Essential Oils as a Potential Treatment Option for Pediculosis

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Key words

pediculosis, Pediculidae, pthiridae, *Pediculus humanus capitis, Pediculus humanus humanus, Pthirus pubis*, treatment, eco-friendly pediculicides

received March 1, 2020
revised April 3, 2020
accepted April 11, 2020

Bibliography

DOI https://doi.org/10.1055/a-1161-9189
published online May 4, 2020 | Planta Med 2020; 86: 619–630 © Georg Thieme Verlag KG Stuttgart · New York | ISSN 0032-0943

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ABSTRACT

Pediculosis is a prevalent ectoparasite infestation caused by lice. The head louse (*Pediculus humanus capitis*) and body louse (*Pediculus humanus humanus*) are obligatory parasites whose only known hosts are humans. Pediculosis is probably the most common ectoparasitic infestation, affecting up to 80% of the population in several countries, and particularly prevalent in the infant population worldwide. Several treatment options, including shampoos and creams containing insecticides, have been introduced for the treatment of pediculosis. Recently, the use of synthetic chemicals to control human lice has raised concerns pertaining to human health and the environment. Therefore, increasing efforts have been undertaken to develop effective pediculicides with low environmental toxicity and minimal environmental residual activity. In this study, we focus on the essential oils derived from 22 plant genera, their constituents, and the major factors that play important roles in the effectiveness of these oils in the treatment of pediculosis. Furthermore, we discuss the advantages and limitations of the mentioned essential oils, and ultimately suggest those demonstrating the most effective *in vitro* pediculicidal activities. The genera such as *Aloysia, Cinnamomum, Eucalyptus, Eugenia, Lavandula, Melaleuca, Mentha, Myrcianthes, Origanum, Pimpinella*, and *Thymus* appear to be more efficient against lice. These genera are rich in anethole, 1,8-cineole, cinnamaldehyde, *p*-cymene, eugenol, linalool, limonene, pulegone, terpinen-4-ol, and thymol compounds.

Introduction

Pediculosis is a widespread obligate ectoparasitic infestation caused by lice [1]. It is an important health problem with a global prevalence. Pediculosis is caused by two genera of blood-sucking lice: *Pthirus* and *Pediculus*. The genus *Pthirus* includes a single species, namely, *Pthirus pubis* (the pubic louse). The genus *Pediculus* consists of *Pediculus humanus capitis* (head lice) and *Pediculus humanus humanus* (body lice) (and one additional species in monkeys) subspecies, both of which are great concerns to public health [2]. *P. humanus capitis* is considered to be the causative agent of one-third of childhood infections, behind asthma and attention deficit disorder [3]. It is widespread globally and occurs across all ethnic groups as well as all socioeconomic levels [4, 5]. *P. humanus humanus* is common among socioeconomic groups such as the homeless, prisoners, and war refugees, which do not have ready access to standard conditions of hygiene. The body louse is considered to act as a vector of some pathogens such as *Rickettsia prowazekii* (epidemic typhus), *Bartonella quintana* (trench fever), and *Borrelia recurrentis* (relapsing fever) as well as *Acinetobacter* sp. [6].

Over the past 60 years, the treatment for pediculosis has relied mainly on the use of topical insecticides, including organochlorines (e.g., lindane introduced in 1960), organophosphorus (e.g., malathion in 1971), carbamates (e.g., carbaryl in 1977), and pyrethroids (e.g., permethrin in 1992) [7–11]. The persistent application of these chemicals has led to several reports of lice resistance from different countries such as the UK, France, and Denmark

[12–14]. Hence, there is an urgent need to develop alternative approaches for louse management. Over the past decade, some novel compounds such as dimeticone, isopropyl myristate, and benzyl alcohol [15, 16], or neurotoxic compounds such as spinosad and ivermectin, were developed against louse species [17, 18]. Recently, natural products with pediculicidal properties, such as essential oils, have been used as therapeutic alternatives to the synthetic insecticides [7, 19, 20].

Here, we present a detailed review of the relevant literature on essential oils with emphasis on their laboratory method of evaluation (*in vitro*), constituents, and the major factors influencing the efficiency of essential oils in the treatment of pediculosis. In addition, we also discuss the advantages and limitations of each group of essential oils in the treatment of pediculosis in detail, and ultimately suggest the groups that are the most effective against louse ectoparasites.

Essential Oils

Essential oils are blends of approximately 10 to 80 different metabolites extracted from plants through steam- or hydro-distillation [21]. Essential oils are commonly derived from plants belonging mainly to the families Myrtaceae, Lauraceae, Lamiaceae, and Asteraceae [22]. They are often extracted from various plant organs, such as flowers (e.g., *Citrus bergamia*), leaves (e.g., *Citronella* sp., *Eucalyptus* sp.), wood (e.g., *Santalum* sp.), roots (e.g., *Chrysopogon zizanioides*), rhizomes (e.g., *Zingiber officinale*), fruits (e.g., *Pimpinella anisum*), and seeds (e.g., *Myristica fragrans*) [22]. The compositions of essential oils are highly variable. They usually contain two or three major terpene or terpenoid components of low molecular weight, which often determine the biological properties of the essential oils [21]. They are biodegradable, with low environmental toxicity and minimal environmental residual activity due to being highly volatile, and are well accepted by people who want to discontinue the use of synthetic chemicals [22]. They have previously been reported to be highly effective in the treatment of pediculosis [23]. The potency of essential oils against lice varies considerably across species.

Ex vivo pediculicidal activity of essential oils

During the past few years, an increasing number of publications, including research articles, books, and media, pinpoint a rise in incidence of lice infestations and highlight the consequences of such infestations on the human health. To shed light on the past and present applications of essential oils against louse ectoparasites, a systematic review of the released literature, including research articles, books, and theses, was performed. Seven medical databases, including Scopus, PubMed, Science Direct, ProQuest, Web of Science, Springer, Medline, Embase, and Google Scholar, were explored with articles published from 1890 to 2019. The search strategy was performed using key words such as scientific species names as well as trivial names used for the lice and their corresponding genera and species, and also included various scientific thematic issues of research (biology, epidemiology, medical, control, etc.). The quest was performed using five languages (English, French, German, Portuguese, and Spanish). The relevant articles that met the aforementioned criteria were selected. Duplicated articles, articles with unrelated topics and abstract, or with commercial publicity were excluded.

To evaluate the efficacy of essential oils against pediculosis, a database containing information on essential oils derived from 106 plant species belonging to 57 genera was gathered for this review. Then, the essential oils that have been demonstrated to be effective against the louse species are presented and discussed in detail in the subsequent sections. The names and characteristics of the major essential oils previously reported to be effective against louse ectoparasites are presented in ▶ **Table 1**.

Lavandula

The genus *Lavandula* consists of over 20 species that initially originated from the Mediterranean region and have varying growth habits, morphological characters, and chemical compositions. Three *Lavandula* species, namely *Lavandula angustifolia* (fine lavender), *Lavandula latifolia* (spike lavender), and *Lavandula intermedia* (lavandin), are mainly used to extract essential oils [24]. Lavender oils have been reported to possess antimicrobial, antifungal, and insecticidal properties [25]. Lavender oils have historically been recommended in the treatment of pediculosis [26, 27] and reported to be effective, with a more than 80% knockdown effect against head lice in a laboratory study [28]. Furthermore, lavender and their components, such as linalool, are used as mosquito repellents [29]. Lavender oils are also effective against other insects and acari (e.g., *Plutella xylostella, Dermanyssus gallinae*, and *Dermatophagoides* spp.) [30]. The main constituents of lavender oil are linalool and linalyl acetate, concentrations of which may vary significantly across oils derived from different cultivars [25].

Eucalyptus

The genus *Eucalyptus* comprises about 900 species, of which over 300 species contain volatile essential oils in their leaves [31]. They were originally native to Australia and have been cultivated worldwide for industrial and medicinal purposes. The essential oils of some *Eucalyptus* species (e.g., *Eucalyptus globulus*) exhibited high activity against head lice [32, 33]. In addition, other species of *Eucalyptus*, including *Eucalyptus sideroxylon, Eucalyptus cinerea, Eucalyptus viminalis, Eucalyptus saligna, Eucalyptus grandis*, and *Eucalyptus camaldulensis* or their hybrids, were also reported to have significant pediculicidal effects against head lice [34]. Furthermore, the oils extracted from some *Eucalyptus* species (e.g., *Eucalyptus citriodora*) have been used as insect repellents [35]. Overall, *Eucalyptus* species found to be effective against head lice have a high content of 1,8-cineole as the main component [34, 36].

Cinnamomum

The genus *Cinnamomum* comprises about 250 species. Two well-known species of this genus are *Cinnamomum zeylanicum* and *Cinnamomum cassia* [37]. They have antioxidant, anti-inflammatory, antidiabetic, antimicrobial, and anticancer properties [37]. Essential oil from the bark/leaf of *C. zeylanicum* significantly inhibited the adults as well as eggs of *P. humanus capitis* [38, 39]. Other species of *Cinnamomum*, including *C. cassia* and *Cinnamomum porphyrium,* have also been reported to kill head lice [40]. In addition, *Cinnamomum* species can repel or kill a variety of insects, includ-

▸ **Table 1** The major essential oils together with their characteristics reported to be effective against louse ectoparasites.

Family	Genus	Species	Lice species	Methodology				Concentration	LT_{50} (min)	KT_{50} (min)	Mortality (%)	Major component	Reference
				Filter paper	Immersion	Fumigation	Direct contact						
Anacardiaceae	*Schinus*	*areira*	PC			X		50 µL		10.80		α-Phellandrene, myrcene, limonene	[51]
Apiaceae	*Pimpinella*	*anisum*	PH		X			1 %			100	E-anethol	[38]
			PC	X				0.25 mg/cm²		45.37		E-anethol	[40]
Asteraceae	*Tagetes*	*minuta*	PC	X				100 ppm	16.40			β-Ocimene, tagetone	[68]
Cupressaceae	*Juniperus*	*oxycedrus*	PC	X				0.25 mg/cm²	19.20			Cadinene, α-cedrene, camphor, guaiacol	[36]
Lamiaceae	*Origanum*	*majorana*	PC	X				0.25 mg/cm²	11.40			1,8-Cineole, linalool	[36]
			PC	X				0.08 mg/cm²				1,8-Cineole, linalool	[76]
		Vulgare	PH		X			1 %			100	Carvacrol, thymol	[38]
	Thymus	*vulgaris*	PH		X			1 %			83.9	Thymol, 1,8-cineole	[38]
			PC			X		50 µL		18.25		Thymol, *p*-cymene, carvacrol	[51]
			PC	X				0.21 mg/cm²		9.90		Thymol, *p*-cymene, carvacrol	[51]
			PC	X				0.25 mg/cm²		29.92		Thymol, O-cimene, γ-terpinene	[40]
	Lavandula	sp.	PC		X			5 %		83.00[a]		Linalool, linalyl acetate	[106]
	Mentha	*spicata*	PC	X				0.25 mg/cm²		8.84		1-Carvone, eugenol, limonene	[40]
		pulegium	PC					0.25 mg/cm²	7.00			Pulegone, piperitenone, menthone	[36]
		piperita	PC		X			5 %		81.30[a]		Menthol, menthone	[106]
	Salvia	*officinalis*	PC	X				0.25 mg/cm²	18.00			Thujone, camphor	[36]
	Rosmarinus	*officinalis*	PC	X				0.25 mg/cm²	14.30			1,8-Cineole, α-pinene, camphor	[36]
	Aniba	*rosaeodora*	PC	X				0.25 mg/cm²	22.40			Linalool	[36]
Lauraceae	*Cinnamomum*	*cassia*	PC	X				0.25 mg/cm²		11.38		Cinnamaldehyde	[40]
		zeylanicum	PC	X				0.25 mg/cm²	37.38			Cinnamaldehyde, benzaldehyde, eugenol	[39]
			PH		X			1 %			100	Eugenol	[38]
		porphyrium	PC			X		60 µL		1.12		NA	[110]
	Litsea	*cubeba*	PC	X				1.75 mg/cm²	30			Geranial, neral, limonene	[56]

continued

▶ Table 1 *Continued*

Family	Genus	Species	Lice species	Methodology				Concentration	LT_{50} (min)	KT_{50} (min)	Mortality (%)	Major component	Reference
				Filter paper	Immersion	Fumigation	Direct contact						
Myrtaceae	*Myrcianthes*	*pseudomato*	PC			X		60 µL		4.09		1,8-Cineole, *β*-caryophyllene	[110]
		cisplatensis	PC			X		60 µL		1.29		1,8-Cineole, limonene	[67]
	Myrtus	*communis*	PC	X				0.25 mg/cm^2	19.20			*α*-Pinene, 1,8-cineole, limonene	[36]
	Eugenia	*caryophyllata*	PC	X				0.25 mg/cm^2	19.60			Eugenol, acetyl eugenol, *β*-caryophyllene	[36]
			PC	X				0.25 mg/cm^2	18.80			Eugenol, acetyl eugenol	[62]
			PC	X				1.75 mg/cm^2	10			Eugenol, acetyl eugenol	[56]
			PC	X				0.25 mg/cm^2		19.73		Eugenol, caryophyllene	[40]
	Melaleuca	*alternifolia*	PC	X				10 %			70	Terpinen-4-ol, 1,8 cineole	[13]
			PH	X				10 %			90	Terpinen-4-ol	[52]
			PC	X				1 %			100	Terpinen-4-ol	[55]
			PH		X			1 %			93.20	Terpinen-4-ol, 1,8-cineole	[38]
	Eucalyptus	*globulus*	PC	X				0.25 mg/cm^2	4.20			1,8-Cineole	[36]
			PC	X				0.225 mg/cm^2				1,8-Cineole	[33]
			PC	X				0.25 mg/cm^2	5.13			1,8-Cineole	[36]
			PC	X				0.25 mg/cm^2		43.16		1,8-Cineole, O-cymene	[40]
		globulus ssp. *globulus*	PC			X		60 µL		27.73		1,8-Cineole	[50]
		globulus ssp. *maidenii*	PC			X		60 µL		31.39		1,8-Cineole	[50]
		camaldulensis	PC			X		60 µL		35.01		1,8-Cineole, *p*-cymene, spathulenol	[34]
		grandis	PC			X		60 µL		25.57		*α*-Pinene, 1,8-cineole	[34]
		E. grandis x *E. camaldulensis*	PC			X		60 µL		13.63		1,8-Cineole, *α*-pinene	[34]
		E. grandis x *E. tereticornis*	PC			X		60 µL		12.99		1,8-Cineole, *α*-pinene	[34]
		sp.	PC		X			5 %		73.30[a]		1,8-Cineole	[106]
		sideroxylon	PC			X		60 µL		24.75		1,8-Cineole	[50]
		cinerea	PC			X		60 µL		12		1,8-Cineole	[67]
		viminalis	PC			X		60 µL		14.90		1,8-Cineole	[67]
		saligna	PC			X		60 µL		17.39		1,8-Cineole	[67]

continued

▶ Table 1 *Continued*

Family	Genus	Species	Lice species	Methodology				Concentration	LT_{50} (min)	KT_{50} (min)	Mortality (%)	Major component	Reference
				Filter paper	Immersion	Fumigation	Direct contact						
Verbenaceae	*Aloysia*	*citriodora* (2)	PC			X		60 µL		3.02		Limonene, citronellal, α-curcumene	[110]
		citriodora	PC			X		50 µL		38.35		Limonene, citronellal, α-curcumene	[51]
			PC	X				0.21 mg/cm^2		18.01		Limonene, citronellal, α-curcumene	[51]
		polystachia	PC			X		50 µL		20.64		Limonene, carvone	[51]
			PC	X				0.21 mg/cm^2		12.93		Limonene, carvone	[51]
	Lippia	*multiflora*	PH				X	10 %		21.95		Linalool, geraniol, limonene	[104]
Zingiberaceae	*Hedychium*	*spicatum*	PC		X			5 %			100	1,8-Cineole	[86]
	Elletaria	*cardamomum*	PC	X				0.25 mg/cm^2	25.40			1,8-Cineole, α-terpinyl acetate	[36]

Direct contact: droplet deposition onto dorsal part of the louse; LT_{50}: lethal time needed to kill 50 % of insects; KT_{50}: required times to knockdown half the number of insects; a: percent of KD_{50}; PC: *Pediculus capitis*; PH: *Pediculus humanus*

ing *Anopheles gambiae* and *Plodia interpunctella* [29, 41]. The main components of *Cinnamomum* species are cinnamaldehyde, benzaldehyde, and eugenol [39].

Mentha

The genus *Mentha* has a cosmopolitan distribution and comprises a large number of species, including *Mentha piperata* (peppermint), *Mentha spicata* (spearmint), and *Mentha pulegium* (pennyroyal). Essential oils extracted from the leaves of *Mentha* species have been studied for their activity against gastrointestinal disorders as well as for their anti-inflammatory properties [42]. These species have also been reported to inhibit head lice [28, 36]. Moreover, they have repellent and insecticidal/acaricidal activities against mosquitoes, *Ixodes ricinus*, and *Dermatophagoides* spp. [43, 44]. The compositions of these essential oils are highly variable, and the main components include menthol, menthone, carvone, pulegone, piperitenone, and limonene (▶ **Table 1**) [45].

Aloysia

The genus *Aloysia* comprises about 30 species that are generally known as "bee brushes". They are native to the Americas, where they are distributed in temperate and subtropical climates. Essential oils extracted from *Aloysia* species have been studied for their anti-oxidant, antimicrobial, and anti-inflammatory properties [46]. Furthermore, they also inhibit *Leishmania* parasites (e.g., *Leishmania amazonensis*) and insects (e.g., *Culex quinquefasciatus* and *Nezara viridula*) [47–49]. Some *Aloysia* species such as *Aloysia polystachya* and *Aloysia citriodora* have been demonstrated to be effective against head lice [50, 51]. The major components of *Aloysia* species are limonene, carvone, citronellal, and α-curcumene [51].

Melaleuca

Melaleuca alternifolia, belonging to the plant family Myrtaceae, is native to Australia and a source of tea tree essential oil. Tea tree oil is reported to have a wide variety of biological properties, including antimicrobial, anti-inflammatory, and acaricidal activities [52, 53]. Tea tree oil was reported to be potentially effective against both head and body lice [52, 54, 55]. The main components of *M. alternifolia* are terpinen-4-ol, γ-terpinene, α-terpinene, and α-terpineol [56].

Pimpinella

The genus *Pimpinella* includes herbaceous plants, of which *Pimpinella anisum,* the most popular condiment plant species, is cultivated worldwide for its aromatic seeds (aniseeds) [57]. Anis seeds have digestive and antimicrobial properties and inhibit insects, including *Culex pipiens* and *Lucilia sericata* [58–60]. Moreover, *P. anisum* was found to be effective against both head and body lice [34, 36]. The most important component of aniseed essential oil is *trans*-anethole [40].

Eugenia

Eugenia is an evergreen tropical plant genus comprising about 1000 species. The most economically important species of this genus is *Eugenia caryophyllata* (*Syzygium aromaticum*). The dried flower of clove is a popular kitchen spice used in both food and medicine (anesthetic, analgesic, antimicrobial, antioxidant, anti-inflammatory, and anticancer agents) [61]. *E. caryophyllata* (clove oil) was reported to display high pediculicidal activity against head lice [40, 56], which was comparable to that of commercial insecticides *d*-phenothrin and pyrethrum [62]. In addition, clove oil and its major component (eugenol) have repellant, acaricidal, and insecticidal activities (against *Aedes* and *Anopheles* mosquitoes, *D. gallinae*, and *Sarcoptes scabiei*) [29, 63]. The major component of clove oil is eugenol, followed by acetyl eugenol and *β*-caryophyllene [56, 62].

Schinus

The genus *Schinus* includes 25 species native to Central and South America [64]. They possess antioxidant, antimicrobial [65], and insecticidal [66] properties. Essential oils extracted from the leaves and fruits of *Schinus areira* were found to be effective against head lice [51]. The dominant compounds found in leaf essential oils of *S. areira* were monoterpene hydrocarbons, namely, *α*-pinene, *β*-pinene, camphene, and *α*-phellandrene [51, 67].

Tagetes

Tagetes is a genus of herbaceous plants comprising 30 species, some of which are cultivated for ornamental or medicinal purposes (e.g., *Tagetes erecta, Tagetes minuta* or *Tagetes glandulifera, Tagetes patula*, and *Tagetes tenuifolia*). Some species such as *T. minuta* were found to have significant pediculicidal activity against head lice [68]. *Tagetes* plants also repel or kill a wide range of insects such as mosquitoes (*Aedes* and *Anopheles*), *Phlebotomus duboscqi, Cimex lectularius, Ceratitis capitata*, and *Triatoma infestans* [69–71]. Major components of *T. minuta* are beta-ocimene and tagetone [72].

Juniperus

The genus *Juniperus*, which is widely distributed in the northern hemisphere, is a well-known source of cedarwood oil. It is used in traditional medicine due to its antiseptic, neuroprotective, and anti-inflammatory properties [73]. Furthermore, it also has antileishmanial [74] and acaricidal (e.g., *Dermatophagoides farinae*) activities [75]. Some species such as *Juniperus oxycedrus* were found to be effective against head lice [36]. The main components of *J. oxycedrus* are cadinene, *α*-cedrene, camphor, and guaiacol [75].

Origanum

Origanum is a genus of perennial herbs native to Europe, North Africa, and most of temperate Asia. This genus includes important groups of culinary herbs, including marjoram (*Origanum majorana*) and oregano (*Origanum vulgare*). These species are also effective against head lice [38, 76]. In addition, they have antibacterial and antifungal properties. They also display activity against hematophagous mosquitoes (*Aedes, Culex*, and *Anopheles*) [77, 78], *I. ricinus* [43], and *Psoroptes cuniculi* [79]. The main components of *Origanum* species are 1,8-cineole, linalool, and carvacrol [67, 76].

Thymus

The genus *Thymus* comprises 350 species of aromatic perennial culinary herbs native to the temperate regions of Europe, North Africa, and Asia. *Thymus* species have antioxidant and antibacterial properties as well as insecticidal/acaricidal activities against *Tetranychus urticae, Blatta lateralis*, and mosquitoes (*Culex, Aedes*, and *Anopheles*) [80–83]. Among *Thymus* species, *Thymus vulgaris* has been found to be effective against both head and body lice [40, 51]. The major constituents of *Thymus* species are thymol, carvacrol, and *p*-cymene [40, 51].

Hedychium

The genus *Hedychium* consists of about 80 perennial herbaceous species characterized by scented flowers. *Hedychium spicatum* (spiked ginger lily), which originated in the southeast Asian countries, is a widely known species of this genus [84]. *Hedychium* species have been reported to possess antibacterial, antifungal, and anthelmintic activities [84, 85]. *H. spicatum* possesses strong pediculicidal activity against head lice [86]. Its major component is 1,8-cineole.

Elettaria

Elettaria is a genus of plants native to India and Sri Lanka. The essential oil derived from *Elettaria cardamomum* (cardamom oil) is reported to be effective against head lice [32]. It is also active against *D. gallinae* [87]. Its major components are 1,8-cineole and *α*-terpinyl acetate [88].

Salvia

The genus *Salvia* comprises roughly 1000 species that have been demonstrated to possess significant antitumor [89], antiprotozoal [90], and insecticidal activities against *Anopheles, Aedes*, and *Culex* mosquitoes [91]. Some species, such as *Salvia officinalis* (sage), were reported to be effective against head lice [32]. The main components of *S. officinalis* are *α*-thujone, camphor, 1,8-cineole, and *β*-thujone.

Rosmarinus

The genus *Rosmarinus* includes perennial culinary herbs native to the Mediterranean basin. *Rosmarinus* species possess antioxidant, antibacterial, and antileishmanial properties [92]. *Rosmarinus officinalis* has been demonstrated to be effective against head lice [32]. In addition, it is effective against *I. ricinus* and mosquitoes [93]. The major components of *R. officinalis* are 1,8-cineole, *α*-pinene, and camphor [38, 92].

Aniba

Aniba is a genus of plants native to the Brazilian Amazon. It comprises 41 species, including *Aniba rosaeodora*, which have been reported to have sedative, antiviral, anticonvulsant, and antidepressant activities [94, 95]. *A. rosaeodora* has been reported to be highly effective against head lice [32]. Linalool has been identified as its major constituent [95].

Litsea

The genus *Litsea* comprises approximately 200 plant species that are mainly distributed in the tropical and subtropical regions [93].

Litsea species have been reported to display anti-inflammatory, antibacterial, antifungal [96, 97], and repellent/insecticidal activities [98, 99]. Recently, an essential oil derived from the fruits of *Litsea cubeba* was reported to be effective against head lice [56]. Its main components are citral (geranial, neral, and limonene) [56].

Myrcianthes

Myrcianthes is a genus of plants native to Central and South America as well as west India. *Myrcianthes* species have been reported to have antimicrobial, antiviral, and insecticidal properties [100, 101]. Among *Myrcianthes* species, *Myrcianthes pseudomato* and *Myrcianthes cisplatensis* have been found to be effective against head lice [67]. The main components of *M. ciplatensis* are limonene, 1,8-cineole, and α-terpineol [67], whereas those of *M. pseudomato* are 1,8-cineole and β-caryophyllene [100].

Myrtus

The genus *Myrtus* comprises two species, namely, *Myrtus nivellei* and *Myrtus communis*. The latter is an evergreen shrub native to the Mediterranean littoral region, utilized for its antiseptic, anti-inflammatory, anti-plasmodial, and insecticidal activities against *C. pipiens* and *A. gambiae* [102, 103]. It is also effective against head lice [32]. The main components of *M. communis* are α-pinene, 1,8-cineole, and limonene [102].

Lippia

Lippia is a genus of flowering plants including 200 species of which *Lippia multiflora* has been reported to have antimicrobial, antimalarial, and scabicidal properties [104, 105]. In addition, it has been reported to be effective against both head and body lice [104]. The main components of *L. multiflora* are limonene, geraniol, and linalool [104].

Apart from the aforementioned genera, several other essential oils have been assessed against louse ectoparasites and have been reported to be ineffective. A list of essential oils ineffective against lice is presented in **Table 1S**, Supporting Information.

Key Factors Influencing the Pediculicidal Activity of Essential Oils

The pediculicidal potential of essential oils against lice species may vary significantly depending on intrinsic and extrinsic factors such as the method of evaluation used and the chemical composition.

Method of evaluation

Essential oils are assessed mainly by four different methods. The most frequently used methods for the assessment of essential oils are impregnated filter paper contact and fumigation.

Filter paper contact: This method involves impregnating a filter paper placed at the bottom of a petri dish with a given concentration of the essential oil. Then, the lice are placed inside the petri dish and the mortality parameters such as LT_{50} (time needed to kill 50% of the insects) or KT_{50} (time required to knock down 50% of the insects) are recorded at the end of the contact time [39, 40, 56].

Immersion: In this method, lice are dipped in the essential oil solution for a predetermined period of time (seconds to minutes) and then the knockdown or mortality rate is recorded [38, 106].

Fumigation: This method uses a closed fumigation chamber (petri dish) containing a microslide on which drops of essential oil and the lice are placed separately. Consequently, the lice are exposed to vapors from the oil [67]. In another variant of this technique, called "vapor phase toxicity", a fine voile sieve is used to prevent the direct contact of lice with the paper impregnated with essential oil [36, 51].

Direct contact: This involves depositing the measured oil drops directly on the dorsal part of the louse body [107]. Then, LC_{50} (concentration sufficient to kill 50% of the lice) or KT_{50} are calculated at the end of the experiment [104, 107].

In addition to the aforementioned methods, the factors of contact time, concentration, and solvent type are crucial in determining the efficiency of the essential oil against louse ectoparasites.

Contact time: Contact time is one of the factors influencing the efficacy of essential oils and varies according to the applied method. Moreover, the contact time varies between different assays within the same method. In the immersion bioassay, immersion time ranges from 10 s to 2 min [38, 106]. In the filter paper contact method, some investigators set the contact time at 15–30 min [55, 56], while others place the lice on impregnated filter papers throughout the experiment (1–5 h) [39]. Similarly, in a fumigation test, lice are placed inside a petri dish chamber throughout the time of observation (~ 1 h) [67]. Longer time of exposure might influence the efficacy of the essential oil. As an example, the mortality rate of body lice exposed to tea tree essential oil for 30 to 210 min is increased from 10 to 90% [52].

Concentration: The concentrations of essential oils vary widely depending on the method used. For filter paper contact, the concentrations range from 0.21 mg/cm^2 to 1.75 mg/cm^2; 1–10% for both direct contact and immersion assays and 50–60 µL for the fumigation assay. This variation can lead to differences in the efficacy of the oils (▸ **Table 1**). Using the filter paper contact assay, Candy et al. [56] observed that essential oil from *E. caryophyllata* at a concentration of 1.75 mg/cm^2 could kill head lice almost two times faster (LT_{50} = 10 min) compared to Yang et al. [62], who observed an LT_{50} of 18.80 min at the 0.25 mg/cm^2 concentration of the same oil.

Solvent: Essential oils are often dissolved in various solvents such as acetone [62], alcohol [106], ethylhexyl stearate [55], poloxamer [108], and mineral and vegetable oils [56]. However, certain solvents could influence the pediculicidal activity. For example, it has been demonstrated that ethanol and other alcohols may exert their own toxicity on the tested lice [106]. Oily excipients have also been shown to exert toxicity on lice.

Chemical composition (formulation)

The chemical composition of a plant essential oil depends on several parameters, most important of which are the environmental conditions.

Geographical variation: Essential oils derived from the same plant species originating from different geographical areas may have similar or radically different chemical compositions due to the climatic and soil variability [109] and can vary from year to year. For example, in bioassays tested using the same method (filter paper) and concentration, Yones et al. [40] and Gutiérrez et al. [51] observed different LT_{50}s for *T. vulgaris* essential oils. The differences in their results were attributed to the difference in the chemical composition of plants originating from two different geographical areas, namely, Argentina and Egypt (▶ **Table 1**). Even within the same country, the chemical composition of essential oil obtained from the same plant species collected from two different locations may vary greatly. This was demonstrated by the main components of essential oils obtained from *S. areira* collected from different locations in Argentina being different (*α*-pinene, *β*-pinene, T-cadinol, and limonene stated by Toloza et al. [67] compared to *α*-pinene, camphene, myrcene, *α*-phellandrene, and limonene reported by Gutiérrez et al. [51]). Another study demonstrated different pediculicidal activities of two chemotypes of *Chenopodium ambrosioides*, wherein chemotype (1) had a KT_{50} of 42 min while chemotype (2) was ineffective with a $KT_{50} > 60$ min [110]. The differences in efficacy of these two chemotypes were attributed to variations in chemical composition; *C. ambrosioides* (1) had *trans*-carveol, *trans*-pinocarvyl acetate, and *cis*-carveol as main components, while *C. ambrosioides* (2) had ascaridole as its main component [50].

Discussion

Insecticides such as organochlorine, pyrethroid, and carbamate were introduced in the 20th century as treatments for pediculosis. They initially displayed high efficacy in killing lice. However, the repeated use of these chemicals resulted in the development of resistance among louse populations globally [14, 54], which posed a major challenge in the treatment of pediculosis. During the last decade, efforts have focused on developing new methods or formulations that are efficient against lice. These efforts have included exploring the potential of essential oils in the treatment of pediculosis. Numerous essential oils have been shown to be effective in eliminating lice. In the present study, we have conducted an exhaustive review of 172 research articles, books, and theses in order to evaluate the advantages and limitations of each group of essential oils in detail, and ultimately demonstrate the most effective ones against lice.

At present, there is no definitive and absolute treatment for pediculosis [111–113]. The use of essential oils derived from plants could have some benefits. A possible advantage of essential oils over some conventional insecticide treatments may be their ovicidal activity, which is seen in most of the oils discussed above [40, 51, 55, 62, 114]. Compounds with ovicidal effects may be particularly beneficial in the control of pediculosis, as they would eliminate the need for multiple treatments to kill newly hatched nymphs. Another advantage of essential oils is their activity on insecticide-resistant lice [50, 76, 106].

Based on the published literature, the modes of evaluation and properties of the oils used in research investigations vary widely, leading to differences in results. Several factors may influence the rate of efficacy of essential oils. One such factor is the method applied to test the essential oil against louse species. Different methods involve different ways of exposure and biological availability of the active component of the oils [106]. For example, *Eucalyptus* oil was 50-fold more active in contact assays carried out in closed containers compared to open ones, possibly due to the fumigation action and vapor pressure [36]. Similarly, Toloza et al. [34] reported high fumigant activity of eucalyptus oil and its major component against head lice. In contrast, *A. polystachya* and *T. vulgaris* were considerably more effective through filter paper contact than fumigation (▶ **Table 1**) [51]. Differences in efficacy between these methods could be attributed to the efficacy of the mode of absorption (penetration) of the active constituent by the lice, which depends on the vapor pressure, density, viscosity, and lipophilicity of the essential oil constituents [40, 51, 67, 106]. Lipophilic and viscous compounds might perform better in contact bioassays because they can directly penetrate the cuticular layer of the lice [106]. In the fumigation assay, the components may be inhaled via the respiratory system, which depends on the vapor pressure of the compound [106]. These factors influence the eventual mode of action of essential oils on human lice.

Apart from the method, factors such as the concentration used, exposure time, main constituents, and the origin of the essential oils may also influence the results. The incorporation of solvents to solubilize essential oils is an important factor because certain solvents (e.g., alcohol) could enhance or diminish the pediculicidal activity of the formulation [50]. The presence of alcohol as a solvent in the formulation of tea tree oil (*M. alternifolia*) makes it difficult to confirm whether the observed pediculicidal effect is attributable to the tea tree oil or the solvent used [13]. Therefore, a neutral solvent can be added to the experiments as a control. In addition, other constituents in minor quantities may also have a possible synergistic or antagonistic activity [41, 107]. Among the 22 genera of essential oils discussed above, which were reported to have pediculicidal activities, certain genera such as *Aloysia, Cinnamomum, Eucalyptus, Eugenia, Lavandula, Melaleuca, Mentha, Myrcianthes, Origanum, Pimpinella*, and *Thymus* have demonstrated high efficacy in killing the lice, which makes them strong candidates for clinical assays [23, 115–117]. Some major components of these plants belong to mono-oxygenated classes (1,8-cineole, linalool, pulegone, terpinen-4-ol, thymol), phenylpropanoids (anethole, cinnamaldehyde, eugenol), and monoterpene hydrocarbons (*p*-cymene, limonene) (▶ **Table 1**). Most of these components exert neurotoxic effects on insects. Their neurotoxic effects involve several mechanisms, in particular, via GABA and octopamine synapses, and the inhibition of acetylcholinesterase [118–121].

Furthermore, some essential oils, although highly effective against lice, cannot be directly formulated as pediculicidal products. Despite the high efficacy of some of these oils, their application has been restricted or banned due to high toxicity or objectionable odor [22, 122, 123]. Essential oils are environmentally safer because they are not persistent [122], but some have been shown to have high mammalian toxicity and may cause skin irritation [123, 124]. However, in terms of mammalian toxicology, just the fact that a product is naturally occurring does not necessarily make it safe. On the other hand, the concentrations of essential oils used in the *ex vivo* bioassays are quite low (generally below 5%, mostly even below 1%), whereas the essential oil-based products for the treatment of lice infestations typically contain at least 10% essential oil, which is around the threshold level of the concentration capable of causing vesicant reactions on human skin [110]. A clinical trial of a pediculicide containing more > 10% of eucalyptus essential oils plus 1% *Leptospermum petersonii* demonstrated satisfactory results [125]. In addition, some essential oils (e.g., *M. pulegium, S. officinalis*) and their compounds (e.g., pulegone, carvacrol, thujone, camphor, and menthol belonging to the chemical families of ketones and phenols) can be mildly to severely toxic to mammals. They often exert irritant, allergic, analgesic, or hepatotoxic, abortifacient, and hormone-like effects [123–129].

Conclusion

In the search for alternative nonchemical insecticides to be used in the treatment of pediculosis, some essential oils have been demonstrated to be as effective as traditional insecticides against *P. humanus*. In this review, 22 plant genera demonstrating effective *in vitro* pediculicidal activities were discussed. Among them, genera such as *Aloysia, Cinnamomum, Eucalyptus, Eugenia, Lavandula, Melaleuca, Mentha, Myrcianthes, Origanum, Pimpinella*, and *Thymus* appear to be more efficient. These genera are rich in anethole, 1,8-cineole, cinnamaldehyde, *p*-cymene, eugenol, linalool, limonene, pulegone, terpinen-4-ol, and thymol compounds. Current information indicates that the majority of the essential oils are safe to the users and environment, with few exceptions. Therefore, essential oils have immense potential to substitute synthetic insecticides, the use of which has generated resistance and toxicity problems. However, each essential oil must be evaluated for its potential threat to human health due to the intrinsic allergenicity of some of their components.

Supporting information

An additional list including the names and characteristics of the major essential oils previously reported to be inefficient against louse ectoparasites according to the literature is given in **Table 1S**.

Contributors' Statement

Conception and design of the work: K. C., M. A., and A. I. Data collection: K. C., M. A., V. A., R. D., and C. B. Analysis and interpretation of the data: K. C., M. A., R. D., and A. I. Drafting of the manuscript: K. C., M. A., R. D., and A. I. Critical revision of the manuscript: M. A., R. D., C. B., A. I.

Conflict of Interest

The authors declare that they have no conflict of interest.

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