36(5):838-844.
218. Suthisut D, Fields PG, Chandrapatya A. Contact toxicity, feeding reduction, and repellency of essential oils from three plants from the Ginger Family (Zingiberaceae) and their major components *against Sitophilus zeamais*

and *Tribolium castaneum*. J Econ Entomol. 2011;104(4):1445-1454.

219. Willis MD, Saunders ME, Ramoutar D, Szymczyk JM, Krenick FN, Rohrbacher A. Insecticidal compositions and methods of using the same. U.S. Patent No. 8,658,223, February 25; 2014.
220. Caballero-Gallardo K, Olivero-Verbel J, Stashenko EE. Repellent activity of essential oils and some of their individual constituents against *Tribolium castaneum* Herbst. J. Agric. Food Chem. 2011;59(5): 1690-1696.
221. Fang R, Jiang CH, Wang XY, Zhang HM, Liu ZL, Zhou L, Deng ZW. Insecticidal activity of essential oil of *Carum carvi* fruits from China and its main components against two grain storage insects. Molecules. 2010;15(12):9391-9402.
222. Enan EE. Molecular and pharmacological analysis of an octopamine receptor from American cockroach and fruit fly in response to plant essential oils. Arch Insect Biochem Physiol. 2005a;59(3):161–171.
223. Enan EE. Molecular response of *Drosophila melanogaster* tyramine receptor cascade to plant essential oils. Insect Biochem Molec Biol. 2005b; 35(4):309–321.
224. Rattan RS. Mechanism of action of insecticidal secondary metabolites of plant origin. Crop Prot. 2010;29(9):913–920.
225. Ryan MF, Byrne O. Plant- insect coevolution and inhibition of acetylcholinesterase. J Chem Ecol. 1988; 14(10):1965-1975.
226. Obeng-Ofori D, Reichmuth CH, Bekele AJ, Hassanali A. Toxicity and protectant potential of camphor, a major component of essential oil of *Ocimum kilimandscharicum*, against four stored product beetles. Int J Pest Manage. 1998;44(4):203-209.
227. Simas NK, Lima EC, Conceição SR, Kuster RM, Oliveira Filho AM. Produtos naturais para o controle da transmissão da dengue–atividade larvicida de *Myroxylon balsamum* (Óleo vermelho) e de terpenóides e fenilpropanóides. Quim Nova. 2004;27(1):46–49.
228. Michaelakis A, Papachristos D, Kimbaris A, Polissiou M. Larvicidal evaluation of three *Mentha* species essential oils and their isolated major components against the West Nile virus mosquito. Hellenic Plant Prot J. 2011;4(2):35–43.
229. Lima TC, Silva TKM, Silva FL, Barbosa-Filho JM, Marques MOM, Santos RLC, Sousa, DP. Larvicidal activity of *Mentha* x *villosa* Hudson essential oil, rotundifolone and derivatives. Chemosphere. 2014;104: 37-43.
230. Santos SRL, Silva VB, Melo, MA, Barbosa JDF, Santos RLC, Sousa DP, Cavalcanti SCH. Toxic effects on and structure–toxicity relationships of phenylpropanoids, terpenes, and related compounds in *Aedes aegypti* larvae. Vector Borne Zoonotic Dis. 2010;10(10):1049–1054.
231. Lopez O, Fernandez-Bolanos JG, Gil MV. New trends in pest control: The search for greener insecticides. Green Chem. 2005;6:431–442.
232. Katiki LM, Barbieri AME, Araujo RC, Veríssimo CJ, Louvandini H, Ferreira JFS. Synergistic interaction of ten essential oils against *Haemonchus contortus in vitro.* Vet Parasitol. 2017;243(30):47-51.
233. Pavela R. Essential oils for the development of eco-friendly mosquito larvicides: A review. Ind. Crops Products. 2015;76:174–187.
234. Regnault-Roger, C, Vicent C, Arnason JT. Essential oils in insect control: Low-risk products in a high-stakes world. Annu Rev Entomol. 2012;57:405–24.
235. Pavela R. Insecticidal properties of several essential oils on the house fly (*Musca domestica* L.). Phytoth Res. 2008;22(2): 274-278.
236. Khater, HK, Khater DF. The insecticidal activity of four medicinal plants against the blowfly *Lucilia sericata* (Diptera: Calliphoridae). Intern J Dermatol. 2009;48:492-497.
237. Palacios SM, Bertoni A, Rossi Y, Santander R, Urzúa A. Insecticidal activity of essential oils from native medicinal plants of Central Argentina against the house fly, *Musca domestica* (L.). Paras Res. 2009a;106(1): 207-212.
238. Palacios SM, Bertoni A, Rossi Y, Santander R, Urzúa A. Efficacy of essential oils from edible plants as insecticides against the house fly, *Musca domestica* L. Molecules. 2009b;14(5):1938-1947.
239. Rossi YE, Canavoso L, Palacios SM. Molecular response of *Musca domestica* L. to *Mintostachys verticillata* essential

oil,(4R)(+)-pulegone and menthone. Fitoterapia. 2012;83(2):336-342.

240. Morey RA, Khandagle AJ. Bioefficacy of essential oils of medicinal plants against housefly, *Musca domestica* L. Paras Res. 2012;111(4): 1799-1805.
241. Rossi YE, Palacios SM. Fumigant toxicity of *Citrus sinensis* essential oil on *Musca domestica* L. adults in the absence and presence of a P450 inhibitor. Acta Trop. 2013;127(1):33-37.
242. Bosly AH. Evaluation of insecticidal activities of *Mentha piperita* and *Lavandula angustifolia* essential oils against house fly, *Musca domestica* L. (Diptera: Muscidae). J Entomol Nematol. 2013;5(4):50-54.
243. Benelli G, Canale A, Flamini G, Cioni PL, Demi F, Ceccarini L, Macchia M, Conti, B. Biotoxicity of *Melaleuca alternifolia* (Myrtaceae) essential oil against the Mediterranean fruit fly, *Ceratitis capitata* (Diptera: Tephritidae), and its parasitoid *Psyttalia concolor* (Hymenoptera: Braconidae). Ind Crops Prod. 2013;50:596-603.
244. Khater HF. Bioactivities of some essential oils against the camel nasal botfly, *Cephalopina titillator.* Parasitol Res. 2014;113: 593-605.
245. Rossi YE, Palacios SM. Insecticidal toxicity of *Eucalyptus cinerea* essential oil and 1, 8-cineole against *Musca domestica* and possible uses according to the metabolic response of flies. Ind Crops Prod. 2015;63:133-137.
246. Pinto ZT, Sánchez FF, Santos ARD, Amaral ACF, Ferreira JLP, Escalona-Arranz JC, Queiroz MMC. Chemical composition and insecticidal activity of *Cymbopogon citratus* essential oil from Cuba and Brazil against housefly. Rev Bras Parasit Vet. 2015;24(1):36-44.
247. Pinto ZT, Fernandéz-Sanchez F, Santos AR, Amaral ACF, Ferreira JLP, Escalona-Arranz JC, Queiroz MMC. Effect of *Cymbopogon citrates* (Poaceae) oil and citral on post-embryonic time of blowflies. J Entomol Nematol. 2015;7(6):54-64.
248. Kumar P, Mishra S, Malik A, Satya S. Biocontrol potential of essential oil monoterpenes against housefly, *Musca domestica* (Diptera: Muscidae). Ecotox Environm Saf. 2014;100:1-6.
249. Hoda SM, Fahmy MM, Attia MM, Rabab M, Shalaby HA, Massoud AM. The insecticidal activity of two medicinal plants (*Commiphora molmol*) and (*Balanites aegyptiaca*) against the blowfly *Lucilia sericata* (Diptera: Calliphoridae). Int. J. Adv. Res. Biol. Sci. 2016;3(3):144-158.
250. Chaaban A, Souza ALF, Martins CEN, Bertoldi FC, Molento MB. Chemical composition of the essential oil of *Tagetes minuta* and its activity against *Cochliomyia macellaria* (Diptera: Calliphoridae). Europ J Med Plants. 2017a;18(1):1-10.
251. Chaaban A, Martins CEN, Bretanha LC, Micke GA, Carrer AR, Rosa NF, Ferreira L, Molento MB. Insecticide activity of *Baccharis dracunculifolia* essential oil against *Cochliomyia macellaria* (Diptera: Calliphoridae). Natural Prod Res; 2017b. DOI: 10.1080/14786419.2017.1392947
252. Chaaban A, Santos VMC, Gomes E, Martins CEN, Amaral W, Deschamps C, Molento MB. Chemical composition of *Piper gaudichaudianum* essential oil and its bioactivity against *Lucilia cuprina* (Diptera: Calliphoridae). J Essent Oil Res. (in press)
253. Araújo LX, Novato TPL, Zeringota V, Maturano R, Melo D, Da Silva BC, Daemon E., Carvalho MG, Monteiro, CMO. Synergism of thymol, carvacrol and eugenol in larvae of the cattle tick, *Rhipicephalus microplus*, and brown dog tick, *Rhipicephalus sanguineus*. Med Vet Entomol. 2016;30(4):377-382.
254. Afshar FH, Maggi F, Iannarelli R, Cianfaglione K, Isman MB. Comparative toxicity of *Helosciadium nodiflorum* essential oils and combinations of their main constituents against the cabbage looper, *Trichoplusia ni* (Lepidoptera). Ind Crops Prod. 2017;98:46-52.
255. Wagner H, Ulrich-Merzenich G. Synergy research: approaching a new generation of phytopharmaceuticals. Phytomedicine. 2009;16:97–110.
256. Bassolé IHN, Juliani HR. Essential oils in combination and their antimicrobial properties. Molecules. 2012;17(4):3989-4006.
257. Benelli G, Pavela R, Iannarelli R, Petrelli R, Cappellacci L, Cianfaglione K, Afshar FH, Nicoletti M, Canale A, Maggi F. Synergized mixtures of Apiaceae essential oils and related plant-borne compounds: larvicidal effectiveness on the filariasis vector *Culex quinquefasciatus* Say. Ind Crops Prod. 2017;96:186-195.

258. Kilani S, Ledauphin J, Bouhlel I, Sghaier MB, Boubaker J, Skandrani I, Mosrati R, Ghedira K, Barillier D, Chekir-Ghedira L. Comparative study of *Cyperus rotundus* essential oil by a modified GC/MS analysis method. Evaluation of its antioxidant, cytotoxic, and apoptotic effects. Chem Biod. 2008;5(5):729-742.
259. Tokarnia CH, Armién AG, Barros SSD, Peixoto PV, Döbereiner J. Estudos complementares sobre a toxidez de *Lantana camara* (Verbenaceae) em bovinos. Pesq Vet Bras. 1999;19(3-4):128-132.
260. Ngassoum MB, Yonkeu S, Jirovetz L, Buchbauer G, Schmaus G, Hammerschmidt FJ. Chemical composition of essential oils of *Lantana camara* leaves and flowers from Cameroon and Madagascar. Flav Fragr J. 1999;14(4):245-250.
261. Dua VK, Pandey AC, Dash AP. Adulticidal activity of essential oil of *Lantana camara* leaves against mosquitoes. Indian J Med Res. 2010;131:434-439.
262. Mukandiwa L, Ahmed A, Eloff JN, Naidoo V. Isolation of seselin from *Clausena anisata* (Rutaceae) leaves and its effects on the feeding and development of *Lucilia cuprina* larvae may explain its use in ethnoveterinary medicine. J Ethnophar. 2013;150(3):886-891.

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