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# Essential oils and their compounds as *Aedes aegypti* L. (Diptera: Culicidae) larvicides: review

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**Abstract** This review aims to describe essential oils and their constituent compounds that exhibit bioactivity against *Aedes aegypti* L. (Diptera: Culicidae) larvae, the immature stage of the primary vector of dengue. This review is based on original articles obtained by searching on major databases. Our literature review revealed that 361 essential oils from 269 plant species have been tested for their larvicidal activity. More than 60 % of these essential oils were considered active ( $LC_{50} < 100$  mg/L), and the majority of these active oils were derived from species belonging to Myrtaceae, Lamiaceae, and Rutaceae. The most active essential oils exhibited effective concentrations comparable with the dosage recommended for the use of temephos in container breeding. Approximately 27 % of the plants studied for their larvicidal activity against *A. aegypti* were collected in Brazil. Essential oils rich in phenylpropanoids, oxygenated sesquiterpenes, and monoterpene hydrocarbons were found to be the most active. When the isolates were tested, phenylpropanoids and monoterpene hydrocarbons were the most active compound classes. We describe the plant parts used and the major constituents of the essential oils. In addition, we discuss factors affecting the activity (such as plant parts, age of the plant, chemotypes, larval source, and methods used), structure–activity relationships, and mechanisms of action of the essential oils and their compounds. Essential oils have been widely investigated and show high larvicidal activity against *A. aegypti*. This review reveals that the essential oils are effective alternatives for the

production of larvicides, which can be used in vector-borne disease control programmes.

## Introduction

The incidence of dengue has increased 30-fold in recent decades worldwide. In 2012, dengue was considered the most important mosquito-borne viral disease in the world, being endemic in over 100 countries of the tropical and subtropical regions where over 2.5 billion people live. Approximately 40 % of the world's population is now at risk of infection by dengue virus; it is estimated that among this population, 50–100 million are infected annually, with 500,000 cases being severe. Approximately 2.5 % of those affected die and most of them are children living in Asian and Latin American countries (World Health Organization (WHO) 2009a; 2012a, b).

According to the WHO (2012c), *Aedes (Stegomyia) aegypti* L. (Diptera: Culicidae) is the primary vector of dengue. This mosquito is a highly anthropophilic species. It has adapted to the urban environment and uses man-made containers for oviposition and development of the aquatic stages of its life cycle. Virus transmission to humans occurs through the bites of infected female mosquitoes, which are daytime feeders (Eldridge 2005; Klowden 2007).

Unfortunately, there is no effective vaccine against dengue virus, which would ideally provide protection against all four virus serotypes. As a consequence, controlling the spread of dengue requires that mosquitoes be targeted directly (Konishi 2011; Gupta and Reddy 2013). Although there are no specific drugs available that prevent viral propagation, larvicides have been employed to combat dengue proliferation (Gubler 2011).

The organophosphate temephos is the most appropriate larvicide to be used in public health programmes (Tikar et al. 2008; WHO 2009b). However, the continued and repeated use of temephos has contributed to the development of

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resistant strains of vector-borne diseases by different mechanisms (WHO 1992; Braga and Valle 2007; Melo-Santos et al. 2010; Polson et al. 2011).

To circumvent these problems, it is critical to identify novel larvicides with different modes of action in order to increase the available choices of pesticides for use in public health control (Góis et al. 2013; Govindarajan et al. 2013). The ideal insecticide should be effective, ecologically sound, sustainable, and cost effective and exhibit low mammalian toxicity. Additionally, larvicides should not significantly change the characteristics of environmental water (WHO 2006).

For dengue control, an integrated approach should be the best option. To reach effective dengue control measures, it is necessary to consider problems such as unplanned urbanization, inadequate water supply, and poor basic sanitary conditions (Gupta and Reddy 2013). The WHO (2012d) reported four categories of vector control in the *Handbook for Integrated Vector Management*. Among them, botanical preparations are cited as a biological method of control.

Plant–insect relationships are a reason for interest in the search for herbal products. For thousands of years, plants and insects have evolved in parallel. This co-evolution has led to the development, in many plants, of chemical and physical mechanisms of defence against insects (Ryan and Byrne 1988). In addition, plant parts and plant derivatives have been traditionally used by human communities to control pest species of insects (Dharmagadda et al. 2005; Shaalan et al. 2005; Prophiro et al. 2012). Azadirachtin, anabasin, quassia, nicotine, pyrethrins, D-limonene, and carvacrol were important botanical insecticides used before the advent of synthetic chemicals (Wood 2012). Citronella oil is used extensively as an insect repellent (EPA 1999; Kongkaew et al. 2011); similarly, *Eucalyptus* oil is used as an insect repellent or an antifeedant agent against herbivores (Batish et al. 2008).

All these factors have attracted the attention of researchers that aim to identify new plant-based insecticides (Shaalan et al. 2005; Cheah et al. 2013; Kovendan et al. 2013), especially for the control of *A. aegypti* propagation by larvicidal agents (Geris et al. 2012; Warikoo and Kumar, 2013). Some studies have focused on the use of essential oils from plants as potential bioactive agents against *A. aegypti* larvae (Magalhães et al. 2010; Vila et al. 2010; Park et al. 2011; Govindarajan et al. 2012). Essential oils are considered the best alternative for the control of disease vectors (Warikoo et al. 2011; Bilal and Hassan 2012; Maheswaran and Ignacimuthu, 2012; Kumar et al. 2013; Liu et al. 2013). They are complex mixtures of volatile secondary metabolites that can mainly be categorized as phenylpropanoids or mono-, sesqui-, and diterpenes (Baser and Buchbauer 2010).

Literature reviews of plant-based products with biological activity have illustrated a significant contribution to the development of new alternatives for improving human health (Amaral et al. 2006; Krishnaiah et al. 2011; Lang and

Buchbauer 2011; Kumar et al. 2012; Unnati et al. 2013). Considering the literature reviews about insecticidal plant extracts (Sukumar et al. 1991; Shaalan et al. 2005; Koul et al. 2008; Zoubiri and Baaliouamer 2011; Ghosh et al. 2012), we limited this review to studies of larvicidal activity of essential oils against *A. aegypti*. We explored the relationship between oil constituents and larvicidal activity with the aim of contributing to the search for new alternatives for dengue control. We present a review based on original articles that were chosen by searching major databases such as Biological Abstracts, Chemical Abstracts, Web of Science, SciFinder, PubMed, Scopus, ScienceDirect, and Scielo. Patents were identified by searching the European Patent Office database. The keywords employed in the literature review were ‘essential oils’, ‘larvicidal activity’, ‘larvicide’, and ‘*Aedes aegypti*’.

### Essential oils and their compounds as larvicides against *A. aegypti*

In 2005, the WHO published the Guidelines for Laboratory and Field Testing of Mosquito Larvicides, aiming to standardize the procedures for testing the mechanisms of action of larvicides. This document defines the sequential phases for evaluating larvicide compounds and their preparation. It is recommended that the studies begin in the laboratory in order to determine the potential of the tested samples. Then, small- and large-scale field trials should be performed to analyse the effects on non-target organisms, as well as the efficacy and residual effects under different ecological settings. These guidelines illustrate that the potency of a chemical against a particular species of mosquito larvae must be compared with other insecticides (WHO 2005).

Several authors developed their own criteria to characterize the potency of mosquito larvicides based on natural products (Chantraine et al. 1998; Massebo et al. 2009; Magalhães et al. 2010). Komalamisra et al. (2005) considered products showing  $LC_{50} < 50$  mg/L active,  $50 \text{ mg/L} < LC_{50} < 100$  mg/L moderately active,  $100 \text{ mg/L} < LC_{50} < 750$  mg/L effective, and  $LC_{50} > 750$  mg/L inactive. Kiran et al. (2006) considered compounds with  $LC_{50} < 100$  mg/L as exhibiting a significant larvicidal effect.

As the WHO has not established a standard criterion for determining the larvicidal activity of natural products, in this review, we used the classification established by Cheng et al. (2003) in which the compounds with  $LC_{50} > 100$  mg/L were considered not active, with  $LC_{50} < 100$  mg/L were active, and those with  $LC_{50} < 50$  mg/L were highly active. In addition, the samples that had their results expressed as mortality percentage were considered active when they were able to kill almost 100 % of larvae at 100 mg/L.

Our literature review showed that 361 essential oils from 269 plant species have been tested for their larvicidal activity against *A. aegypti*. According to the classification of Cheng et al. (2003), we considered more than 60 % of these essential oils as active ( $LC_{50} < 100$  mg/L) in our review. This result confirms the ecological role of essential oils in nature; many essential oils serve to protect plants by defence mechanisms against pathogens and predators (Grodnitzky and Coats 2002; Bakkali et al. 2008). Hence, plant essential oils have great potential in dengue control. Table 1 lists these plant species as well as their essential oil characteristics.

The studies of essential oil as *A. aegypti* larvicide used species distributed among 29 families. Myrtaceae, Zingiberaceae, Asteraceae, and Lamiaceae accounted for 14.5, 12.5, 12, and 12 % of the studied species, respectively. The majority of the active oils are from species that belong to Myrtaceae (13.5 %), Lamiaceae (10.5 %), and Rutaceae (8.2 %). According to Sukumar et al. (1991), Regnault-Roger (1997), Magalhães et al. (2010), and Park et al. (2011), species that belong to Myrtaceae, Apiaceae, Piperaceae, Lamiaceae, Rutaceae, Asteraceae, Meliaceae, and Zingiberaceae have the potential to be used as insecticides.

The most active essential oils were from the woods of *Callitris glaucophylla* Joy ( $LC_{50} = 0.69$  mg/L), *Juniperus virginiana* L. ( $LC_{50} = 1$  mg/L), *Thymus serpyllum* L. ( $LC_{50} = 1$  mg/L), and *Amyris balsamifera* L. ( $LC_{50} = 1$  mg/L) (Amer and Mehlhorn 2006; Shaalan et al. 2006). Their  $LC_{50}$  values are comparable with the dosage recommended for the use of temephos (1 mg/L) in container breeding (WHO 2012e).

Essential oils were extracted from the entire plant or from specific parts of the plant. In the analyses, we found that leaves were the most commonly used part of the plant. However, only 50 % of the oils extracted from plant leaves exhibited high larvicidal activity ( $LC_{50} < 50$  mg/L), whereas almost 80 % of the essential oils extracted from plant seeds showed high activity.

Approximately 27 % of the plants studied for their larvicidal activity against *A. aegypti* were collected in Brazil, of which 77 % were collected from the northeast of Brazil. Essential oils from these plants have been the most studied. These data support the importance of Brazilian biodiversity. According to Oliveira et al. (2012), 20 % of the plants species of the world are native to Brazil; however, these plants have not been optimally used and should be further studied.

Essential oils rich in phenylpropanoids, oxygenated sesquiterpenes, and monoterpene hydrocarbons were found to be the most active; all phenylpropanoid-rich essential oils exhibited larvicidal activity. The essential oils that were not active according to the criterion used are listed in Table 2. The botanical families Asteraceae and Zingiberaceae showed the highest ratio of inactive species.

To further understand the relationship between essential oils and their larvicidal activity, some authors isolated and tested the major compounds of these oils. In most of these studies, it was observed that the whole essential oil was as active as their isolated compounds. Phenylpropanoids and monoterpene hydrocarbons were the most active compound classes. Table 3 lists the isolated compounds that were considered active ( $LC_{50} < 100$  mg/L).

The oxygenated sesquiterpenes  $\beta$ -eudesmol and caryophyllene oxide, which are major compounds of the active essential oils from *Guatteria friesiana* Erkens & Maas and *Guatteria blepharophylla* Mart., respectively (Aciole et al. 2011), were not active when tested isolated, although the whole oil showed high activity (Cheng et al. 2009a, b). This can be explained by the interactions between the constituents present in oils. Other compounds that were considered inactive ( $LC_{50} > 100$  mg/L) are listed in Table 4.

The studies performed by Magalhães et al. (2010), Aciole et al. (2011), and Lima et al. (2011) achieved results that demonstrated the high larvicidal activity of oxygenated sesquiterpene-rich essential oil. Lima et al. (2011) correlated the activity of *Spondias purpurea* L. essential oil with the high concentration of these compounds in blend. Simas et al. (2004) noted that oxygenated sesquiterpenes were more effective than monoterpenes and phenylpropanoids. On the basis of these results, the authors hypothesized that lipophilicity is an important tool for the larvicidal activity on *A. aegypti*.

Essential oils are complex chemical mixtures of major and minor compounds. In general, the bioactivity of essential oils is correlated with their major substances. However, it is important to note that these secondary metabolites can facilitate interactions that increase or decrease the larvicidal activity of tested oils compared with the activities of their isolated constituents (Waliwitiya et al. 2009). The synergistic phenomenon exists in botanical preparations by the interaction between molecules that are both major and minor components of the preparations. In some cases, the bioactivity of the blend is higher than those of purified compounds (Lahlou 2004a; Shaalan et al. 2005).

Cheng et al. (2009c) found that the leaf essential oil from *Cryptomeria japonica* (Thunb. ex L. f.) D. Don ( $LC_{50} = 28.4$  mg/L) was more toxic to *A. aegypti* larvae than its major constituents, 16-kaurene ( $LC_{50} = 57.0$  mg/L), and elemol ( $LC_{50} > 100.0$  mg/L), both of which are present in the samples at proportions approaching 20 %. The authors suggest that the minor compounds 3-carene ( $LC_{50} = 25.3$  mg/L), terpinolene ( $LC_{50} = 32.1$  mg/L),  $\alpha$ -terpinene ( $LC_{50} = 28.1$  mg/L), and  $\gamma$ -terpinene ( $LC_{50} = 26.8$  mg/L) also contribute to the larvicidal activity, since they exhibited great larvicidal potential.

In a study performed by Silva et al. (2008),  $\beta$ -caryophyllene and caryophyllene oxide were identified as the major compounds of the leaf essential oil of *Hyptis*

**Table 1** Plant essential oils considered active ( $LC_{50} < 100$  mg/L) against *Aedes aegypti* L. (Diptera: Culicidae) larvae

Family and plant species	Part used	Plant origin	Major constituents	$LC_{50}$ (mg/L)	Reference
<b>Acoraceae</b>					
<i>Acorus calamus</i> L.	Roots	Pakistan	NI	99.41	Manzoor et al. (2013)
<b>Amaranthaceae</b>					
<i>Chenopodium ambrosioides</i> L.	Aerial	Cuba	$\alpha$ -Terpineol	35	Leyva et al. (2009a)
	Aerial	Ethiopia	NI	9.1	Massebo et al. (2009)
<b>Anacardiaceae</b>					
<i>Anacardium humile</i> A. St.-Hil.	Leaves	Brazilian Savanna	NI	20.9	Porto et al. (2008)
<i>Schinus molle</i> L.	Leaves	Ethiopia	NI	9.6	Massebo et al. (2009)
	Seeds	Ethiopia	NI	14.5	Massebo et al. (2009)
	Seeds	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
	Seeds	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Spondias purpurea</i> L.	Leaves	Northeast of Brazil	Caryophyllene oxide and $\alpha$ -cadinol	39.7	Lima et al. (2011)
<b>Annonaceae</b>					
<i>Guatteria blepharophylla</i> Mart.	Leaves	Brazilian Amazon	Caryophyllene oxide	58.72	Aciole et al. (2011)
<i>Guatteria friesiana</i> Erkens & Maas	Leaves	Brazilian Amazon	$\beta$ -Eudesmol	52.6	Aciole et al. (2011)
<i>Guatteria hispida</i> (R.E.Fr.) Erkens & Maas	Leaves	Brazilian Amazon	$\beta$ -Pinene and $\alpha$ -pinene	85.74	Aciole et al. (2011)
<i>Rollinia leptopetala</i> R.E. Fr.	Stems	Northeast of Brazil	Spathulenol	34.7	Feitosa et al. (2009)
<b>Apiaceae</b>					
<i>Anethum graveolens</i> L.	Aerial	Germany	NI	50	Amer and Mehlhorn (2006)
<i>Apium graveolens</i> L.	Seeds	Thailand	(R)-(+)-Limonene	42.07	Pitasawat et al. (2007)
	Leaves	South Korea	4-Chloro-4,4-dimethyl-3-(1-imidazolyl)-valerophenone and 1-dodecanol	59.32	Nagella et al. (2012)
<i>Carum carvi</i> L.	Seeds	Thailand	Carvone	54.62	Pitasawat et al. (2007)
	Fruits	South Korea	NI	NI <sup>a</sup>	Lee (2006)
<i>Cuminum cyminum</i> L.	Fruits	South Korea	NI	NI <sup>a</sup>	Lee (2006)
	Fruits	South Korea	NI	NI <sup>a</sup>	Lee (2006)
<i>Daucus carota</i> L.	Root	South Korea	NI	NI <sup>a</sup>	Lee (2006)
<i>Eryngium</i> sp. L.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Ferula galbanifera</i> Mill.	Steam bark	South Korea	NI	NI <sup>a</sup>	Lee (2006)
<i>Foeniculum vulgare</i> Mill.	Fruits	Thailand	<i>trans</i> -Anethole	49.32	Pitasawat et al. (2007)
	Seeds	Bolivia	NI	24.3	Chantraine et al. (1998)
<i>Heracleum pastinacifolium</i> subsp. <i>transcaucasicum</i> P.H. Davis	Fruits	NI	Octyl acetate	69.72	Tabanca et al. (2012a)
<i>Heracleum pastinacifolium</i> subsp. <i>incanum</i> P.H. Davis	Fruits	NI	Hexyl butyrate	71.85	Tabanca et al. (2012a)
<i>Pimpinella anisum</i> L.	Seeds	India	NI	<100	Prajapati et al. (2005)

**Table 1** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
<i>Trachyspermum ammi</i> (L.) Sprague	Seeds	NI	Thymol	NI <sup>a</sup>	Seo et al. (2012)
Araliaceae					
<i>Dendropanax moribifera</i> Leveille	Flower	South Korea	$\gamma$ -Elemene	62.32	Chung et al. (2009)
Aristolochiaceae					
<i>Asarum heterotropoides</i> Leveille	Root	Korea	Methyleugenol and safrole	23.82	Perumalsamy et al. (2009, 2010)
Asteraceae					
<i>Baccharis</i> sp. L.	Aerial	Bolivia	NI	14.7	Chantraine et al. (1998)
<i>Coreopsis fasciculata</i> Wedd.	Aerial	Bolivia	NI	26.5	Chantraine et al. (1998)
<i>Eupatorium betonicaeforme</i> (DC.) Baker	Root	Northeast of Brazil	$\beta$ -Caryophyllene	NI <sup>a</sup>	Albuquerque et al. (2004)
<i>Gynoxis</i> sp. Cass.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Helichrysum italicum</i> G. Don f.	NI	France	NI	100	Amer and Mehlhorn (2006)
<i>Pectis oligocephala</i> Baker	Aerial	Northeast of Brazil	<i>p</i> -Cymene and thymol	NI <sup>a</sup>	Albuquerque et al. (2007)
<i>Senecio adenophylloides</i> Sch. Bip.	Leaves	Bolivia	NI	43.4	Chantraine et al. (1998)
<i>Tagetes erecta</i> L.	Leaves	India	NI	15.37	Pathak et al. (2000)
	Leaves and Stem	Northeast of Brazil	Piperitone	79.78	Marques et al. (2011)
<i>Tagetes filifolia</i> Lag.	Aerial	Peru	<i>trans</i> -Anethole	47.7	Ruiz et al. (2011)
<i>Tagetes minuta</i> L.	Aerial	Peru	<i>trans</i> -Ocimenone	52.3	Ruiz et al. (2011)
<i>Tagetes patula</i> L.	Leaves	India	Limonene and terpinolene	13.57	Dharmagadda et al. (2005)
<i>Tagetes pusilla</i> Kunth	Seeds	Bolivia	NI	14.1	Chantraine et al. (1998)
Boraginaceae					
<i>Auxemma glazioviana</i> Taub.	Heartwood	Northeast of Brazil	$\alpha$ -Bisabolol and $\alpha$ -cadinol	2.53	Costa et al. (2004)
	Heartwood	Northeast of Brazil	$\alpha$ -Bisabolol, $\alpha$ -cadinol, and T-murolol	2.98	Costa et al. (2004)
<i>Cordia curassavica</i> (Jacq.) Roem. & Schult.	Leaves	Southeast of Brazil	<i>cis</i> -Isolongifolone	87.70	Aciole (2009)
	Leaves	Northeast of Brazil	$\alpha$ -Pinene	97.7	Santos et al. (2006)
<i>Cordia leucomalloides</i> Taroda	Leaves	Northeast of Brazil	$\delta$ -Cadinene and ( <i>E</i> )-caryophyllene	63.1	Santos et al. (2006)
Burseraceae					
<i>Boswellia carteri</i> Birdw.	Resins	Somalia	NI	10	Amer and Mehlhorn (2006)
<i>Commiphora myrrha</i> (T. Nees) Engl.	Stem bark	South Korea	NI	NI <sup>a</sup>	Lee (2006)
Convolvulaceae					
<i>Ipomoea cairica</i> (L.) Sweet	NI	India	NI	22.3	Thomas et al. (2004)
Cupressaceae					
<i>Callitris glaucophylla</i> Joy Thomps. & L.P. Johnson	Wood	Australia	Guaiol and citronellic acid	0.69	Shaaan et al. (2006)
<i>Calocedrus formosana</i> (Florin) Florin	Heartwood	Taiwan	NI	75.2	Cheng et al. (2003)
	Bark	Taiwan	NI	51.8	Cheng et al. (2003)



**Table 1** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
<i>Chamaecyparis formosensis</i> Matsum.	Leaves	Taiwan	NI	56.3	Cheng et al. (2003)
	Wood	Taiwan	Myrtenol	38.6	Kuo et al. (2007)
<i>Cryptomeria japonica</i> (Thunb. ex L. f.) D. Don	Leaves	Taiwan	16-Kaurene and elemol	28.4 – 56.7	Cheng et al. (2009c)
<i>Cunninghamia konishii</i> Hayata	Leaves	Taiwan	NI	37.6	Cheng et al. (2003)
	Bark	Taiwan	NI	48.1	Cheng et al. (2003)
	Heartwood	Taiwan	NI	72	Cheng et al. (2003)
	Sapwood	Taiwan	NI	82.7	Cheng et al. (2003)
	Wood	Taiwan	Cedrol	85.7	Cheng et al. (2013)
<i>Cupressus arizonica</i> var. <i>glabra</i> (Sudw.) Little	Leaves	Taiwan	α-Pinene	91.7	Cheng et al. (2013)
	Female cones	USA	α-Pinene	33.7	Ali et al. (2013a)
	Wood-bark	USA	α-Pinene and <i>epi</i> -zonarene	44.6	Ali et al. (2013a)
	Male cones	USA	α-Pinene and <i>epi</i> -zonarene	53.6	Ali et al. (2013a)
<i>Juniperus macropoda</i> Bois.	Needle-twigs	USA	α-Pinene	55.5	Ali et al. (2013a)
	Fruit	India	NI	< 100	Prajapati et al. (2005)
<i>Juniperus virginiana</i> L.	Wood	USA	NI	1	Amer and Mehlhorn (2006)
<i>Juniperus communis</i> L.	Wood	South Korea	NI	NI <sup>a</sup>	Lee (2006)
	NI	Austria	NI	50	Amer and Mehlhorn (2006)
<i>Taiwania cryptomerioides</i> Hayata	Heartwood	Taiwan	NI	79.8	Cheng et al. (2003)
<b>Euphorbiaceae</b>					
<i>Croton argyrophylloides</i> Müll. Arg.	Aerial	Northeast of Brazil	β- <i>trans</i> -Guaiene	94.6	Lima et al. (2013)
<i>Croton nepetaefolius</i> Baill.	Aerial	Northeast of Brazil	Methyleugenol	66.4	Lima et al. (2013)
	Leaves	Northeast of Brazil	Methyleugenol	84	Morais et al. (2006)
<i>Croton regelianus</i> Müll. Arg.	Leaves	Northeast of Brazil	Ascaridole	24.22	Torres et al. (2008)
	Leaves	Northeast of Brazil	<i>p</i> -Cymene	66.74	Torres et al. (2008)
<i>Croton sonderianus</i> Müll. Arg.	Aerial	Northeast of Brazil	Spathulenol	54.5	Lima et al. (2013)
<i>Croton zehntneri</i> Pax & K. Hoffm.	Aerial	Northeast of Brazil	( <i>E</i> )-Anethole	26.2	Lima et al. (2013)
	Leaves	Northeast of Brazil	( <i>E</i> )-Anethole	28	Morais et al. (2006)
	Leaves	Northeast of Brazil	( <i>E</i> )-Anethole	56.2	Santos et al. (2007)
	Stalkes	Northeast of Brazil	( <i>E</i> )-Anethole and <i>p</i> -anisaldehyde	51.3	Santos et al. (2007)
	Inflorescence	Northeast of Brazil	( <i>E</i> )-Anethole	57.5	Santos et al. (2007)
<b>Fabaceae</b>					
<i>Bauhinia acuruana</i> Moric	Leaves	Northeast of Brazil	epi-α-Cadinol and spathulenol	56.22	Góis (2010)
<i>Copaifera multijuga</i> Haynet	Resin	Brazilian Amazon	β-Caryophyllene	18	Trindade et al. (2013)
<i>Hymenaea courbaril</i> L.	Ripe fruit peels	Northeast of Brazil	α-Copaene and spathulenol	14.8	Aguiar et al. (2010)
	Unripe fruit peels	Northeast of Brazil	Germacrene D and β-caryophyllene	28.4	Aguiar et al. (2010)

**Table 1** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
<i>Myroxylon pereirae</i> (Royle) Klotzsch	Resin	NI	Benzyl benzoate	NI <sup>a</sup>	Seo et al. (2012)
<b>Lamiaceae</b>					
<i>Hyptis martiusii</i> Benth.	Leaves	Northeast of Brazil	δ-3-Carene and 1,8-cineol	18.5	Costa et al. (2005)
<i>Lavandula gibsoni</i> J. Graham	Aerial	India	α-Terpinolen and thymol	48.32	Kulkarni et al. (2013)
<i>Lavandula officinalis</i> Chaix	Flowering tops	South Korea	NI	NI <sup>a</sup>	Lee (2006)
<i>Lepechinia meyenii</i> (Walp.) Epling	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Mentha piperita</i> L.	Leaves	India	NI	26.19	Pathak et al. (2000)
	Leaves	India	NI	47.54	Kalaivani et al. (2012)
<i>Mentha spicata</i> L.	Leaves	India	Carvone	56.08	Govindarajan et al. (2012)
	Leaves	Ethiopia	NI	67.8	Massebo et al. (2009)
<i>Nepeta cataria</i> L.	NI	NI	(E),(Z)-Nepetalactone and (Z),(E)-nepetalactone	70	Zhu et al. (2006)
<i>Ocimum americanum</i> L.	Leaves and branches	Northeast of Brazil	(E)-Methyl-cinnamate	67	Cavalcanti et al. (2004)
<i>Ocimum basilicum</i> L.	Leaves	Pakistan	NI	75.35	Manzoor et al. (2013)
<i>Ocimum gratissimum</i> L.	Aerial	Northeast of Brazil	Eugenol	60	Cavalcanti et al. (2004)
<i>Ocimum lamiifolium</i> Hochst. Ex Benth.	Leaves	Ethiopia	NI	8.6	Massebo et al. (2009)
<i>Ocimum sanctum</i> L.	Leaves	India	NI	29.76	Pathak et al. (2000)
	NI	Nigeria	Methyleugenol	85.11	Gbolade and Lockwood (2008)
	NI	India	NI	92.48	Tennyson et al. (2013)
<i>Ocimum suave</i> Willd.	Leaves	Ethiopia	NI	29.8	Massebo et al. (2009)
<i>Origanum marjorana</i> L.	Leaves	South Korea	NI	NI <sup>a</sup>	Lee (2006)
<i>Plectranthus amboinicus</i> (Lour.) Spreng.	Leaves	Northeast of Brazil	Carvacrol	51.8	Lima et al. (2011)
<i>Plectranthus mollis</i> Spreng.	Aerial	India	Piperitone oxide and fenchone	25.39	Kulkarni et al. (2013)
<i>Pogostemon patchouli</i> Pellet.	Whole plant	NI	NI	NI <sup>a</sup>	Seo et al. (2012)
<i>Thymus serpyllum</i> L.	NI	Turkey	NI	1	Amer and Mehlhorn (2006)
<i>Thymus vulgaris</i> L.	Leaves	Ethiopia	NI	17.3	Massebo et al. (2009)
<b>Lauraceae</b>					
<i>Cinnamomum camphora</i> (L.) J. Presl	NI	Taiwan	NI	10	Amer and Mehlhorn (2006)
<i>Cinnamomum cassia</i> (L.) C. Presl	NI	NI	Cinnamaldehyde	80	Zhu et al. (2006)
<i>Cinnamomum impressicostatum</i> Kosterm.	Leaves	Malaysia	Benzyl benzoate and α-phellandrene	10.7	Jantan et al. (2005)
	Leaves	Malaysia	NI	13.7	Jantan et al. (2003)
<i>Cinnamomum microphyllum</i> Ridl.	Leaves	Malaysia	Benzyl benzoate	6.7	Jantan et al. (2005)
	Leaves	Malaysia	NI	20.6	Jantan et al. (2003)
<i>Cinnamomum mollissimum</i> Hook. F.	Leaves	Malaysia	Benzyl benzoate	10.2	Jantan et al. (2005)



**Table 1** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
<i>Cinnamomum osmophloeum</i> Kaneh.	Leaves	Taiwan	NI	86.8	Cheng et al. (2003)
	Leaves	Taiwan	<i>trans</i> -Cinnamaldehyde	36	Cheng et al. (2004)
	Leaves	Taiwan	<i>trans</i> -Cinnamaldehyde and cinnamyl acetate	44	Cheng et al. (2004)
<i>Cinnamomum pubescens</i> Kochummen	Leaves	Malaysia	Benzyl benzoate	12.8	Jantan et al. (2005)
<i>Cinnamomum rhyncophyllum</i> Miq.	Leaves	Malaysia	Benzyl benzoate	6.0	Jantan et al. (2005)
<i>Cinnamomum scortechinii</i> Gamble	Leaves	Malaysia	β-Phellandrene and linalool	21.5	Jantan et al. (2005)
<i>Cinnamomum sintoc</i> Blume	Leaves	Malaysia	Safrole	41	Jantan et al. (2005)
<i>Cinnamomum zeylanicum</i> Blume.	Leaves	Northeast of Brazil	Eugenol	79.75	Mendes (2011)
<b>Meliaceae</b>					
<i>Guarea humaitensis</i> T.D. Penn.	Branches	Brazilian Amazon	Caryophyllene epoxide	48.6	Magalhães et al. (2010)
<i>Guarea scabra</i> A. Juss.	Leaves	Brazilian Amazon	<i>cis</i> -Caryophyllene	98.6	Magalhães et al. (2010)
<b>Myristicaceae</b>					
<i>Myristica fragrans</i> Houtt.	NI	India	NI	93.62	Tennyson et al. (2013)
<b>Myrtaceae</b>					
<i>Eucalyptus benthamii</i> var <i>Benthamii</i> Maiden & Cabbage	Leaves	Argentina	α-Pinene	NI <sup>a</sup>	Lucia et al. (2012)
<i>Eucalyptus botryoides</i> Smith	Leaves	Argentina	<i>p</i> -Cymene, α-eudesmol, and 1,8-cineol	NI <sup>a</sup>	Lucia et al. (2012)
<i>Eucalyptus camaldulensis</i> Dehnh.	Leaves	Argentina	1,8-Cineol, <i>p</i> -cymene and β-phellandrene	26.75	Lucia et al. (2008)
	Leaves	Taiwan	α-Pinene, <i>p</i> -cymene, and α-phellandrene	31	Cheng et al. (2009b)
<i>Eucalyptus citriodora</i> Hook.	Leaves	Ethiopia	NI	38.7	Massebo et al. (2009)
	NI	NI	<i>p</i> -Menthane-3,8-diol	58	Zhu et al. (2006)
<i>Eucalyptus dives</i> Schauer	Leaves	Australia	NI	NI <sup>a</sup>	Amer and Mehlhorn (2006)
<i>Eucalyptus dunnii</i> Maiden	Leaves	Argentina	1,8-Cineol and γ-terpinene	25.23	Lucia et al. (2008)
<i>Eucalyptus fastigata</i> Deane & Maiden	Leaves	Argentina	<i>p</i> -Cymene	NI <sup>a</sup>	Lucia et al. (2012)
<i>Eucalyptus globulus</i> Labill.	Leaves	Ethiopia	1,8-Cineol	52.9	Massebo et al. (2009)
<i>Eucalyptus grandis</i> W. Hill	Leaves	Argentina	α-Pinene	32.4	Lucia et al. (2007)
<i>Eucalyptus gunnii</i> Hook. F.	Leaves	Argentina	1,8-Cineol and <i>p</i> -cymene	21.13	Lucia et al. (2008)
<i>Eucalyptus nobilis</i> L.A.S. Johnson & K.D. Hill	Leaves	Argentina	1,8-Cineol	NI <sup>a</sup>	Lucia et al. (2012)
<i>Eucalyptus radiata</i> ssp. <i>radiata</i> Sieber ex Spreng	Leaves	Argentina	1,8-Cineol	NI <sup>a</sup>	Lucia et al. (2012)
<i>Eucalyptus robusta</i> Smith	Leaves	Argentina	α-Pinene	NI <sup>a</sup>	Lucia et al. (2012)
<i>Eucalyptus saligna</i> Sm.	Leaves	Argentina	1,8-Cineol and <i>p</i> -cymene	22.16	Lucia et al. (2008)
<i>Eucalyptus tereticornis</i> Sm.	Leaves	Argentina	β-Phellandrene and 1,8-cineol	22.14	Lucia et al. (2008)
<i>Eucalyptus urophylla</i> S.T. Blake	Leaves	Taiwan	1,8-Cineol	95.5	Cheng et al. (2009b)
<i>Eugenia melanadenia</i> Krug & Urb.	Leaves	Cuba	1,8-Cineol	85	Aguilera et al. (2003)
<i>Eugenia triquetra</i> O. Berg	Leaves	Venezuela	Linalool and limonene	64.8	Mora et al. (2010)
<i>Melaleuca dissitiflora</i> F. Muell	NI	NI	Terpinen-4-ol	NI <sup>a</sup>	Park et al. (2011)
<i>Melaleuca leucadendron</i> (L.) L.	NI	Cuba	1,8-Cineol, α-pinene, and α-terpineol	41	Leyva et al. (2008)
<i>Melaleuca linariifolia</i> Sm.	NI	NI	Terpinen-4-ol and γ-terpinene	NI <sup>a</sup>	Park et al. (2011)
<i>Melaleuca quinquenervia</i> (Cav.) S. T. Blake	NI	NI	1,8-Cineol and ( <i>E</i> )-nerolidol	NI <sup>a</sup>	Park et al. (2011)
<i>Melaleuca viridiflora</i> Sol. ex Gaertn.	Leaves	South Korea	NI	NI <sup>a</sup>	Lee (2006)

**Table 1** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
<i>Myrtus communis</i> L.	Leaves and Twigs	France	NI	50	Amer and Mehlhorn (2006)
<i>Pimenta dioica</i> (L.) Merr.	Leaves	Southeast of Brazil	Eugenol	38.8	Marinho (2010)
<i>Pimenta pseudocaryophyllus</i> (Gomes) Landrum	Leaves	Southeast of Brazil	Chavibetol (m-eugenol)	44.1	Aciole (2009)
<i>Pimenta racemosa</i> (Mill.) J.W. Moore	Leaves	Cuba	Terpinem-4-ol and 1,8-cineol	27	Leyva et al. (2009a)
	Leaves	South Korea	NI	NI <sup>a</sup>	Lee (2006)
<i>Psidium guajava</i> L.	Leaves	Northeast of Brazil	1,8-Cineol and $\beta$ -caryophyllene	24.7	Lima et al. (2011)
<i>Psidium rotundatum</i> Griseb.	Leaves	Cuba	1,8-Cineol	63	Aguilera et al. (2003)
<i>Syzygium aromaticum</i> (L.) Merr. & L.M. Perry	Flowers	Northeast of Brazil	Eugenol	21.4	Costa et al. (2005)
	NI	NI	Eugenol	62.3	Barbosa et al. (2012a)
	Flowers	NI	Eugenol	63.36	Nascimento (2012)
<b>Pinaceae</b>					
<i>Picea excelsa</i> (Lamb.) Link	NI	Korea	NI	NI <sup>a</sup>	Amer and Mehlhorn (2006)
<i>Pinus caribaea</i> Morelet	Leaves	Cuba	NI	51	Leyva et al. (2009b)
<i>Pinus longifolia</i> Salisb.	NI	India	K-terpineol	82.1	Ansari et al. (2005)
<i>Pinus tropicalis</i> Morelet	Leaves	Cuba	NI	42	Leyva et al. (2009b)
<i>Pinus</i> sp. L. (Turpentine)	Resin	Argentina	$\alpha$ -Pinene and $\beta$ -pinene	14.7	Lucia et al. (2007)
<b>Piperaceae</b>					
<i>Piper aduncum</i> L.	Fruits	Northeast of Brazil	$\beta$ -Pinene	30.2	Costa et al. (2010a)
	Aerial	Brazilian Amazon	Dillapiole	54.5	Almeida et al. (2009)
	NI	Cuba	Dillapiole	57	Leyva et al. (2009a)
<i>Piper auritum</i> Kunth.	Leaves	Cuba	Safrole	17	Leyva et al. (2009a)
<i>Piper betle</i> L.	NI	Indonesia	Citronellal	13.1	Wahyuni (2012)
<i>Piper hostmanianum</i> (Miq.) C. DC.	Leaves	Brazilian Amazon	Asaricin and myristicin	54	Morais et al. (2007)
<i>Piper klotzschianum</i> (Kunth) C. DC.	Seeds	Southeast of Brazil	1-Butyl-3,4-methylenedioxybenzene, limonene, and $\alpha$ -phellandrene	13.27	Nascimento et al. (2013)
	Root	Southeast of Brazil	1-Butyl-3,4-methylenedioxybenzene	10.0	Nascimento et al. (2013)
<i>Piper marginatum</i> Jacq.	Leaves	Northeast of Brazil	Isoelemecin and apiole	8.29	Costa et al. (2010a)
	Leaves	Northeast of Brazil	(Z)-Asarone	23.8	Autran et al. (2009)
	Stem	Northeast of Brazil	(E)-Asarone and patchouli alcohol	19.9	Autran et al. (2009)
	Inflorescence	Northeast of Brazil	Patchouli alcohol and (E)-asarone	19.9	Autran et al. (2009)
<i>Piper nigrum</i> L.	Seeds	Ethiopia	NI	9.1	Massebo et al. (2009)
	Seeds	Sri Lanka	(E)-Caryophyllene and caryophyllene oxide	50	Amer and Mehlhorn (2006)
	Seeds	Northeast of Brazil	(E)-Caryophyllene, caryophyllene oxide, and Sabinene	75.8	Costa et al. (2010a)
<i>Piper permucronatum</i> Yunck.	Leaves	Brazilian Amazon	Dillapiole and myristicin	36	Morais et al. (2007)

**Table 1** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
<b>Poaceae</b>					
<i>Cymbopogon citratus</i> (DC.) Stapf	Leaves	Northeast of Brazil	Geranial	69	Cavalcanti et al. (2004)
<i>Cymbopogon martini</i> (Roxb.) Will. Watson	NI	India	NI	87.88	Tennyson et al. (2013)
<i>Cymbopogon winterianus</i> Jowitt ex Bor	Leaves	Northeast of Brazil	NI	98	Mendonça et al. (2005)
<i>Vetiveria zizanioides</i> (L.) Nash	Root	Bolivia	NI	31.5	Chantraine et al. (1998)
<b>Ranunculaceae</b>					
<i>Nigella sativa</i> L.	Leaves	Ethiopia	NI	32.1	Massebo et al. (2009)
<b>Rutaceae</b>					
<i>Amyris balsamifera</i> L.	Wood	Haiti	NI	1	Amer and Mehlhorn (2006)
	Wood	Haiti	Elemol and eudesmol	52	Zhu et al. (2006)
<i>Chloroxylon swietenia</i> DC.	Leaves	India	Geijerene	16.5	Kiran et al. (2006)
	Stems	India	Geijerene and limonene	20.4	Kiran et al. (2006)
<i>Citrus bergamia</i> Risso	Fruit peels	South Korea	NI	NI <sup>a</sup>	Lee (2006)
<i>Citrus limon</i> (L.) Osbeck	Fruit peels	Italy	NI	10	Amer and Mehlhorn (2006)
<i>Citrus sinensis</i> (L.) Osbeck	NI	India	NI	85.93	Tennyson et al. (2013)
<i>Ruta graveolens</i> L.	Aerial	NI	Undecan-2-one	21.25	Tabanca et al. (2012b)
<i>Clausena excavata</i> Burm. f.	Leaves	Taiwan	Safrole and terpinolene	37.1	Cheng et al. (2009a)
	Twigs	Taiwan	Safrole	40.1	Cheng et al. (2009a)
<i>Feronia limonia</i> (L.) Swingle	Leaves	India	Estragole and $\beta$ -pinene	11.59	Senthilkumar et al. (2013)
<i>Murraya koenigii</i> (L.) Spreng.	Leaves	India	NI	29.96	Pathak et al. (2000)
<i>Toddalia asiatica</i> (L.) Lam.	Fruits	Kenya	Linalool	40.6	Nyahanga et al. (2010)
	Leaves	Kenya	Sabinene	99.7	Nyahanga et al. (2010)
<i>Zanthoxylum armatum</i> DC.	Seeds	India	Linalool	54	Tiwary et al. (2007)
<i>Zanthoxylum articulatum</i> Engler	Leaves	Northeast of Brazil	Viridiflorol	77.62	Feitosa et al. (2007)
<i>Zanthoxylum limonella</i> Alston	Fruits	Thailand	(R)-(+)-Limonene	24.6	Pitasawat et al. (2007)
<i>Zanthoxylum Oxyphyllum</i> Edgew.	Leaves	India	Methyl heptyl ketone	7.52	Borah et al. (2012)
<b>Santalaceae</b>					
<i>Santalum album</i> L.	Wood	India	Guaiol, elemol, and eudesmol	10	Amer and Mehlhorn (2006)
<b>Scrophulariaceae</b>					
<i>Capraria biflora</i> L.	Leaves	Northeast of Brazil	$\alpha$ -Humulene	73.39	Souza et al. (2012a)
<i>Stemodia maritima</i> L.	Stem	Northeast of Brazil	$\beta$ -Caryophyllene and caryophyllene oxide	22.9	Arriaga et al. (2007)
	Leaves		$\beta$ -Caryophyllene	55.4	Arriaga et al. (2007)
<b>Verbenaceae</b>					
<i>Lantana camara</i> L.	Leaves	Northeast of Brazil	Bicyclogermacrene and ( <i>E</i> )-caryophyllene	42.3	Costa et al. (2010b)

**Table 1** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
<i>Lippia adoensis</i> Hochst.	Leaves	Ethiopia	NI	47.1	Massebo et al. (2009)
<i>Lippia citriodora</i> Kunth.	NI	France	NI	100	Amer and Mehlhorn (2006)
<i>Lippia gracilis</i> Schauer	Leaves	Northeast of Brazil	Carvacrol	26.3	Santiago et al. (2006)
	Leaves	Northeast of Brazil	Carvacrol	98	Silva et al. (2008)
	Leaves	Northeast of Brazil	Thymol	19.5	Costa et al. (2005)
	NI	Northeast of Brazil	Thymol	25.5	Lima et al. (2013)
	Leaves	Northeast of Brazil	Thymol	56	Morais et al. (2006)
<i>Lippia sidoides</i> Cham.	Leaves	Northeast of Brazil	Thymol	63	Cavalcanti et al. (2004)
	Leaves	Northeast of Brazil	Thymol	63	Cavalcanti et al. (2004)
	Leaves	Northeast of Brazil	Thymol	63	Cavalcanti et al. (2004)
	Leaves	Northeast of Brazil	Thymol	63	Cavalcanti et al. (2004)
<b>Zingiberaceae</b>					
<i>Alpinia purpurata</i> (Viell.) K. Schum.	Red flower	Northeast of Brazil	β-Caryophyllene and β-pinene	80.7	Santos et al. (2012)
	Pink flower	Northeast of Brazil	β-Pinene and β-caryophyllene	71.5	Santos et al. (2012)
<i>Curcuma aromatica</i> Salisb.	Rhizomes	Thailand	1H-3a,7-Methanoazulene and curcumene	36.3	Choochote et al. (2005)
<i>Curcuma domestica</i> Valetton	Rhizomes	Malaysia	NI	20.9	Jantan et al. (2003)
<i>Curcuma longa</i> L.	Rhizomes	Cuba	Turnerone, curcumene, and zingiberene	25	Leyva et al. (2008)
<i>Curcuma xanthorrhiza</i> Roxb.	Rhizomes	Malaysia	NI	74.2	Jantan et al. (2003)
<i>Curcuma zedoaria</i> Roxb.	Rhizomes	Thailand	1,8-Cineol and <i>p</i> -cymene	31.87	Pitasawat et al. (2007)
	Rhizomes	Thailand	β-Tumerone	33.45	Champakaew et al. (2007)
<i>Etilingera elatior</i> (Jack) R.M. Sm.	Porcelain flower	NI	Dodecanal	26.62	Silva et al. (2013)
	Red flower	NI	Dodecanal and dodecanol	33.47	Silva et al. (2013)
	Pink flower	NI	Dodecanal, dodecanol, and α-pinene	42.22	Silva et al. (2013)
<i>Hedychium coccineum</i> Buch.-Ham. ex Sm.	Rhizome	USA	Linalool	NI <sup>a</sup>	Sakhanokho et al. (2013)
<i>Hedychium</i> ‘Kinkaku’	Rhizome	USA	1,8-Cineol and β-pinene	NI <sup>a</sup>	Sakhanokho et al. (2013)
<i>Hedychium</i> ‘Tai Golden Goddess’	Rhizome	USA	1,8-Cineol	NI <sup>a</sup>	Sakhanokho et al. (2013)
<i>Zingiber officinale</i> Roscoe	Rhizome	India	NI	40.5	Kalaivani et al. (2012)
	Rhizome	NI	α-Zingiberene	76.07	Silva (2012)
	Rhizome	India	NI	100	Prajapati et al. (2005)

NI information is not available

<sup>a</sup> Results expressed as percentage of larval mortality

*pectinata* (L.) Poit. This oil exhibited an LC<sub>50</sub> value of 366 mg/L against *A. aegypti* larvae, whereas the LC<sub>50</sub> value of β-caryophyllene was 1,202 mg/L and that of caryophyllene oxide was 125 mg/L.

Through this review, we observed that the lowest LC<sub>50</sub> values of essential oils were lower than that of their isolated compounds. For example, among the oils tested, the wood essential oil from *C. glaucophylla* (LC<sub>50</sub>=0.69 mg/L) showed

**Table 2** Plant essential oils considered not active ( $LC_{50} > 100$  mg/L) against *Aedes aegypti* L. (Diptera: Culicidae) larvae

Family and plant species	Part used	Plant origin	Major constituents	$LC_{50}$ (mg/L)	Reference
<b>Amaranthaceae</b>					
<i>Achyranthes aspera</i> L.	Leaves	India	NI	761	Khandagle et al. (2011)
	Stems	India	NI	668	Khandagle et al. (2011)
<b>Anacardiaceae</b>					
<i>Schinus pearcei</i> Engl.	Leaves	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Schinus polygamus</i> (Cav.) Cabrera	Leaves	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Schinus terebenthifolia</i> Raddi	Fruits	Southeast of Brazil	$\delta$ -3-Carene	117.34	Cole (2008)
	Fruits	Southeast of Brazil	$\delta$ -3-Carene	NI <sup>a</sup>	Silva et al. (2010)
<b>Annonaceae</b>					
<i>Rollinia leptopetala</i> R.E. Fr.	Leaves	Northeast of Brazil	Linalool and 1,8-cineol	104.7	Feitosa et al. (2009)
<b>Apiaceae</b>					
<i>Coriandrum sativum</i> L.	Seed	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Cuminum cyminum</i> L.	Seed	India	NI	>150	Prajapati et al. (2005)
<b>Asteraceae</b>					
<i>Eupatorium buniifolium</i> Hook. ex Arn.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Ageratum conyzoides</i> L.	Leaves	Northeast of Brazil	NI	148	Mendonça et al. (2005)
<i>Artemisia abrotanum</i> L.	NI	Cuba	NI	193	Leyva et al. (2008)
<i>Artemisia afra</i> Jacq. ex Willd.	Flowering	NI	NI	NI <sup>a</sup>	Seo et al. (2012)
<i>Artemisia vulgaris</i> L.	Leaves	Northeast of Brazil	NI	114.1	Lavor et al. (2012)
<i>Baccharis dracunculifolia</i> DC.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Baccharis genistelloides</i> (Lam.) Pers.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Baccharis latifolia</i> (Ruiz & Pav.) Pers.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Baccharis pentandlii</i> DC.	Leaves	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Baccharis salicifolia</i> (Ruiz & Pav.) Pers.	Leaves	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Chrysanthemum parthenium</i> (L.) Bernh.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Coniza rurigena</i> Neck.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Eupatorium betonicaeforme</i> (DC.) Baker	Aerial	Northeast of Brazil	$\beta$ -Caryophyllene	NI <sup>a</sup>	Albuquerque et al. (2004)
<i>Gnaphalium gaudichaudianum</i> DC.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Parastrephia lepidophylla</i> (Wedd.) Cabrera	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Pectis apodocephala</i> Baker	Aerial	Northeast of Brazil	Citral	NI <sup>a</sup>	Albuquerque et al. (2007)
<i>Pluchea fastigiata</i> Griseb.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Porophyllum ruderale</i> (Jacq.) Cass.	Leaves and flowers	Northeast of Brazil	(E)- $\beta$ -Ocimene	173.65	Fontes-Jr et al. (2012)
<i>Saussurea lappa</i> (Decne.) Sch. Bip.	Roots	Pakistan	NI	128.89	Manzoor et al. (2013)
<i>Senecio hebetatus</i> Wedd.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Tagetes elliptica</i> Sm.	Aerial	Peru	6,7-Epoxy myrcene and dihydrotagetone	111	Ruiz et al. (2011)
<i>Tagetes minuta</i> L.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<b>Cupressaceae</b>					
<i>Calocedrus formosana</i> (Florin) Florin	Sapwood	Taiwan	NI	104.8	Cheng et al. (2003)
<i>Cunninghamia lanceolata</i> (Lamb.) Hook.	Heartwood	Taiwan	NI	106.4	Cheng et al. (2003)
	Sapwood	Taiwan	NI	172.2	Cheng et al. (2003)
<i>Taiwania cryptomerioides</i> Hayata	Sapwood	Taiwan	NI	240	Cheng et al. (2003)

**Table 2** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
<b>Cyperaceae</b>					
<i>Cyperus scariosus</i> R. Br.	Flower	India	NI	>250	Prajapati et al. (2005)
<b>Euphorbiaceae</b>					
<i>Croton argyrophylloides</i> Müll. Arg.	Leaves	Northeast of Brazil	$\alpha$ -Pinene	102	Morais et al. (2006)
<i>Croton heliotropiifolius</i> Kunth	Leaves	Northeast of Brazil	$\beta$ -Caryophyllene	544	Doria et al. (2010)
	Leaves	Northeast of Brazil	$\beta$ -Caryophyllene	550.68	Silva (2006)
<i>Croton pulegioidorus</i> Baill.	Leaves	Northeast of Brazil	$\beta$ -Caryophyllene	158.81	Silva (2006); Doria et al. (2010)
<i>Croton sonderianus</i> Müll. Arg.	Leaves	Northeast of Brazil	$\beta$ -Phelandrene and $\beta$ -trans-guaiene	104	Morais et al. (2006)
<b>Fabaceae</b>					
<i>Copaifera reticulata</i> Ducke	Resin	NI	NI	NI <sup>a</sup>	Seo et al. (2012)
<i>Pterodon polygalaeflorus</i> Benth.	Dried fruits	Northeast of Brazil	$\beta$ -Caryophyllene	134.9	Pimenta et al. (2006)
<b>Lamiaceae</b>					
<i>Hedeoma mandoniana</i> Wedd.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Hyptis fruticosa</i> Salzm. Ex Benth.	Leaves	Northeast of Brazil	1,8-Cineol	502	Silva et al. (2008)
<i>Hyptis pectinata</i> (L.) Poit.	Leaves	Northeast of Brazil	$\beta$ -Caryophyllene and caryophyllene oxide	366	Silva et al. (2008)
<i>Hyptis suaveolens</i> (L.) Poit.	Leaves and branches	Northeast of Brazil	1,8-Cineol and trans-caryophyllene	261	Cavalcanti et al. (2004)
<i>Lavandula hybrida</i> E. Rev. ex Briq.	Flowering	NI	NI	NI <sup>a</sup>	Seo et al. (2012)
<i>Lepechinia floribunda</i> (Benth.) Epling	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Lepechinia graveolens</i> (Regel) Epling	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Mentha arvensis</i> L.	Leaves	Pakistan	NI	114.33	Manzoor et al. (2013)
	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Mentha piperita</i> L.	Leaves	India	Menthol	111.9	Kumar et al. (2011)
<i>Minthostachys andina</i> (Britton ex Rusby) Epling	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Ocimum basilicum</i> L.	Leaves	India	NI	200	Prajapati et al. (2005)
	Leaves	India	NI	148.5	Kalaivani et al. (2012)
	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Rosmarinus officinalis</i> L.	Shoot	India	NI	>250	Prajapati et al. (2005)
	NI	NI	NI	>500	Waliwitiya et al. (2009)
<i>Salvia hankei</i> E. Peter	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Satureja boliviana</i> (Benth.) Briq.	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<b>Lauraceae</b>					
<i>Aniba duckei</i> Kosterm.	Leaves	Brazilian Amazon	Linalool	250.61	Teles (2009)
<i>Cinnamomum cordatum</i> Kosterm.	Leaves	Malaysia	Linalool and methyl cinnamate	183.6	Jantan et al. (2005)
<i>Cinnamomum osmophloeum</i> Kaneh.	Leaves	Taiwan	T-cadinol and $\alpha$ -cadinol	108	Cheng et al. (2004)
	Leaves	Taiwan	Camphor	115	Cheng et al. (2004)
	Leaves	Taiwan	NI	120	Cheng et al. (2003)
	Leaves	Taiwan	Linalool	177	Cheng et al. (2004)
<i>Cinnamomum zeylanicum</i> Blume.	Bark	India	NI	>150	Prajapati et al. (2005)
<i>Guarea convergens</i> T.D. Penn.	Branches	Brazilian Amazon	$\alpha$ -Santalene and $\alpha$ -copaene	145	Magalhães et al. (2010)
<i>Guarea silvatica</i> C. DC.	Leaves	Brazilian Amazon	Caryophyllene oxide	117.8	Magalhães et al. (2010)



**Table 2** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
	Branches	Brazilian Amazon	Spathulenol	273.6	Magalhães et al. (2010)
<b>Myrtaceae</b>					
<i>Eucalyptus cinerea</i> F. Muell. ex Benth.	Leaves	Argentina	1,8-Cineol	NI <sup>a</sup>	Lucia et al. (2008)
<i>Eucalyptus citriodora</i> Hook	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
	NI	NI	NI	NI <sup>a</sup>	Park et al. (2011)
<i>Eucalyptus dives</i> Schauer	NI	NI	NI	NI <sup>a</sup>	Park et al. (2011)
<i>Eucalyptus globulus</i> Labill.	NI	India	NI	106.21	Tennyson et al. (2013)
	NI	NI	1,8-Cineol	NI <sup>a</sup>	Park et al. (2011)
<i>Eucalyptus globulus</i> subsp. <i>maidenii</i> (F. Muell.) J.B. Kirkp.	Leaves	Argentina	1,8-Cineol	NI <sup>a</sup>	Lucia et al. (2008)
<i>Eucalyptus globulus</i> subsp. <i>globulus</i> Labill.	Leaves	Argentina	1,8-Cineol	NI <sup>a</sup>	Lucia et al. (2008)
<i>Eucalyptus polybractea</i> R. T. Baker	NI	NI	NI	NI <sup>a</sup>	Park et al. (2011)
<i>Eucalyptus radiata</i> Sieber ex DC	NI	NI	NI	NI <sup>a</sup>	Park et al. (2011)
<i>Eucalyptus sideroxylon</i> A. Cunn. ex Woolls	Leaves	Argentina	1,8-Cineol	NI <sup>a</sup>	Lucia et al. (2008)
<i>Eucalyptus smithii</i> R. T. Baker	NI	NI	NI	NI <sup>a</sup>	Park et al. (2011)
<i>Eucalyptus viminalis</i> Labill.	Leaves	Argentina	1,8-Cineol	NI <sup>a</sup>	Lucia et al. (2008)
<i>Leptospermum petersonii</i> F. M. Bailey	NI	NI	NI	NI <sup>a</sup>	Park et al. (2011)
<i>Melaleuca cajuputi</i> Powell	Leaves	NI	NI	NI <sup>a</sup>	Seo et al. (2012)
<i>Melaleuca uncinata</i> R. Br.	NI	NI	NI	NI <sup>a</sup>	Park et al. (2011)
<i>Myrcia ovata</i> Cambess.	Leaves	Northeast of Brazil	Neral and geranial	192	Lima et al. (2011)
<i>Plinia cerrocampanensis</i> Barrie	Leaves	Panama	α-Bisabolol	NI <sup>a</sup>	Vila et al. (2010)
<i>Syzygium aromaticum</i> (L.) Merr. & L.M. Perry	NI	India	NI	135.20	Tennyson et al. (2013)
<i>Syzygium jambolana</i> (Lam.) DC.	Leaves and branches	Northeast of Brazil	(Z)-Ocimene and (E)-ocimene	433	Cavalcanti et al. (2004)
<b>Pinaceae</b>					
<i>Cedrus atlantica</i> (Endl.) Manetti ex Carrière	Wood	India	NI	947.09	Tennyson et al. (2013)
<i>Pinus radiata</i> D. Don	NI	India	NI	182.28	Tennyson et al. (2013)
<b>Piperaceae</b>					
<i>Piper gaudichaudianum</i> Kunth	Leaves	Brazilian Amazon	Viridiflorol and aromadendrene	121	Morais et al. (2007)
<i>Piper humaytanum</i> Yunck.	Leaves	Brazilian Amazon	Caryophyllene oxide and β-selinene	156	Morais et al. (2007)
<i>Piper tuberculatum</i> Jacq.	Leaves	Northeast of Brazil	NI	106.3	Lavor et al. (2012)
<b>Poaceae</b>					
<i>Cymbopogon citratus</i> (DC.) Stapf	Leaves	Pakistan	NI	136.28	Manzoor et al. (2013)
	Aerial	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Cymbopogon nardus</i> (L.) Rendle	NI	India	NI	1374.05	Tennyson et al. (2013)
<i>Cymbopogon flexuosus</i> (Nees ex Steud.) Wats.	Leaves	Northeast of Brazil	NI	121.6	Lavor et al. (2012)
	NI	India	NI	138.36	Tennyson et al. (2013)
<b>Ranunculaceae</b>					
<i>Nigella sativa</i> L.	Seed	India	NI	>250	Prajapati et al. (2005)
<b>Rutaceae</b>					
<i>Clausena anisata</i> (Willd.) Hook. f. ex Benth	Leaves	India	β-Pinene and sabinene	130.19	Govindarajan (2010)
<i>Clausena dentata</i> (Willd.) Roem.	Leaves	India	Sabinene, biofloratriene, and borneol	140.2	Rajkumar and Jebanesan (2010)
<i>Citrus limonia</i> (L.) Osbeck	Fruit peels	Northeast of Brazil	Limonene	519	Cavalcanti et al. (2004)
<i>Citrus sinensis</i> (L.) Osbeck	Fruit peels		Limonene	538	Cavalcanti et al. (2004)

**Table 2** (continued)

Family and plant species	Part used	Plant origin	Major constituents	LC <sub>50</sub> (mg/L)	Reference
Verbenaceae					
		Northeast of Brazil			
<i>Aloysia gratissima</i> (Gillies & Hook.) Tronc.	Leaves	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Lantana montevidensis</i> (Spreng) Briq.	Leaves	Northeast of Brazil	(Z)-Caryophyllene and valencene	117	Costa et al. (2010b)
Zingiberaceae					
<i>Alpinia zerumbet</i> (Pers.) B.L. Burtt & R.M. Sm.	Leaves and branches	Northeast of Brazil	1,8-Cineol and terpinen-4-ol	313	Cavalcanti et al. (2004)
<i>Boesenbergia pandurata</i> (Roxb.) Schltr.	Rhizome	Malaysia	NI	149.2	Jantan et al. (2003)
<i>Costus albiflora</i> A. Chev. ex Koechlin	Root	Bolivia	NI	NI <sup>a</sup>	Chantraine et al. (1998)
<i>Curcuma aeruginosa</i> Roxb.	Rhizome	Malaysia	NI	103.1	Jantan et al. (2003)
<i>Curcuma longa</i> L.	Rhizome	India	NI	>100	Prajapati et al. (2005)
	Rhizome	India	NI	115.6	Kalaivani et al. (2012)
<i>Hedychium bousigonianum</i> Pierre ex Gagnep.	Rhizome	USA	1,8-cineol and $\beta$ -pinene	NI <sup>a</sup>	2013
<i>Hedychium</i> ‘Dave Case’	Rhizome	USA	1,8-Cineol and ( <i>E</i> )-nerolidol	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium</i> ‘Dr. Moy’	Rhizome	USA	1,8-Cineol	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium elatum</i> Horan.	Rhizome	USA	$\beta$ -Pinene and linalool	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium flavescens</i> Carey ex Roscoe	Rhizome	USA	Linalool and $\beta$ -pinene	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium flavum</i> Roxb.	Rhizome	USA	1,8-Cineol and $\beta$ -pinene	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium forrestii</i> Diels	Rhizome	USA	Linalool	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium</i> ‘Pink Sparks’	Rhizome	USA	1,8-Cineol and $\alpha$ -humulene	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium</i> ‘Pink V’	Rhizome	USA	1,8-Cineol	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium</i> ‘Tai Conch Pink’	Rhizome	USA	1,8-Cineol and ( <i>E</i> )-nerolidol	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium</i> ‘Tai Emperor’	Rhizome	USA	1,8-Cineol and $\alpha$ -pinene	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium</i> ‘Tai Empress’	Rhizome	USA	1,8-Cineol	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium</i> ‘Tai Mammoth’	Rhizome	USA	1,8-Cineol and linalool	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium</i> ‘Tai Monarch’	Rhizome	USA	Linalool and 1,8-cineol	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium thyrsoforme</i> Sm.	Rhizome	USA	1,8-Cineol and $\beta$ -pinene	NI <sup>a</sup>	Sakhanokho et al. 2013
<i>Hedychium</i> ‘White Starburst’	Rhizome	USA	1,8-Cineol and $\beta$ -pinene	NI <sup>a</sup>	Sakhanokho et al. (2013)
<i>Zingiber cassumunar</i> Roxb.	Rhizome	Malaysia	NI	NI	Jantan et al. (2003)
<i>Zingiber officinale</i> Roscoe	Rhizome	Malaysia	NI	197.2	Jantan et al. (2003)
	Rhizome	India	NI	154	Khandagle et al. (2011)
<i>Zingiber zerumbet</i> (L.) Roscoe ex Sm.	Rhizome	Malaysia	NI	102.6	Jantan et al. (2003)

NI information is not available.

<sup>a</sup> Results expressed as percentage of larval mortality

the highest larvicidal potential, whereas the lowest LC<sub>50</sub> value exhibited for an isolated compound (phenylpropanoids benzyl benzoate and benzyl salicylate) from essential oil was 6.8 mg/L.

The blends of compounds, rather than isolated ones, confer the ecological role of essential oils on plant defence. This shows us the importance of the complexity of chemical composition of the natural products. Understanding the mechanisms involved in synergistic phenomenon is meaningful for the improvement of essential oil-based larvicidal products.

These results support the idea of using complex natural product without the isolation of the active compound. The production and marketing of essential oil can be much cheaper than that of larvicide compounds since the necessary process for the isolation or synthesis of the latter is more expensive. Therefore, it is possible to obtain an essential oil-based, economically viable larvicidal product obtained from a renewable resource, with greater acceptance by the population. Thus, scientific research in this segment should be encouraged to contribute to the development of such larvicidal products.

**Table 3** Metabolites from essential oils considered active ( $LC_{50} < 100$  mg/L) against *Aedes aegypti* L. (Diptera: Culicidae) larvae

Classes	Constituents	$LC_{50}$ (mg/L)	Reference
Monoterpene hydrocarbons	$\delta$ -3-Carene	25.3	Cheng et al. (2009a)
		19.2	Perumalsamy et al. (2009)
		60	Kim et al. (2008)
	(-)-Camphene	67	Perumalsamy et al. (2009)
		19.2	Cheng et al. (2009b)
		37.1	Cheng et al. (2009c)
	<i>p</i> -Cymene	43.3	Cheng et al. (2009a)
		51	Santos et al. (2010)
		69.4	Cheng et al. (2013)
		NI <sup>a</sup>	Park et al. (2011)
		69.28	Perumalsamy et al. (2009)
	Fenchene	18.1	Cheng et al. (2009b)
		19.4	Cheng et al. (2009a)
		12.01	Govindarajan et al. (2012)
	R-(+)-Limonene	27	Santos et al. (2011)
		24.47	Perumalsamy et al. (2009)
		37	Silva et al. (2008)
		71.9	Cheng et al. (2013)
		NI <sup>a</sup>	Park et al. (2011)
	S-(-)-Limonene	30	Santos et al. (2011)
		NI <sup>a</sup>	Park et al. (2011)
	$\beta$ -Myrcene	27.9	Cheng et al. (2009a)
		35.8	Cheng et al. (2009c, 2013)
		66.42	Perumalsamy et al. (2009)
	$\alpha$ -Phellandrene	16.6	Cheng et al. (2009b)
		23.08	Perumalsamy et al. (2009)
	$\alpha$ -Pinene	15.4	Lucia et al. (2007)
		79.1	Cheng et al. (2009c)
	(+) - $\alpha$ -Pinene	50.92	Perumalsamy et al. (2009)
		74.3	Simas et al. (2004)
	(-)- $\alpha$ -Pinene	64.80	Perumalsamy et al. (2009)
		27.69	Govindarajan (2010)
	$\beta$ -Pinene	12.1	Lucia et al. (2007)
		22.39	Perumalsamy et al. (2009)
	(+) - $\beta$ -Pinene	42.5	Simas et al. (2004)
		15.40	Perumalsamy et al. (2009)
	(-)- $\beta$ -Pinene		

**Table 3** (continued)

Classes	Constituents	$LC_{50}$ (mg/L)	Reference
Terpenoids	Sabinene	21.2	Govindarajan (2010)
		27.3	Rajkumar and Jebanesan (2010)
	$\alpha$ -Terpinene	74.1	Cheng et al. (2013)
		14.7	Cheng et al. (2009b)
		28.1	Cheng et al. (2009c)
		NI <sup>a</sup>	Park et al. (2011)
	$\gamma$ -Terpinene	17.11	Perumalsamy et al. (2009)
		26.8	Cheng et al. (2009a)
		30.7	Cheng et al. (2009b, c)
		56	Santos et al. (2011)
		95	Silva et al. (2008)
		NI <sup>a</sup>	Park et al. (2011)
	Terpinolene	28.4	Cheng et al. (2009b, c)
		32.1	Cheng et al. (2009a)
		15.32	Perumalsamy et al. (2009)
Oxygenated monoterpenes	Ascaridole	9.6	Torres et al. (2008)
		43.5	Rajkumar and Jebanesan (2010)
	Borneol	94.9	Perumalsamy et al. (2009)
		67.02	Perumalsamy et al. (2009)
	Camphene	58.9	Lima et al. (2011)
		69	Santos et al. (2010)
	Carvacrol	70	Silva et al. (2008)
		32.88	Govindarajan et al. (2012)
	<i>cis</i> -Carveol	23.69	Govindarajan et al. (2012)
		118	Santos et al. (2011)
	RS-Carvone	152	Santos et al. (2011)
		43.8	Simas et al. (2004)
	R-(-)-Carvone	124	Santos et al. (2011)
		47.9	Lima et al. (2011)
	S-(+)-Carvone	57.2	Lucia et al. (2007)
		74.9	Perumalsamy et al. (2009)
Other terpenoids	1,8-Cineol	49.9	Ali et al. (2013b)
		49.3	Ali et al. (2013b)
	Citronellol	81.6	Simas et al. (2004)
		58.5	Ali et al. (2013b)
	Geraniol	38.64	Govindarajan (2010)
		96.6	Perumalsamy et al. (2009)
	Geranyl formate	48.7	Waliwitiya et al. (2009)
	Linalool		
	Pulegone		

**Table 3** (continued)

Classes	Constituents	LC <sub>50</sub> (mg/L)	Reference
	Terpinen-4-ol	64.76	Perumalsamy et al. (2009)
	Thymol	53.5	Waliwitiya et al. (2009)
		79	Silva et al. (2008)
		81	Santos et al. (2010)
		NI <sup>a</sup>	Carvalho et al. (2003)
	3,5-dimethoxytoluene	64.05	Perumalsamy et al. (2009)
	3,4,5-Trimethoxytoluene	67.13	Perumalsamy et al. (2009)
	Verbenone	93.16	Perumalsamy et al. (2009)
	Germacrene D	18.76	Govindarajan (2010)
	Geijerene	63.6	Kiran et al. (2006)
Sesquiterpene hydrocarbons	β-Caryophyllene	43.4	Kiran et al. (2006)
		88.3	Perumalsamy et al. (2009)
	Pregeijerene	28.3	Kiran et al. (2006)
	β-Bisabolol	33.2	Rajkumar and Jebanesan (2010)
Oxygenated Sesquiterpenes	(E),(E)-Farnesol	13	Simas et al. (2004)
	(E)-Nerolidol	9.0	Chantraine et al. (1998)
		13.4	Ali et al. (2013b)
		17.0	Simas et al. (2004)
		NI <sup>aa</sup>	Park et al. (2011)
Diterpenes	16-Kaurene	57	Cheng et al. (2009c)
Phenylpropanoids	(E)-Anethole	14.8	Chantraine et al. (1998)
		42	Cheng et al. (2004)
		88.5	Waliwitiya et al. (2009)
		69.2	Santos et al. (2007)
	(E)-Asarone	27	Perumalsamy et al. (2009; 2010)
	(Z)-Asarone	16 <sup>b</sup>	Ciccia et al. (2000)
	Benzyl benzoate	6.8	Jantan et al. (2005)
	Benzyl salicylate	6.8	Jantan et al. (2005)
	(E)-Cinnamaldehyde	24.4	Simas et al. (2004)
		29	Cheng et al. (2004)
		51.3	Kim et al. (2008)
	Cinnamyl acetate	33	Cheng et al. (2004)
	Methyl cinnamate	16.8	Jantan et al. (2005)
		26	Cheng et al. (2004)
	Ethyl cinnamate	39.5	Kim et al. (2008)
		33	Cheng et al. (2004)
	Ethyl- <i>p</i> -methoxycinnamate	18.9	Kim et al. (2008)

**Table 3** (continued)

Classes	Constituents	LC <sub>50</sub> (mg/L)	Reference
	<i>p</i> -Methoxycinnamic acid	61	Kim et al. (2008)
	Eugenol	33	Cheng et al. (2004)
		44.5	Simas et al. (2004)
		79.39	Nascimento (2012)
		82.8	Pandey et al. (2013)
		88	Santos et al. (2010)
		89.9	Jantan et al. (2005)
	Methyleugenol	57.65	Perumalsamy et al. (2009, 2010)
	Estragole	12.7	Govindarajan (2010)
		46.4	Perumalsamy et al. (2009)
	Myristicin	72.98	Perumalsamy et al. (2009)
	Safrole	49	Simas et al. (2004)
		32.1	Jantan et al. (2005)
		9.88	Perumalsamy et al. (2009)
	2,2-Dimethyl-6-vinylchroman-4-one	NI <sup>a</sup>	Albuquerque et al. (2004)
	2-Senecioid-4-vinylphenol	NI <sup>a</sup>	Albuquerque et al. (2004)
	Hexyl butyrate	74.9	Tabanca et al. (2012a)
Others	Undecan-2-one	14.37	Tabanca et al. (2012b)

NI information is not available

<sup>a</sup> Results expressed as percentage of larval mortality

<sup>b</sup> Result expressed as LC<sub>90</sub> (in milligrams per litre)

An additional way to develop more effective natural products for use in mosquito control is by adding the synthetic compound piperonyl butoxide (PBO) to natural compounds. PBO is an inhibitor of microsomal mono-oxygenases, which are involved in the metabolism and detoxification of insecticides (Kumar et al. 2002). Waliwitiya et al. (2009) reported the synergistic effect of PBO and phytochemicals. Their study showed that plant-based products containing PBO were more active, such that their required concentrations were comparable to those of conventional larvicides.

### Factors affecting the larvicidal potential of essential oils and their compounds

The toxic potential of essential oils and their compounds against *A. aegypti* larvae may vary significantly according to intrinsic and extrinsic factors. Plant species, plant parts, age of

**Table 4** Metabolites from essential oils considered not active ( $LC_{50} > 100$  mg/L) against *Aedes aegypti* L. (Diptera: Culicidae) larvae

Classes	Constituents	$LC_{50}$ (mg/L)	Reference
Monoterpene hydrocarbons	3-Carene	150	Santos et al. (2010)
	Myrcene	>500	Waliwitiya et al. (2009)
		NI <sup>a</sup>	Chantraine et al. (1998), Park et al. (2011)
	$\alpha$ -Phellandrene	NI <sup>a</sup>	Park et al. (2011)
	$\alpha$ -Pinene	>100	Cheng et al. (2013)
		>500	Waliwitiya et al. (2009)
		NI <sup>a</sup>	Chantraine et al. (1998), Park et al. (2011)
	$\beta$ -Pinene	>500	Waliwitiya et al. (2009)
		NI <sup>a</sup>	Park et al. (2011)
	(+)-Borneol	>100	Kim et al. (2008)
Oxygenated monoterpenes	(-)-Borneol	>100	Kim et al. (2008)
	Borneol	610	Santos et al. (2010)
		>500	Waliwitiya et al. (2009)
	Borneol acetate	>500	Waliwitiya et al. (2009)
	Isoborneol	598	Santos et al. (2010)
	(-)-Camphene	>100	Kim et al. (2008)
		220	Santos et al. (2010)
	(+)-Camphene	406	Santos et al. (2010)
	Camphor	271.5	Jantan et al. (2005)
		>500	Waliwitiya et al. (2009)
		657	Santos et al. (2010)
	1,4-Cineol	751	Santos et al. (2010)
	1,8-Cineol	>100	Kim et al. (2008)
		642.4	Jantan et al. (2005)
		1,381	Silva et al. (2008)
		1,419	Santos et al. (2010)
		NI <sup>a</sup>	Chantraine et al. (1998), Park et al. (2011)
	Citral	NI	Ali et al. (2013b)
	Citronellal	262.9	Waliwitiya et al. (2009)
		>100	Simas et al. (2004)
	Citronellyl formate	>100	Ali et al. (2013b)
	Eucarvone	130.35	Perumalsamy et al. (2009)
	Geranic acid	>100	Ali et al. (2013b)
	Geraniol	415	Pandey et al. (2013)
	Limonene oxide	517	Santos et al. (2011)
	Linalool	>100	Simas et al. (2004), Ali et al. (2013b)
		157.4	Jantan et al. (2005)
		242.6	Pandey et al. (2013)
		>500	Waliwitiya et al. (2009)
		NI <sup>a</sup>	Chantraine et al. (1998), Park et al. (2011)
	Menthol	>100	Simas et al. (2004)
		365.8	Pandey et al. (2013)

**Table 4** (continued)

Classes	Constituents	$LC_{50}$ (mg/L)	Reference
		404	Santos et al. (2011)
	Menthone	508	Santos et al. (2011)
	Isomenthone	NI	Ali et al. (2013b)
	Pulegone	NI <sup>a</sup>	Chantraine et al. (1998)
	Isopulegol	297	Santos et al. (2011)
	Neoisopulegol	554	Santos et al. (2011)
	Terpineol	331.7	Pandey et al. (2013)
	$\alpha$ -Terpineol	>100	Cheng et al. (2013)
		111.78	Perumalsamy et al. 2009
		NI <sup>a</sup>	Chantraine et al. (1998), Park et al. (2011)
	(+)- $\alpha$ -Terpineol	>100	Kim et al. (2008)
	(-)- $\alpha$ -Terpineol	>100	Kim et al. (2008)
	Terpinen-4-ol	220.5	Jantan et al. 2005
Sesquiterpene hydrocarbons		NI <sup>a</sup>	Chantraine et al. (1998), Park et al. (2011)
	(-)-Terpinen-4-ol	>100	Cheng et al. (2009c)
	$\beta$ -Caryophyllene	1,038	Doria et al. (2010)
		1,202	Silva et al. (2008)
		NI <sup>a</sup>	Park et al. (2011)
Oxygenated sesquiterpenes	$\alpha$ -Cedrene	>100	Cheng et al. (2013)
	$\beta$ -Cedrene	>100	Cheng et al. (2013)
	$\alpha$ -Humulene	NI <sup>a</sup>	Park et al. (2011)
	$\alpha$ -Cadinol	>100	Cheng et al. (2013)
	Caryophyllene oxide	125	Silva et al. (2008)
Phenylpropanoids	Cedrol	>100	Cheng et al. (2013)
	Elemol	>100	Cheng et al. (2009c)
	$\beta$ -Eudesmol	>100	Cheng et al. (2009c)
	Eugenol	142.9	Waliwitiya et al. (2009)
Others	Methyleugenol	350.9	Jantan et al. (2005)
	Hexyl isobutyrate	106.3	Tabanca et al. (2012a)
	Hexyl-2-methyl butyrate	107.7	Tabanca et al. (2012a)
	Octyl acetate	148.9	Tabanca et al. (2012a)

NI information is not available

<sup>a</sup> Results expressed as percentage of larval mortality

the plant, chemotypes, and geographic conditions (such as season, rainfall, humidity percentage, temperature, sunlight, and altitude) in which the plant was collected, larval source, and methods used, in general, induce different larval responses (Morais 2009; Barbosa et al. 2012b).

Cheng et al. (2003) demonstrated that essential oils from the heartwood, bark, leaves, and sapwood of *Calocedrus formosana* (Florin) Florin presented different degrees of activity, e.g. essential oil from sapwood was less toxic than essential oil from leaves. Similar results were observed in the same study for heartwood and sapwood oil of *Taiwania*



*cryptomerioides* Hayata; the essential oil obtained from heartwood was active against *A. aegypti* larvae ( $LC_{50}$ =79.8 mg/L) and that from sapwood was inactive ( $LC_{50}$ =240 mg/L).

Arriaga et al. (2007) revealed that the essential oil from the stem of *Stemodia maritima* L. exhibited an  $LC_{50}$  of 22.9 mg/L, whereas the essential oil from the leaves of this species was less active ( $LC_{50}$ =55.4 mg/L). The essential oil from *Rollinia leptopetala* R.E. Fr. stem ( $LC_{50}$ =34.7 mg/L) was also more active than that from its leaves ( $LC_{50}$ =104.7 mg/L) (Feitosa et al. 2009). These results can be explained by the differences in the chemical composition of essential oils from distinct plant parts.

Cheng et al. (2009c) compared the larvicidal potential of essential oils from leaves of *C. japonica* at different ages (58, 42, and 26 years old). Although the percentage of the two major compounds (16-kaurene and elemol) in the oils were not significantly different among the three samples, their toxicity against *A. aegypti* larvae varied. The 58-year-old tree was the most active, showing a  $LC_{50}$  of 28.4 mg/L, compared with the 42-year-old ( $LC_{50}$ =39.2 mg/L) and the 26-year-old tree ( $LC_{50}$ =56.7 mg/L). These results indicated that essential oils obtained from the trees at different ages have a significant influence on *A. aegypti* larvicidal activity.

Five chemotypes of indigenous *Cinnamomum osmophloeum* Kaneh. exhibited different larvicidal potential; the linalool type, camphor type, and mixed type (T-cadinol and  $\alpha$ -cadinol) were considered inactive ( $LC_{50}$ >100 mg/L), whereas the cinnamaldehyde type and cinnamaldehyde/cinnamyl acetate types were highly active ( $LC_{50}$ <50 mg/L) (Cheng et al. 2004).

Additionally, the different ecological niches of mosquito larvae can influence their susceptibility to toxic compounds. It was hypothesized that the field-collected larvae are more resistant to chemicals than those reared in laboratory because the former are better adapted to adjust to environmental variations and have a higher genetic variability (George and Vincent 2005; Sun et al. 2006). Simas et al. (2004) tested (*R*)-(-)-carvone against larvae reared in laboratory for more than 10 years and showed that this compound has a good larvicidal potential ( $LC_{50}$ =43.8 mg/L). However (*R*)-(-)-carvone was not active ( $LC_{50}$ =158 mg/L) when tested against larvae collected in fields that are known to have larvae strains resistant to temephos (Santos et al. 2011).

Barbosa et al. (2012a) tested some compounds and *Syzygium aromaticum* (L.) Merr. essential oil against a field-collected strain that is resistant to temephos and also tested them against the Rockefeller strain, which is susceptible to temephos. It was possible to observe different results for both strains, such as in the case of eugenol, which exhibited  $LC_{50}$  values of 93 and 71 mg/L in field-collected and Rockefeller larvae, respectively. However, the results do not illustrate a statistically significant difference. This finding indicates that

*S. aromaticum* essential oil and analysed compounds like eugenol do not exhibit cross-resistance with temephos.

Another factor that can change the potential of compounds is the larval instar (Thanigaivel et al. 2012). There are four mosquito larval stages (Consoli and Oliveira 1994). Waliwitiya et al. (2009) investigated the toxicity of several monoterpenes, *trans*-anethole, and *Rosmarinus officinalis* L. essential oil against *A. aegypti* larvae of first to fourth instars; they observed that the activity of the samples decreased according to larval growth. During larval growth, the larvae acquire higher capacity of detoxification and development alterations in cuticle thickness. These larval features may contribute to decreased larvicidal efficacy of a compound.

Different methodologies and analyses used in the experiments can also lead to contradictory results (Santos et al. 2010; Patil et al. 2011; Barbosa et al. 2012a). For example, methyleugenol was reported to be active ( $LC_{50}$ =57.6 mg/L) by Perumalsamy et al. (2010) and inactive ( $LC_{50}$ =350.9 mg/L) by Jantan et al. (2005). Silva et al. (2008) showed that the  $LC_{50}$  value of  $\beta$ -caryophyllene was 1,202 mg/L, whereas Perumalsamy et al. (2009) observed an  $LC_{50}$  value of 88.3 mg/L. Likewise, different larvicidal activities against *A. aegypti* larvae have been reported for other compounds such as 1,8-cineol,  $\alpha$ -pinene,  $\beta$ -pinene, (-)-camphene, and linalool in different studies. These varying results probably stem from differences in the methodology performed to measure the larvicidal activity (Tables 3 and 4).

According to Lahlou (2004a), the biological tests results are dependent of laboratory conditions (temperature and photoperiod), materials, and models used for the experimentation. Standardization of the testing procedures is desirable in order to provide data, which can be compared and utilized by national authorities, from scientific researchers who carried out analyses in different laboratories and institutions (WHO 2009b).

## Structure–activity relationships of essential oil compounds

The relation between larvicidal effect and essential oil chemical composition is difficult to determine because the interactions among the compounds may influence the activity of the mixture. Thus, some authors have identified chemical structural characteristics of major compounds of essential oils that may contribute to the understanding of larvicidal effects (Santos et al. 2010, 2011; Barbosa et al. 2012a).

Lipophilicity plays a key role in modulating larvicidal activity. The association between lipophilic compounds and protein deactivation/enzyme inhibition may be a reasonable explanation for this fact (Ryan and Byrne 1988). It was confirmed in a chemometric study applied to active compounds such as terpenes and phenylpropanoids. In this study, the larvicidal activity was strongly correlated with the independent variables having a hydrophobic profile (Scotti et al.



2013). We will explain in more detail the important structural characteristics for effective larvicidal activity of monoterpenes, sesquiterpenes, and phenylpropanoids and their derivatives.

Phenol (**1**) exhibited an  $LC_{50}$  value of 194 mg/L for *A. aegypti* larvae, whereas compounds that have lipophilic groups like CH chains outside a phenyl ring, e.g. thymol (**2**) ( $LC_{50}$ =81 mg/L) and carvacrol (**3**) ( $LC_{50}$ =69 mg/L), displayed larvicidal activity higher than phenol (Santos et al. 2010).

The double bonds are important in the larvicidal activity of natural molecules because hydrogenation of these bonds decreases the lipophilic character of these compounds, restricting their passage through the larvae cuticle (Lomonaco et al. 2009). It is interesting to note the importance of exocyclic double bonds, for instance, in the comparison between  $\alpha$ -pinene (**4**) and  $\beta$ -pinene (**5**). According to Simas et al. (2004), Lucia et al. (2007), and Peumalsamy et al. (2009),  $\beta$ -pinene, which possesses exocyclic double bond, is more toxic to *A. aegypti* larvae than  $\alpha$ -pinene, which has endocyclic double bond (Table 2). Santos et al. (2011) demonstrated that the  $LC_{50}$  value of R-limonene (**6**) (with endo- and exocyclic double bonds) was 27 mg/L. The  $LC_{50}$  value of  $\gamma$ -terpinene (**8**), a compound with two endocyclic double bonds, was 56 mg/L.

The phenylpropanoids benzyl benzoate and benzyl salicylate were the most active compounds. The higher number of conjugated double bonds in the aromatic ring contributes to their high larvicidal potential. In general, aromatic molecules are more toxic to *A. aegypti* larvae than are aliphatic ones. The electronic density and aromatic ring planarity seem to influence positively the effectiveness of these substances (Santos et al. 2010).

Similarly, a high number of hydroxyl groups decrease potency (Scotti et al. 2013). López et al. (2005) reported that this structural characteristic prevents molecule penetration through the mosquito cuticle, which prevents the compound from reaching its specific targets. Although carvacrol (**3**) and thymol (**4**) have conjugated double bonds in their aromatic rings, they also have a hydroxyl group each and thus do not exhibit high larvicidal activity against *A. aegypti* (Santos et al. 2010). The same chemical structure without the hydroxyl group, represented by *p*-cymene (**9**), was more potent ( $LC_{50}$ =51 mg/L).

Barbosa et al. (2012a) evaluated structure–activity relationships of eugenol derivatives (**10**). The lowest potency was observed for the compound in which the double bond on the side chain was removed to add a hydroxyl (**11**) ( $LC_{50}$ =1,415.1 mg/L). The derivative that was more potent than eugenol ( $LC_{50}$ =93.3 mg/L) was 1-ethoxy-2-methoxy-4-(2-propen-1-yl)-benzene (**12**) ( $LC_{50}$ =67.2 mg/L). This compound is different from eugenol because the phenolic proton of eugenol was removed and an ethyl group was added instead.

In general, acetylation of the hydroxyl group in oxygenated monoterpenes increases their activity (e.g.  $LC_{50}$  of eugenyl acetate was 50.2 mg/L). Some structural features such as

shape, degree of unsaturation, and functional groups influence their larvicidal activity (Pandey et al. 2013).

A compound having an aliphatic aldehyde conjugated with an aromatic ring is quite potent. This fact was reinforced by comparing the larvicidal activity of (*E*)-cinnamaldehyde (**13**) ( $LC_{50}$ =24.4 mg/L) with that of citronellal (**14**), which is not aromatic and was inactive for larvae of *A. aegypti* (Simas et al. 2004). The studies by Cheng et al. (2004) and Santos et al. (2010) have also confirmed this data. The first study illustrated that the  $LC_{50}$  of benzaldehyde (**15**) after 48 h was 33 mg/L. The second study compared the bioactivity of phenol (**1**) ( $LC_{50}$ =194 mg/L) and salicylaldehyde (**16**) ( $LC_{50}$ =136 mg/L).

Some essential oils compounds have stereoisomers. The chiral compounds are recognized by receptors and enzymes in different ways. This influences their mode of action and leads to different biological activity (Lahlou 2004b). Table 2 shows different larvicidal potential for  $\alpha$ -pinene and  $\beta$ -pinene enantiomers. In addition, the larvicidal potential of enantiomers (*S*)-(+)-carvone (**17**) ( $LC_{50}$ =124 mg/L) and (*R*)-(–)-carvone (**18**) ( $LC_{50}$ =152 mg/L) and (+)-camphene (**19**) ( $LC_{50}$ =406 mg/L) and (–)-camphene (**20**) ( $LC_{50}$ =220 mg/L) was significantly different. In contrast, (*R*)-(+)-limonene (**6**) ( $LC_{50}$ =27 mg/L) and (*S*)-(–)-limonene (**7**) ( $LC_{50}$ =30 mg/L) exhibited similar activity profiles (Santos et al. 2010, 2011).

According to Santos et al. (2011), neo-isopulegol (**21**) exhibited an  $LC_{50}$  value of 554 mg/L. It was less potent than its diastereoisomer isopulegol (**22**) ( $LC_{50}$ =297 mg/L). However, this difference was not observed between borneol (**23**) ( $LC_{50}$ =610 mg/L) and isoborneol (**24**) ( $LC_{50}$ =598 mg/L) (Fig. 1) (Santos et al. 2010).

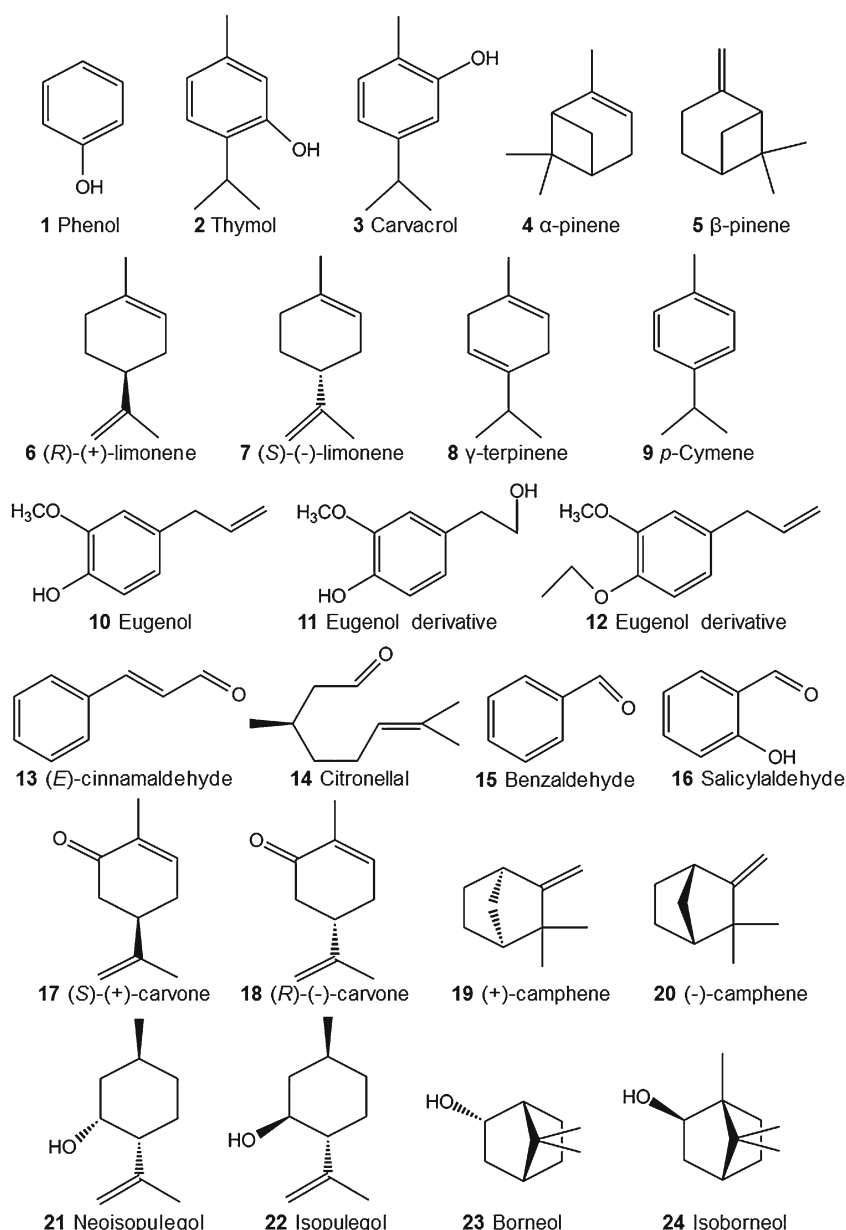
The evaluation of structure–activity relationships of larvicidal compounds may contribute to the search for additional compounds with similarly high or even higher activity. This knowledge may indicate synthesis pathways for the production of insecticides more effective and less toxic and, in addition, can promote the understanding of the mode of action of these larvicidal compounds.

## Mode of action

Few studies have investigated the larvicidal mechanisms of action of essential oils and their compounds against *A. aegypti* larvae. Essential oils are complex mixtures of chemical compounds. Hence, several mechanisms of toxicity on insects could be involved. Protein denaturalization, enzymatic inhibition, and membrane disintegration are some of the suggested modes (Regnault-Roger 1997; Cavalca et al. 2010).

Insecticides can affect insects by various modes of action. They may be ingested and absorbed through the digestive tract. The respiratory system and the body may be the target by fumigants, suffocants, and desiccants. Furthermore, some

**Fig. 1** Chemical structures of some compounds studied for their larvicidal activity against *Aedes aegypti* L. (Diptera: Culicidae)



compounds may act as hormones inhibiting the growth and development of the insect (Hemingway and Ranson 2005).

According to Cantrell et al. (2010), larvicide compounds act by absorption through the cuticle, via the respiratory tract, and/or enter by ingestion via the gastrointestinal tract. Once in the interior of the larva, the substances can reach the site of action or can cause systemic effects by diffusion into different tissues (Souza et al. 2012b).

In addition, the lipophilicity of the essential oils constituents enables disruption and penetration through the lipoprotein matrix of the insect cell membrane (Satyan et al. 2009). Franzios et al. (1997) indicate that many essential oils deter insect feeding, while some others act as insect growth regulators through analogs or antagonistic effects to endogenous hormones.

Some authors have suggested that the rapid effect on some natural larvicides is indicative of their neurotoxic mode of action. The symptoms of most larvae treated with essential oils are caused by toxicity to the neuromuscular system. These symptoms are excitation, convulsions, hyperactivity, and hyperextension of the legs and abdomen, followed by paralysis (fast knock-down) and death (Enan 2001; Isman 2006). According to Kostyukovsky et al. (2002), these effects are similar to those produced by conventional insecticides as temephos, an organophosphate cholinesterase inhibitor used in vector-borne disease control programmes (WHO 2009b).

Ryan and Byrne (1988) reported that five oxygenated monoterpenes were reversible competitive inhibitors of acetylcholinesterase (AChE) isolated from electric eels. Both

in vitro and in vivo experiments confirmed this. Nevertheless, in the studies by Kostyukovsky et al. (2002) and López and Pascual-Villalobos (2010), natural terpenes such as fenchone,  $\gamma$ -terpinene, geraniol, linalool, and (*S*)-carvone only inhibited AChE from *Electrophorus electricus* L. (Gymnotiformes: Gymnotidae) and from *Rhyzopertha dominica* F. (Coleoptera: Bostrichidae) at high concentrations, indicating that the AChE inhibition is not the main mode of action of these essential oil compounds.

Another potential target for the larvicidal activity of essential oil constituents is the octopaminergic system of insects. Octopamine is a biogenic monoamine that is present in neuronal and non-neuronal tissues of invertebrates. This compound acts as a neurotransmitter, neurohormone, and neuromodulator. Its physiological role is analogous to that of norepinephrine in vertebrates, influencing many features of animal physiology and behaviour, such as flight, energy metabolism regulation, and heart rate (Roeder 1999; Pflüger and Stevenson 2005). The octopamine receptors (ORs) are membrane-bound receptors that belong to the family of G protein-coupled receptors. Generally, interactions with ligands modulate effects via changes in intracellular calcium concentrations  $[Ca^{2+}]_i$  and via activation or inhibition of adenylyl cyclase (Evans 1984).

Enan (2001) suggested that the toxicity of eugenol and  $\alpha$ -terpineol to *Periplaneta americana* L. (Blattaria: Blattellidae) (American cockroaches) uses the octopaminergic system as a primary target. The involvement of octopamine/octopamine receptor is indicated by toxicity signs as acceleration of heart-beat, effects on cyclic adenosine monophosphate (cAMP) production in the nervous system, and a decrease in binding octopamine receptors. Kostyukovsky et al. (2002), by in vitro studies using abdominal segments from *Helicoverpa armigera* Hübn (Lepidoptera: Noctuidae) (cotton bollworm moth) as a source of ORs, indicated that the mode of action of two essential oil terpenes on insects was a competitive activation of ORs. Enan (2005) proposed that ORs mediate the toxicity of cinnamic alcohol, eugenol, (*E*)-anethol, and 2-phenylethyl propionate against *Drosophila melanogaster* Meigen (Diptera: Drosophilidae) and *P. americana*, via cellular changes such as receptor binding, cAMP production, and  $[Ca^{2+}]_i$  mobilization.

In a recent protein-ligand docking study, eugenol, geraniol, 1,8-cineol, and carvacrol as well as octopamine and acetylcholine were allowed to dock against OR and acetylcholinesterase protein models of *A. aegypti* and *Homo sapiens*. The study objective was to predict and rank the association between the ligands and the target proteins on two animal systems. The compounds docked with all the protein models, although they performed better against the protein models of *A. aegypti* than the human protein models (Khanikar et al. 2013).

Another receptor may be involved with the mode of action of essential oils. The insecticidal activity of the oxygenated

monoterpene thymol was mediated by interferences of ionotropic GABA receptors. In addition, thymol was more potent on a recombinant insect GABA receptor than on mammalian GABA<sub>A</sub> receptors. However, the thymol-binding site on the GABA receptor has not been identified because thymol did not act via the site of action on the investigated allosteric modulators such as benzodiazepines,  $\beta$ -carboline, barbiturates, propofol, loreclezole, and steroids (Priestley et al. 2003).

All the aforementioned facts indicate that these compounds may be considered safe to humans. Further studies should be carried out to confirm the mosquito larvicidal modes of action of essential oil constituents. With these data, it will be possible to find pharmacophore models that are necessary for molecular recognition by the receptors. Therefore, these findings can serve as a means to develop products more effective and less toxic to non-target organisms compared with the conventional larvicides used in vector-borne disease control programmes.

Essential oils comprise a complex mixture of constituents, and their larvicidal activity seems to have no specific site of action. Therefore, it is likely very difficult for the insect to develop an adaptation that leads to resistance (Wahyuni 2012).

## Patents

The data cited in this paper illustrates the higher larvicidal potential of essential oils and their compounds toward *A. aegypti*. Thus, some patent applications were published with the purpose to regulate the production of formulations for use against *A. aegypti* larvae in the field.

One patent proposed a mosquito larvicide formulation in which the active agent is D-limonene, which is present in orange oil and ethyl lactate (WO2005034631A2). US patent application no. US3954991 also relates to the use of limonene. In this patent, however, limonene is condensed with sesamol to produce two novel compounds that are highly effective at killing mosquito larvae.

Two monoterpenes widely found in essential oils, *p*-cymene and thymol, were incorporated into a formulation that can be used as a larvicide and adulticide against mosquitoes belonging to the genus *Aedes* and *Anopheles* (US2009036547A1). The inventors reported that this composition is also useful against strains resistant to conventional insecticides. Japanese patent application no. 2000026210A includes spathulenol as an active ingredient of a formula insecticide to be used against *A. aegypti* and *Culex pipiens pallens* L. (Diptera: Culicidae).

French patent application no. FR2958500 describes a process for the preparation and use of an insecticide, insect repellent, ovicide, larvicide, and nymphicide composition. This composition comprises at least one essential oil or a mixture of them. These essential oils may originate from *Eucalyptus globulus* Labill., *Juniperus communis* L., *Santalum album* L., *Mentha piperita* L., *Eugenia caryophyllata* Thunb., *Pinus*

*sylvestris* L., *R. officinalis* L., *Eucalyptus citriodora* Hook., *Annona squamosa* L., among others.

International publication no. WO2011/032892A1 describes a synergistic combination of compounds for use as an ascaricide, insecticide, pupicide, and/or larvicide that comprises at least two active compounds. These may include fatty alcohols and simple oils as well as essential oils of pepper-mint, tangerine, grapefruit, lemon, and basil.

Although this review highlights the high potential of Brazilian plants, only one Brazilian patent was found in the database. The cited patent reports the use of essential oil from bracts of *Alpinia purpurata* (Viell.) K. Schum. as a larvicide and deterrent against *A. aegypti* (BRPI0805711-7A2).

## Conclusion

In the search for alternative larvicides to be used in vector-borne disease control programmes, plant essential oils have demonstrated to be more active than their individual compounds against *A. aegypti*. This highest bioactivity of essential oils shows us the importance of producing a low-cost larvicide without the need to isolate an active compound, which is an expensive process. For this, selection of chemical markers is essential for the quality control of herbal products.

Although these natural products have been widely investigated, a low number of patents have been applied with the purpose of regulating the production of formulations for use against *A. aegypti* larvae in the field. This review demonstrates the need for standardization of methodologies for the evaluation of larvicides against *A. aegypti*.

The research regarding the search for new larvicides should be performed in a standardized manner. The features from plants (collection, extraction, chemical constitution) and insects (collection, age) and the methodological procedures must be well defined in research. We need to overcome the barriers to commercialization of new botanical insecticides. There has to be a paradigm shift in natural product research, in which studies are conducted with the ultimate goal of producing plant-based larvicides for use in public health programmes.

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