Biomedical Sciences
2020; 6(3): 44-51
http://www.sciencepublishinggroup.com/j/bs
doi: 10.11648/j.bs.20200603.11
ISSN: 2575-3924 (Print); ISSN: 2575-3932 (Online)

Review Article

Efficacy of Plant-based Repellents Against Anopheles Mosquitoes: A Systematic Review

Laura Nyawira Wangai, Kenny Kimani Kamau*, Godwil Munyekenye, David Nderu, Eva Maina, William Gitau, Mary Murigi, Susan Kamau, Mercy Njuguna, Joseph Gichuki, Fredrick Otieno

School of Health Sciences, Kirinyaga University, Kutus, Kenya

Email address:
lwangai@kyu.ac.ke (L. N. Wangai), kkamau@kyu.ac.ke (K. K. Kamau), gmunyekenye@kyu.ac.ke (G. Munyekenye), dnderu@gmail.com (D. Nderu), emaina@kyu.ac.ke (E. Maina), wgichui@kyu.ac.ke (W. Gitau), mmurigi@kyu.ac.ke (M. Murigi), smkamau@kyu.ac.ke (S. Kamau), gichukiyoefu@gmail.com (J. Gichuki), foginga@kyu.ac.ke (F. Otieno)

*Corresponding author

To cite this article:
Laura Nyawira Wangai, Kenny Kimani Kamau, Godwil Munyekenye, David Nderu, Eva Maina, William Gitau, Mary Murigi, Susan Kamau, Mercy Njuguna, Joseph Gichuki, Fredrick Otieno. Efficacy of Plant-based Repellents Against Anopheles Mosquitoes: A Systematic Review. *Biomedical Sciences.* Vol. 6, No. 3, 2020, pp. 44-51. doi: 10.11648/j.bs.20200603.11

Received: June 10, 2020; **Accepted**: June 20, 2020; **Published**: July 4, 2020

Abstract: Mosquitoes are usually targeted using insecticides, insect growth regulators, and microbial agents. Indoor residual spraying and insecticide-treated bed nets. However, these strategies have negative effects on human health, the environment and induce resistance in a number of species. Eco-friendly tools have been recently implemented against mosquito vectors, including plant-based insecticides. To date few studies have adopted World Health Organization (WHO) Pesticide Evaluation Scheme guidelines for repellent testing against mosquitoes. This review presents a summary of recent information on development, and efficacy of plant-based repellents against Anopheles mosquitoes as well as promising new advances in the field. All eligible studies published up to April 2020 were systematically searched in several databases, namely PubMed/Medline, Scopus and Google scholar. The outcomes of interest were percentage repellency, protection time and additional properties identified in repellent compounds. A total of 27 trials met the inclusion criteria. The highest repellency effect against mosquitoes was conferred by citronella, followed by *Ligusticum sinense* extract, *pine*, *Dalbergia sissoo*, and *Rhizophora mucronata* oils with 100% protection for 8 to 14 hours. Furthermore, essential oils from plants such as lavender, camphor, catnip, geranium, jasmine, broad-leaved eucalyptus, lemongrass, lemon-scented eucalyptus, amyris, narrow-leaved eucalyptus, carotin, cedarwood, chamomile, cinnamon oil, juniper, cajeput, soya bean, rosemary, niaouli, olive, tagetes, violet, sandalwood, litsea, galbanum, and *C. longa* also showed >90% repellency within 8 hours against different species of Anopheles. Therefore, the review showed, essential oils and extracts of some plants could be formulated for the development of eco-friendly repellents against Anopheles species. Plant oils may serve as suitable alternatives to synthetic repellents in the future as they are relatively safe, inexpensive, and are readily available in many parts of the world.

Keywords: Plant, Plant Extract, Repellent, Repellency Index, Anopheles, Essential Oil

1. Background

Mosquitoes serve as vectors for a wide variety of human and veterinary pathogens and parasites. Vector-borne diseases such as malaria, dengue, leishmaniasis, filariasis, and Chagas disease cause extensive morbidity and mortality, and are a major economic burden in disease-endemic countries [1, 2]. Malaria, in particular, continues to have a devastating impact on infants and young children in endemic regions. In 2018 alone, over 200 million malaria cases and 0.4 million deaths we reported globally. Most of this burden was experienced by infants and young children in sub-Saharan Africa [3]. Of the 500 species of Anopheles mosquitoes thus far, approximately 50 species can transmit malaria from the bite of an infected female *Anopheles spp.* [1, 2].

Protection from mosquito bites is one of the best approaches to reduce malaria incidences. The use of repellents to protect people from bites of mosquitoes has been acknowledged as part of an overall integrated insect-borne disease control programme [4]. Most commercial repellents are produced by using chemical components such as N, N-diethyl-metatoluamide (DEET), Allethrin, N, N-diethyl mendelic acid amide, and Dimethyl phthalate [5]. It has been reported that these chemical repellents are not safe for public health and should be used with caution. This is because of their detrimental impacts on synthetic fabric and plastic as well as toxic reactions, such as allergy, dermatitis, and cardiovascular and neurological side effects [6, 7]. Prolonged and frequent use of synthetic repellents in mosquito control has resulted to development of resistance to insecticides, resurgence in mosquito populations, and adverse impact on nontarget organisms [8–11]. Accordingly, the idea of using natural mosquito repellent products as an alternative to develop new eco-friendly repellents could be an amicable solution to reverse the undesirable effects on environment and human health. In recent years, interest in plant-based repellents has been revived, as they are a rich source of bioactive phytochemicals that are safe and biodegradable into nontoxic by-products, which could be screened for insecticidal activities and mosquito repellent [12–15]. Many studies have shown that plant extracts or essential oils have repellant properties against malaria vectors around the world.

Most plants produce various compounds to preventing attack from phytophagous (plant eating) insects. These chemicals fall into several categories, including repellents, feeding deterrents, toxins, and growth regulators. Based on chemical properties these compounds can be grouped into five major categories, namely nitrogen compounds (primarily alkaloids), terpenoids, phenolics, proteinase inhibitors, and growth regulators [16]. Although the primary functions of these compounds in plant defense mechanism against phytophagous insects remain unclear, many plant compounds are also effective against mosquitoes and other biting Diptera, especially volatile components released as a consequence of herbivory. The fact that several of these compounds are repellent to haematophagous insects could be an evolutionary relict from a plant-feeding ancestor, as many of these compounds evolved as repellents to phytophagous insects [17], and this repellent response to potentially toxic compounds is well conserved in the lineage of Diptera (True Flies). Plants commonly produce volatile “green leaf volatiles” when leaves are damaged in order to deter herbivores [13], and several reports have shown strong responses of mosquito odour receptors to this class of volatiles including geranyl acetate and citronellal [17], 6-methyl-5- hepten2-one and geranylacetone [18]. Furthermore, the same odour receptors that respond to DEET also respond to thujone eucalyptol and linalool in *Culex quinquefasciatus* [19]. In *Anopheles gambiae*, the DEET receptor OR83b is not only stimulated by citronellal, but it is also modulated by the TRPA1 cation channel [20]. However, it is most likely that many plant volatiles are deterrent or repellent because they have high vapour toxicity to insects [16, 17]. This repellency of plant material has been exploited for thousands of years by man, most simply by hanging bruised plants in houses, a practice that is still in wide use throughout the developing countries [17]. Plants have also been used for centuries in the form of crude fumigants where plants were burnt to drive away nuisance mosquitoes and later as oil formulations applied to the skin or clothes.

A number of studies on use of repellents against malaria vectors have been conducted but it is necessary to synthesize the results of these experiments in order to inform policy decisions on use of topical repellents. Systematic reviews and meta-analysis of randomized and non-randomized studies on topical insect repellents for personal protection have been conducted but these did not expound on the efficacy and future developments of plant-based repellents which be relied on to provide a prolonged and predictable protection from species of Anopheles mosquitoes without causing side effects on human health. [5, 17, 21, 22]. Therefore, this systematic review and meta-analysis of randomized and non-randomized controlled studies was conducted to build more understanding on the efficacy of available insect repellents and elaborate further on future development of plant-based repellents that are effective and environmental-friendly.

2. Methods

All eligible studies on the repellency effects of plant-based repellants against Anopheles spp. published up to April 2020 were systematically searched in electronic databases PubMed, MEDLINE, Web of Science, Scopus and Google Scholar using the following Medical Subject Headings and keywords: (((Plant [Title/Abstract]) OR Plants [Title/Abstract]) OR herbal [Title/Abstract]) AND (botanical [Title/Abstract]) AND ((extract [Title/ Abstract]) OR extracts [Title/Abstract]) AND ((“essential oil” [Title/Abstract]) OR “essential oils” [Title/Abstract]) AND (((((“Insect repellent” [Mesh]) OR repellents) OR repellent) OR repellency) OR repellency index) AND ((“Anopheles” [Mesh]) OR “Anopheles” [Title/Abstract]). The search was limited to English publications. In addition, a manual search was conducted to identify additional pertinent articles using references from retrieved articles.

2.1. Eligibility Criteria

Studies were included in the present systematic review if they met these criteria: (a) full-text publication was written in English, (b) analyzed the repellency effects of plant extracts and essential oils against malaria vectors, Anopheles spp. mosquitoes, and, (c) reported the percentage of repellency or complete protection time. The following studies were excluded: studies exploring the repellency effect of chemical-based products, studies examining the repellency effect of animal extracts, animal models (studies not on human subjects), articles without full texts, reviews, duplicate articles, abstracts, republished data, comments, conference papers, editorials, and studies with insufficient data. In addition, studies were excluded if the information could not be extracted. A screening of titles and abstracts followed by a full-text review was performed by five investigators. All titles and abstracts were screened by five independent investigators for eligibility. If a consensus was reached, a study was excluded or selected for full-text review. If consensus was not reached, another reviewer was consulted to resolve any feasible discrepancies.

2.2. Data Extraction and Analysis

After screening for the eligible studies, the following information was extracted: name of the first author, country of origin, journal details, publication year, condition of study (field or laboratory), plant name, *Anopheles species*, concentration of repellents, repellency percentage and complete protection time using a standardized data collection form. All data were independently extracted by two reviewers and disagreements were solved by discussion, and if necessary, a third author was involved.

3. Results

A total of 285 studies were identified in the initial literature search. Of the 216 studies excluded, 102 were duplicated studies; 39 were not on repellency effect of plants on Anopheles spp., 7 were review publications; 6 investigated the repellency impact of chemical-based repellents or animal extracts; 11 studies were conducted on laboratory animals and 10 studies had not reported adequate data concerning the percentage of repellency or 100% protection time. The primary eligibility process yielded 27 documents. Literature search in the references of reviews and other databases search provided 3 additional articles. A total of 15 studies were conducted in different countries, including Brazil, India and Thailand.

3.1. Essential Oils

Essential oils distilled from members of the *Lamiaceae* (mint family that includes most culinary herbs), *Poaceae* (aromatic grasses) and Pinaceae (pine and cedar family) are commonly used as insect repellents throughout the globe as shown in Table 1. Many members of these families are used in rural communities through burning or hanging them within homes [34]. In Europe and North America there is a strong history of the use of oils that date back to Ancient times. Almost all plants used as repellents are also used for food flavouring or in the perfume industry, which may explain the association with these oils as safer natural alternatives to DEET despite many oils causing contact dermatitis [33]. Many commercial repellents contain several plant essential oils either for fragrance or as repellents including peppermint, lemongrass, geraniol, pine oil, pennyroyal, cedar oil, thyme oil and patchouli. The most effective of these include thyme oil, geraniol, peppermint oil, cedar oil, patchouli and clove that have been found to repel malaria, filarial and yellow fever vectors for a period of 60 -180 mins [44-56]. Most of these essential oils are highly volatile and this contributes to their poor longevity as mosquito repellents. However, this problem can be addressed by using fixatives or careful formulation to improve their longevity. For example, oils from turmeric and hairy basil with addition of 5% vanillin repelled three species of mosquitoes for a period of 6-8 hours depending on the mosquito species [34]. Although essential oils are exempt from registration through the EPA, they can irritate the skin and their repellent effect is dependent on formulation and concentration. Repellents containing only essential oils in the absence of an active ingredient such as DEET should not be recommended as repellents for use in disease endemic areas, and those containing high levels of essential oils could cause skin irritation, especially in the presence of sunlight.

3.2. Citronella

Essential oils and extracts derived from plants in the citronella genus (*Poaceae*) are commonly used as ingredients of plant-based mosquito repellents (Table 1), mainly *Cymbopogon nardus* that is sold in Europe and North America in commercial preparations. The repellency effect of citronella has been documented in several studies describing citronella as an essential oil extracted from the stems and leaves of different species of lemongrass (*Cymbopogon spp.*) [23]. A study on mosquitoes repellency found that citronella obtained from lemongrass has a 100% repellency effect against *Anopheles culicifacies* for 11 hours [24]. Recently, several studies have also reported that citronella can repel different *Anopheles spp.* for 8 to 6 hours [15, 22, 2]. Different concentration of citronella essential oil (100 µl to 0.1 ml) have also been shown to have significant repellency for 4 to 0.8 of 100% protection time against almost all mosquitoes vectors of human importance in a number of studies (field and laboratory- based) across the globe [15, 17, 26–28]. However, the percentage repellency of citronella varies (52 to 85%) depending on the concentration of extracts and mosquito *species* tested. A few studies have analyzed the efficacy of essential oils extracted from citronella for repellency effect against arthropods [29]. Citronella-based repellents only protect from host-seeking mosquitoes for about two hours although formulation of the repellent is very crucial. The results indicate citronella, which contain citronellal, citronellol, geraniol, citral, a pinene, and limonene, is as effective as DEET. However, the oils from citronella are highly volatile thus causing reducing its efficacy and protection. This observation has unraveled the need to mix essential oil of Cymbopogon winterianus with a large molecules such as vanillin (5%), to prolong protection time and reduce the evaporation rate of the volatile oil [30]. Recently, the use of nanotechnology has enabled slow release of oils, thus prolonging protection time [31]. The encapsulated citronella oil nanoemulsion was initially prepared by high-pressure homogenization of 2.5% surfactant and 100% glycerol, to develop stable droplets that increase the retention of the oil and slow down release. The release rate relates well to the protection time so that a decrease in release rate can prolong mosquito protection time [31]. Another strategy adopted to prolong the effect of plant-based repellents is microencapsulation using gelatin-arabic gum microcapsules.

This approach can sustain complete citronella repellency effect for up to 30 days on treated fabric stored at room temperature [32]. The use of such advanced technologies to sustain and improve the performance of natural repellents may transform the repellent market and promote the use of plant oils as eco-friendly and long-lasting mosquito repellents.

Table 1. *Overview of repellent plant efficacy from literature review.*

Author, ref	Location	Plant (*other names*)	Repellent compound
Trongtokit et al., [33, 34]	India	*Eugenia caryophyllus* or *Syzygium aromaticum* or *Eugenia aromaticu*	Eugenol carvacrol thymol cinnamaldehyde
Moore et al., [35] Dugassa et al,.[36]	Australia Brazil Bolivia China India Ethiopia Tanzania Kenya	MYRTACEAE *Corymbia citriodora*	citronellal PMD (by product of hidrodistillation) (p-menthane3,8-diol) citronellol limonene geraniol isopulegol δ-pinene
Lukwa e al., [38]	Kenya Tanzania Ghana Zimbabwe	VERBENACEAE *Lippia spp* (Lemon brush)	myrcene linalool a-pinene eucalypto alloparinol camphor limonene
Govere et al., [39]		*L. javanica*	a –terpeneol verbenone
Seyoum et al., [40, 37]	Kenya Tanzania	*Lantana camara*	Caryophylene
Seyoum et al., [40] White, [41, 40]	Kenya Tanzania Zimbabwe Nigeria Ghana Cameroon Eritrea Ethiopia	LAMIACEAE *Ocimum spp. O. americanum*	p-cymene estragosl linalool linoleic acid eucalyptol eugenol camphor citral thujone limonene ocimene and others
Dugassa et al., [36]	China India Ethiopia Tanzania Kenya	*O. suave*	camphor limonene
Seyoum et al., [37]	Kenya Tanzania Ghana The Gambiae	*Hyptis spp. Hyptis suaveolens*	myrcene
Palsson, [42, 40] Sharma and Ansari [43]	India Sri Lanka China Brazil Bolívia Pakistan Ethiopia Guinea Bissau Kenya Tanzania.	*MELIACEAE Azadirachta indica*	azadirachtin saponins
Tyagi, [44]	Uganda Zimbabwe India	ASTERACEAE *Tagetes minuta*	citronellal PMD
Moore et al., [35]	Indonesia Malaysia Thailand Laos	*Citrus hystrix*	citronellol limonene geraniol isopulegol
Tawatsin et al., [45]	India	ZINGIBERACEAE *Curcuma longa*	Eucalypto alloparinol

Table 1. *Continued.*

Author, ref	Mode of testing	% Repellency protection	Study design
Trongtokit et al., [33, 34]	100% essential oil applied topically	100% protection against *An. albimanus* for 213 minutes	Experimental (laboratory-based)
[34]	100% essential oil applied topically	100% protection against *An. dirus* for 210 min	Laboratory study
Moore et al., [35] Dugassa et al,.[36]	30% PMD applied topically thermal expulsion (leaves)	96.88% protection from mosquitoes for 4 hours 78.7% protection from *An. arabiensis* 76.8% protection from *An. pharaoensis*	field study in Bolivia field study in Ethiopia
Trongtokit et al., [33]	20% PMD (1.7 mg/ cm2) applied topical	100% protection for 11-12 hours against *An. stephensi*	laboratory study
Seyoum et al., [37]	50% PMD applied topical	100% protection from *An. gambiae* and *An. funestus* for 6-7 hours	field study in Tanzania
Dugassa et al., [36]	direct burning of leaves	70.1% protection from *An. arabiensis* 72.9% protection from *An. pharaoensis*	field study in Ethiopia
[37]	periodic thermal expulsion (leaves	74.5% protection from *An. gambiae s.s.*	semi-field study in Kenya
Lukwa e al., [38]	5mg/cm2 plant extract applied topically	100% protection against *An. arabiensis* for 8 hours	laboratory study
Govere et al., [39]	alcohol plant extract applied topically	76.7% protection against *An arabiensis* for 4 hours	field study in India
Seyoum et al., [40] [37]	potted plan periodic thermal expulsion (leaves) potted plant	32.4% protection against *An. gambiae s.s* 42.4% protection against *An. gambiae s.s*	field study in Kenya semi-field study in Kenya
Seyoum et al., [40] White, [41, 40]	fresh plants combined with O. suave bruised and applied topically 100% essential oil combined with vanillin 5% applied topically	37.91% protection against *An. gambiae s.l.* 50% protection against *An. gambiae s.l.* 100% protection against *An. dirus* for 8 hours	field study in Kenya field study in Tanzania Laboratory study
Dugassa et al., [36]	thermal expulsion (leaves)	73.6% protection from *An. arabiensis* 75.1% protection from *An. pharaoensis*	field study in Ethiopia
Tawatsin et al., [45]	direct burning (leaves	71.5% protection from *An. arabiensis* 79.7% protection from *An. pharaoensis*	field study in Ethiopia
Seyoum et al., [37]	smouldering on charcoal	85.4% repellency against mosquitoes for 2 hours	Field-study
Palsson, [42, 40] Sharma and Ansari [43]	direct burning (leaves) periodic thermal expulsion (leaves) 1% neem oil volatilized in a kerosene lamp	76.0% protection from mosquitoes for 2 hours24.5% protection from *An. gambiae s.s* 94.2% protection from *Anopheles spp.*	field study in Guinea Bissau semi-field study in Kenya field study in India
Tyagi, [44]	topically	84.2% protection against *An. stepehensi* for 6 hours	laboratory study

Author, ref	Mode of testing	% Repellency protection	Study design
Moore et al., [35]	100% essential oil combined with vanillin 5% applied topically	100% protection against *An. stephensi* for 8 hours	laboratory study
Tawatsin et al., [45]	100% essential oil combined with vanillin 5% applied topicall	100% protection against *An. dirus* for 8 hour	laboratory study

3.3. Current Developments in Plant-based Repellents Against Mosquitoes

The field of plant-based repellents is advancing with consumer demand for protection against arthropod bites using safe, pleasant to use and environmentally sustainable products. Perhaps the most important consideration is improving the longevity of those repellents that are effective but volatile such as citronella. Several studies looked at improving formulations of plant oils to increase their longevity through development of nanoemulsions [31], enhanced formulations and fixatives [46]; while alternate uses such as spatial activity [47] and excito-repellency [48] have also been investigated. There has been a single clinical study of PMD to lower malaria incidence [49]. This is an exciting discovery since PMD can be recovered by distilling the leaves of *E. citroidora* or chemical modification of citronellal [50] available from plants of the genus *Cymbopogon*. These plants are already commercially cropped in malaria endemic countries including South America, especially Brazil (over 5 million trees), southern China, India, Sri Lanka, Congo (Zaire), Kenya and most countries in southern Africa, where it is grown for essential oil production and timber. Local production of insect repellent would remove the high cost of importation in developing countries. New developments have also been seen in understanding the function of plant-based repellents in insects. Several studies have investigated the behavioural mode of action of repellents through structure-activity studies of contact versus spatial repellency [51], or olfactometry that demonstrated that DEET inhibited mosquito response to human odour whereas Ocimum forskolei repels but does not inhibit response to human odour [52]. Furthermore, it has been shown that citronellal directly activates cation channels, which is similar to the excitorepellent effect of pyrethrin – another plant based terpine [53], unlike DEET which has inhibitory effect [3]. The field of repellent development from plants is extremely fertile due to wealth of insecticidal compounds found in plants as defences against insects. The modern pyrethroids that are the mainstay of the current malaria elimination program that is making excellent progress, are synthetic analogues based on the chemical structure of pyrethrins, discovered in the pyrethrum daisy, Tanacetum cinerariifolium from the Dalmation region and Tanacetum coccineum of Persian origin. The field of plant-based repellent evaluation and development had become far more rigorous in recent years and developments in methods of dispensing plant-based volatiles means that extension in the duration of repellency and consequent efficacy of plant-based repellents will be possible in future.

4. Discussion

Widespread pest and disease vector resistance against chemical control strategies pose a huge impediment toward successful disease and pest control. To overcome this problem, development of effective approaches is paramount. The field of herbal repellents is rapidly evolving with the increased demand for mosquitoes' repellents that are safe, pleasant to usage and eco-friendly. Since high cost of developing repellants could delay development and successful deployment of pest and vector control programs, use of local florae as repellents offer an attractive alternative. Essential oils and plant extracts are emerging as potential agents for Anopheles spp. control because they are easy-to-administer, low-cost, and risk-free properties. In the present systematic review, *L. sinense* extract was found to have the highest repellency effect against Anopheles mosquitoes, followed by citronella, pine, D. sissoo, peppermint and R. mucronata oils. Complete protection time ranged from 9.1 to 11.5 hours. Essential oils from plants such as lavender, camphor, catnip, geranium, jasmine, broad-leaved eucalyptus, lemongrass, lemonscented eucalyptus, amyris, narrow-leaved eucalyptus, carotin, cedarwood, chamomile, cinnamon oil, juniper, cajeput, soya bean, rosemary, niaouli, olive, tagetes, violet, sandalwood, *litsea, galbanum*, and *C. longa* also shown good repellency of up to 8 hours' complete repellency against different species of *Anopheles* genus.

Noteworthy is that the review identified the exact mechanism of action of these plants in preventing Anopheles spp. bites is yet to be fully understood. Nevertheless, Citronella extract, one of the most investigated plant repellency effect of various mosquitoes, has been reported to have active compounds that repel mosquitoes. these include eugenol, eucalyptol, camphor, linalool, citral, and citronellal [54]. Data collected so far propose that these agents interfere with olfactory receptors of mosquitoes [55]. A recent study revealed that *An. gambiae* is able to detect molecules derived from citronellal using olfactory neurons in the antenna that is controlled by TRPA1 gene, activated directly by the molecule with high potency [56]. Another study found that citronellal directly activates cation channels [55], This mechanism is similar to the excite-repellent effect of pyrethrin, a plant-based terpine [17], but contrasts with the inhibitory effect of DEET [56]. Although the protection time of citronella oil is shorter than that of DEET, Citronella oil could provide sufficient protection time against mosquitoes. For other plants, the underlying mechanism remains to be elucidated.

Improving the formulations of plant extracts is key to elevate longevity of volatile plant-based repellents. This could be achieved by developing encapsulated nano emulsions, improved formulations and fixatives. While alternative uses such as excite-repellency and spatial activity have already been examined [56], there is need for caution when interpreting the findings for several reasons. First, a poorly inspected confounding aspect is the effect of sweating on the effectiveness and protection time of repellents, which are water-soluble, might limit the comparison of the effect of repellents. Second, in field studies, the number of human volunteers as well as the season during which a trial is conducted differed among studies included in this review. Climate change could also affect mosquito behavior and the variance is controlled by standardizing humidity temperature in ‘arm-in-cage’ trials; however, these parameters are not always similar in different trials or conform to the mosquito environment standards. Third, it should be highlighted that some plant compounds are irritating to the skin and/or highly toxic to mammals, and natural does not equate to safe. Thus, plants with potential repellency properties should be tested for their possible undesired effects before adoption as alternative mosquito repellant products. Fourth, some studies have shown that formulation play a significant role in the effectiveness of a repellants [34].

A few studies have focused on the search for active compounds than on optimal formulations [34, 54]. In this study, many studies showed the effectiveness of plant repellents against Anopheles spp. mosquitoes. However, when focusing on Anopheles subspecies, there were only a few publications indicating the efficacy of each plant, which resulted in a difficulty to reach a robust conclusion regarding the best herbal candidates to develop new commercial repellents. Thus more research is required. Finally, current studies are difficult to be compared and the repellency effectiveness may also differ among subspecies. Unfortunately, a few studies aimed to compare repellency efficacy of a special plant on subspecies of Anopheles. The heterogeneity in the results of previous studies might be explained by differences in compound concentrations, application dosages, mosquito species, formulations and the assessment method of repellency. For instance, some trials recorded protection time after mosquitoes landed on the subject. Most studies however, recorded time until mosquito bite occurred. Given the heterogeneity in the studies included in the current systematic review, future research assessing the repellent impacts should provide clear description of repellents, characteristics of volunteers in field trials, mosquito species, and outcome measures.

5. Conclusion

The results of this review show that some plants essential oils and extracts have significant repellent activity against Anopheles spp. mosquitoes. The studies conducted in the last two decades have focused on the search for new natural repellents and some plants displayed good repellent properties. However, few natural products have been developed so far. This review calls underscore the need to understand the potential role of plant-derived repellents contribute in disease control.

References

[1] Benelli G. Research in mosquito control: current challenges for a brighter future. Parasitology research. 2015; 114 (8): 2801–2805.

[2] Norris DE. Mosquito-borne diseases as a consequence of land use change. EcoHealth. 2004; 1 (1): 19–24.

[3] Organization WH. World malaria report 2019. 2019;

[4] Organization WH. Guidelines for efficacy testing of mosquito repellents for human skin. Geneva: World Health Organization; 2009.

[5] Patel EK, Gupta A, Oswal RJ. A review on: mosquito repellent methods. IJPCBS. 2012; 2 (3): 310–317.

[6] Diaz JH. Chemical and plant-based insect repellents: efficacy, safety, and toxicity. Wilderness & environmental medicine. 2016; 27 (1): 153–163.

[7] Chavasse DC, Yap HH, Organization WH. Chemical methods for the control of vectors and pests of public health importance. Geneva: World Health Organization; 1997.

[8] Hemingway J, Field L, Vontas J. An overview of insecticide resistance. Science. 2002; 298 (5591): 96–97.

[9] Weill M, Lutfalla G, Mogensen K, Chandre F, Berthomieu A, Berticat C, et al. Insecticide resistance in mosquito vectors. Nature. 2003; 423 (6936): 136–137.

[10] Liu N. Insecticide resistance in mosquitoes: impact, mechanisms, and research directions. Annual review of entomology. 2015; 60: 537–559.

[11] Liu N, Xu Q, Zhu F, Zhang LEE. Pyrethroid resistance in mosquitoes. Insect Science. 2006; 13 (3): 159–166.

[12] Palanisami S, Natarajan E, Rajamma R. Development of eco-friendly herbal mosquito repellent. Journal of innovative biology. 2014; 1 (3): 132–136.

[13] Benelli G, Canale A, Conti B. Eco-friendly contro strategies against the asian tiger mosquito, Aedes albopictus (Diptera: Culicidae): repellency and toxic activity of plant essential oils and extracts. 2014.

[14] Pavela R. Essential oils for the development of eco-friendly mosquito larvicides: a review. Industrial crops and products. 2015; 76: 174–187.

[15] Nerio LS, Olivero-Verbel J, Stashenko E. Repellent activity of essential oils: a review. Bioresource technology. 2010; 101 (1): 372–378.

[16] Edriss AE, Alabjar ZA, Satti AA. Phytochemical screening of important secondary metabolites in some extracts of two Sudanese plants. Global Advanced Research Journal of Environmental Science and Toxicology. 2012; 1 (8): 199–202.

[17] Asadollahi A, Khoobdel M, Zahraei-Ramazani A, Azarmi S, Mosawi SH. Effectiveness of plant-based repellents against different Anopheles species: a systematic review. Malaria Journal. 2019; 18 (1): 436.

[18] Logan JG, Stanczyk NM, Hassanali A, Kemei J, Santana AE, Ribeiro KA, et al. Arm-in-cage testing of natural human-derived mosquito repellents. Malaria journal. 2010; 9 (1): 239.

[19] Kain P, Boyle SM, Tharadra SK, Guda T, Pham C, Dahanukar A, et al. Odour receptors and neurons for DEET and new insect repellents. Nature. 2013; 502 (7472): 507–512.

[20] Xu P, Choo Y-M, De La Rosa A, Leal WS. Mosquito odorant receptor for DEET and methyl jasmonate. Proceedings of the National Academy of Sciences. 2014; 111 (46): 16592–16597.

[21] Shaalan EA-S, Canyon D, Younes MWF, Abdel-Wahab H, Mansour A-H. A review of botanical phytochemicals with mosquitocidal potential. Environment international. 2005; 31 (8): 1149–1166.

[22] Kalita B, Bora S, Sharma AK. Plant essential oils as mosquito repellent-a review. IJRDPL. 2013; 3: 143–150.

[23] Ganjewala D. Cymbopogon essential oils: Chemical compositions and bioactivities. International journal of essential oil therapeutics. 2009; 3 (2–3): 56–65.

[24] Ansari MA, Mittal PK, Razdan RK, Sreehari U. Larvicidal and mosquito repellent activities of Pine (Pinus longifolia, Family: Pinaceae) oil. Journal of vector borne diseases. 2005; 42 (3): 95.

[25] Mehlhorn H, Schmahl G, Schmidt J. Extract of the seeds of the plant Vitex agnus castus proven to be highly efficacious as a repellent against ticks, fleas, mosquitoes and biting flies. Parasitology research. 2005; 95 (5): 363–365.

[26] Amer A, Mehlhorn H. Repellency effect of forty-one essential oils against Aedes, Anopheles, and Culex mosquitoes. Parasitology research. 2006; 99 (4): 478.

[27] Tawatsin A, Asavadachanukorn P, Thavara U, Wongsinkongman P, Bansidhi J, Boonruad T, et al. Repellency of essential oils extracted from plants in Thailand against four mosquito vectors (Diptera: Culicidae) and oviposition deterrent effects against Aedes aegypti (Diptera: Culicidae). Southeast Asian journal of tropical medicine and public health. 2006; 37 (5): 915.

[28] Rajkumar S, Jebanesan A. Repellent activity of selected plant essential oils against the malarial fever mosquito Anopheles stephensi. Trop Biomed. 2007; 24 (2): 71–75.

[29] Lee MY. Essential oils as repellents against arthropods. BioMed research international. 2018; 2018.

[30] Choochote W, Chaithong U, Kamsuk K, Jitpakdi A, Tippawangkosol P, Tuetun B, et al. Repellent activity of selected essential oils against Aedes aegypti. Fitoterapia. 2007; 78 (5): 359–364.

[31] Sakulku U, Nuchuchua O, Uawongyart N, Puttipipatkhachorn S, Soottitantawat A, Ruktanonchai U. Characterization and mosquito repellent activity of citronella oil nanoemulsion. International journal of pharmaceutics. 2009; 372 (1–2): 105–111.

[32] Specos MM, García JJ, Tornesello J, Marino P, Vecchia MD, Tesoriero MD, et al. Microencapsulated citronella oil for mosquito repellent finishing of cotton textiles. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2010; 104 (10): 653–658.

[33] Trongtokit Y, Rongsriyam Y, Komalamisra N, Apiwathnasorn C. Comparative repellency of 38 essential oils against mosquito bites. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 2005; 19 (4): 303–309.

[34] Trongtokit Y, Curtis CF, Rongsriyam Y. Efficacy of repellent products against caged and free flying Anopheles stephensi mosquitoes. Southeast Asian journal of tropical medicine and public health. 2005; 36 (6): 1423.

[35] Moore SJ, Lenglet A, Hill N. Field evaluation of three plant-based insect repellents against malaria vectors in Vaca Diez Province, the Bolivian Amazon. Journal of the American Mosquito Control Association. 2002; 18 (2): 107–110.

[36] Dugassa S, Medhin G, Balkew M, Seyoum A, Gebre-Michael T. Field investigation on the repellent activity of some aromatic plants by traditional means against Anopheles arabiensis and An. pharoensis (Diptera: Culicidae) around Koka, central Ethiopia. Acta tropica. 2009; 112 (1): 38–42.

[37] Seyoum A, P\aalsson K, Kung'a S, Kabiru EW, Lwande W, Killeen GF, et al. Traditional use of mosquito-repellent plants in western Kenya and their evaluation in semi-field experimental huts against Anopheles gambiae: ethnobotanical studies and application by thermal expulsion and direct burning. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2002; 96 (3): 225–231.

[38] Lukwa N, Molgaard P, Furu P, Bogh C. Lippia javanica (Burm F) Spreng: its general constituents and bioactivity on mosquitoes. Tropical biomedicine. 2009; 26 (1): 85–91.

[39] Govere J, Durrheim DN, Du NT, Hunt RH, Coetzee M. Local plants as repellents against Anopheles arabiensis, in Mpumalanga Province, South Africa. The Central African journal of medicine. 2000; 46 (8): 213–216.

[40] Seyoum A, Kabiru EW, Lwande W, Killeen GF, Hassanali A, Knols BG. Repellency of live potted plants against Anopheles gambiae from human baits in semi-field experimental huts. The American journal of tropical medicine and hygiene. 2002; 67 (2): 191–195.

[41] White GB. The insect-repeUent value of Ocimum spp. (Labiatae): traditional anti-mosquito plants. East African medical journal. 1973; 50 (5): 248–52.

[42] P\aalsson K, Jaenson TG. Plant products used as mosquito repellents in Guinea Bissau, West Africa. Acta Tropica. 1999; 72 (1): 39–52.

[43] Sharma VP, Ansari MA. Personal protection from mosquitoes (Diptera: Culicidae) by burning neem oil in kerosene. Journal of medical entomology. 1994; 31 (3): 505–507.

[44] Tyagi BK, Ramnath T, Shahi AK. Evaluation of repellency effect of Tagetus minuta (Family: Compositae) against the vector mosquitoes Anopheles stephensi Liston, Culex quinquefasciatus Say and Aedes aegypti (L.). International pest control. 1997; 39 (6): 184–185.

[45] Tawatsin A, Wratten SD, Scott RR, Thavara U, Techadamrongsin Y. Repellency of volatile oils from plants against three mosquito vectors. Journal of vector ecology. 2001; 26: 76–82.

[46] Trongtokit Y, Rongsriyam Y, Komalamisra N, Krisadaphong P, Apiwathnasorn C. Laboratory and field trial of developing medicinal local Thai plant products against four species of mosquito vectors. Southeast Asian journal of tropical medicine and public health. 2004; 35: 325–333.

[47] Müller GC, Junnila A, Kravchenko VD, Revay EE, Butler J, Schlein Y. Indoor protection against mosquito and sand fly bites: a comparison between citronella, linalool, and geraniol candles. Journal of the American Mosquito Control Association. 2008; 24 (1): 150–153.

[48] Noosidum A, Prabaripai A, Chareonviriyaphap T, Chandrapatya A. Excito-repellency properties of essential oils from Melaleuca leucadendron L., Litsea cubeba (Lour.) Persoon, and Litsea salicifolia (Nees) on Aedes aegypti (L.) mosquitoes. Journal of Vector Ecology. 2008; 33 (2): 305–312.

[49] Hill N, Lenglet A, Arnez AM, Carneiro I. Plant based insect repellent and insecticide treated bed nets to protect against malaria in areas of early evening biting vectors: double blind randomised placebo controlled clinical trial in the Bolivian Amazon. bmj. 2007; 335 (7628): 1023.

[50] Rani MA, Lakshmi CSR. Journal of Pharma Research. Pharmaceuticals. 2012; 7 (9): 10–14.

[51] Paluch G, Grodnitzky J, Bartholomay L, Coats J. Quantitative structure- activity relationship of botanical sesquiterpenes: Spatial and contact repellency to the yellow fever mosquito, Aedes aegypti. Journal of agricultural and food chemistry. 2009; 57 (16): 7618–7625.

[52] Waka M, Hopkins RJ, Glinwood R, Curtis C. The effect of repellents Ocimum forskolei and deet on the response of Anopheles stephensi to host odours. Medical and veterinary entomology. 2006; 20 (4): 373–376.

[53] Soderlund DM, Bloomquist JR. Neurotoxic actions of pyrethroid insecticides. Annual review of entomology. 1989; 34 (1): 77–96.

[54] Maia MF, Moore SJ. Plant-based insect repellents: a review of their efficacy, development and testing. Malaria journal. 2011; 10 (1): S11.

[55] Paluch G, Bartholomay L, Coats J. Mosquito repellents: a review of chemical structure diversity and olfaction. Pest management science. 2010; 66 (9): 925–935.

[56] Du EJ, Ahn TJ, Choi MS, Kwon I, Kim H-W, Kwon JY, et al. The mosquito repellent citronellal directly potentiates Drosophila TRPA1, facilitating feeding suppression. Molecules and cells. 2015; 38 (10): 911.