



Review Article

PLANT ESSENTIAL OILS AS MOSQUITO REPELLENT-A REVIEW

Bhupen Kalita,^{1*} Somi Bora,¹ Anil Kumar Sharma²

1. Girijananda Chowdhury Institute of Pharmaceutical Science, Guwahati, Assam-781017.
2. Kemwell Biopharm Pvt. Ltd. Bangalore, Karnataka-560022.

*Corresponding Author: Email bhupenkalita7@gmail.com

(Received: September 11, 2013; Accepted: November 01, 2013)

ABSTRACT

Malaria is considered endemic in 104 countries and territories around the world necessitating its control. Essential oils belonging to various plant species and possessing mixtures of hydrocarbons have been seen to act as effective repellent against various pests. The monoterpenoids constituting the major component is found to be cytotoxic to plant and animal tissue thus impairing the normal functioning of these tissues. The commercially marketed repellents basically consist of essential oils from plants *Cymbopogon nardus*, *Eucalyptus maculata*, *Cymbopogon excavatus*, *Mentha piperita*, *Azadirachta indica*. The volatile nature of these components due to their short duration of efficacy has urged for the development of novel formulations, use of fixatives such as vanillin and combination essential oil plants as repellents. The easy availability and less adverse environmental impact have led to the increased interest in plant origin insecticides as an alternative to chemical insecticides. The present article envisaged to review the reports of essential oils on its effectiveness as repellent.

Keywords: Repellent, pesticide, mosquito, repellent, essential oil.

INTRODUCTION

Mosquito borne diseases are major human and animal health problem in all tropical and subtropical countries. The diseases transmitted include malaria, filariasis, yellow fever, Japanese encephalitis and dengue fever. There has been exploration of various methods over the centuries to combat threats from mosquito borne diseases. With the beginning of the 20th century there grew an interest for use of biological control agents but this was declined with the discovery of insecticidal properties of DDT in 1939. However its deleterious impact on non-target population and the development of resistance prompted for the search of alternative, simple and sustainable methods of mosquito control [1, 2, and 3].

Considerable research efforts have proved that essential oil compound and their derivatives are an effective and

alternative means of controlling nuisance mosquitoes and their property of rapid degradation in the environment has favoured for its increased specificity [4]. The justification of essential oils as green pesticides lies in the fact that the constituents of all essential oils are moderately toxic or mostly found to be nontoxic to mammals, birds and the aquatic ecosystem [5].

Although there exist several advancements in the field of synthetic drug chemistry and antibiotics but plants still continue to be one of the major raw materials for drugs treating various ailments of human. In fact Clinical and Pharmaceutical investigations have helped in elevating the status of various medicinal plants by identifying the role of active principles present in them and exploring their mode of action in human and animal systems [6]. However essential oils due to their volatile nature demand for frequent re-application to maintain its potency. They evaporate

completely and thereby their effectiveness is short lived and so complete protection cannot be achieved [7]. The review tries to compile the health scenario affected by mosquitoes and discusses the available methods of mosquito control with special focus on essential oils as alternative of synthetic chemicals.

Mosquito borne diseases:

Since ancient times, mosquitoes have been reported as the source of various ailments affecting human. Comprising approximately 3500 species, mosquitoes are found beyond the tropical and subtropical regions of the world. The chief genera which vector human disease causing pathogens are Anopheles (malaria, filariasis), Aedes (yellow fever, dengue, chikungunya) and Culex (West Nile, Japanese encephalitis, filariasis). Over its life span a female mosquito repeatedly takes a blood meal as protein source to complete egg development. By injecting the saliva which may contain pathogens into the host animal, the pathogens thus complete an obligatory life cycle phase and multiply in the mosquito's salivary glands. This thereby makes female mosquito an ideal transmitter of diverse blood borne pathogens and agents of devastating human diseases [8, 9]. Over the years malaria have been considered as one of the leading cause of death in India (Table: 1). History reveals that the highest incidence of malaria in India occurred in the 1950s with an estimated 75 million cases and 0.8 million deaths per year [10]. Malaria is caused by the protozoal parasites Plasmodium vivax Grassi and Feletti, Plasmodium malariae Feletti and Grassi, Plasmodium ovale Stephens, and Plasmodium falciparum Welch, which are transmitted by Anopheles mosquitoes. Studies suggest that for any form of malaria to be endemic in a certain area a number of requirements must be fulfilled, it needs the presence of a large number of competent anopheline mosquitoes with a sufficient preference for human blood and an exposed human population with enough number of malaria carriers and susceptible individuals for the chain of infection to persist [11].

Reports signify that annually 100 million cases of dengue fever and half a million cases of dengue hemorrhagic fever (DHF) occur globally (Table: 2), with an average case of fatality rate around 5%. Potential reasons for the global resurgence and spread of dengue fever and DHF epidemics

are assumed due to population growth, uncontrolled urbanization in tropical and subtropical countries, proliferation of breeding sites for Aedes mosquitoes and the lack of effective mosquito control [12].

One of the leading causes of acute encephalopathy is encephalitis affecting children and adolescents particularly in the tropics. Mosquitoes proliferate in close association with pigs & other animal reservoirs and are found to spread virus of Japanese encephalitis basically in malnourished children of poor families from rural area [13].

Table 1: Countrywide malaria surveillance data (1995-2008)

Year	Total malaria cases (million)	Death due to malaria (thousand)
1995	2.93	1151
1996	3.04	1010
1997	2.66	879
1998	2.22	664
1999	2.28	1048
2000	2.03	932
2001	2.09	1005
2002	1.84	973
2003	1.87	1006
2004	1.92	949
2005	1.82	963
2006	1.79	1707
2007	1.51	1310
2008	1.52	924

Table 2: Severe outbreaks of DF/DHF across India.

Year	Number of DF/DHF cases	Number of death	Region
1996	10252	423	Delhi
2006	12317	184	21 states/Union Territories
2007	5534	69	18 states

Control of Mosquitoes:

The efficient way to control these diseases is to control mosquito vector populations and prevent mosquito bites (Table: 3). Studies reflect that insect repellents play an important role in preventing the mosquito vector, deterring an insect from flying to, landing on or biting human and animal skin. Generally the widely used compounds as insect repellents are synthetic chemical repellents but they bear the disadvantage of being not safe for human, especially children, domestic animals because they may cause skin irritation, hot sensation, rashes or allergy [14].

Table 3: Methods of mosquito control

Chemical methods	Non-chemical methods	Biological methods
Synthetic repellents: DEET, Permethrin	Physical method: Medicated net, Non-medicated net, Mosquito traps	By growing some fish species that feeds on mosquito larvae in water bodies
Natural repellents: Neem oil, Citronella oil	Mechanical methods: Electric mosquito zapper, Mosquito magnet	

Fogging is a temporary method of controlling mosquitoes and such other pests but is particularly necessary in the context of health threats from severe bug populations and for an outdoor activity where these pests are unwanted. The method employs a thermal fogger which produces a pesticide fog or smoke by heating the fogging solution with a coil inside the unit. It is ready-to-use fogging solution and each gallon contains 0.5% Pyrethrins and 5.0% Piperonyl Butoxide. Another revolutionary approach is the transdermal technology to deliver a natural mosquito repellent nutrient directly into the blood stream for a complete 24-hour mosquito protection. The active ingredient in the patch is Vitamin B₁ or Thiamine as it is known to be the most effective natural mosquito repellent discovered to date. It was found that female mosquitoes are repulsive to the scent of Thiamine, therefore the patch works by inducing a controlled amount of Vitamin B₁ into the blood stream [7]. Many synthetic chemicals as mosquito repellent are available

in the market in various form like mosquito repellent cream, mosquito repellent patch, coils, spray, mosquito repellent wipe and mosquito repellent liquid that evaporate on heating. But most of the products are irritant to the users and environment.

Essential oils as green pesticide:

Essential oils are volatile naturally occurring, complex compounds characterized by a strong odour and are formed by aromatic plants as secondary metabolites. They are liquid, volatile, rarely coloured, lipid soluble and soluble in organic solvents with a density generally lower than that of water. There are 17,500 aromatic plant species among higher plants and approximately 3,000 essential oils are known out of which 300 are commercially important for pharmaceuticals, cosmetics and perfume industries apart from pesticidal potential. In nature essential oils play an important role in the protection of the plants as antibacterial, antiviral, antifungal, insecticides and also against herbivores by reducing their appetite for such plants. They also may attract some insects to favour the dispersion of pollens and seeds or to repel the undesirable. Owing to the attraction for natural products like essential oils, despite their wide use and being familiar to us as fragrances, it is important to develop a better understanding of their mode of biological action for new applications in human health, agriculture and the environment. Some of them constitute effective alternatives or complements to synthetic compounds of the chemical industry without showing the same secondary effects [15].

Literature cited indicates that certain natural products *Zanthoxylum armatum* (Rutaceae); *Azadirachta indica* (Maliaceae) and *Curcuma aromatica* (Zingiberaceae) have been investigated for repellent activity against mosquitoes. *Callistemon rigidus* (bottle brush), *A. indica* (neem) and *Z. armatum* (timur) have been reported to have repellent activity against land leeches also. Repellent action of neem oil in the form of mats and neem cream has been evaluated against mosquitoes. Benzene and methanol extracts of *Artemisia vulgaris* have been reported to have repellent activity against *Aedes aegypti*. Quelling, an insect repellent produced in China, derived from the extract of the lemon grass and eucalyptus plants were evaluated against mosquitoes. Essential oil obtained from *Vitex negundo* was used as repellent against *Aedes aegypti*. Repellent

properties of *Lantana camara* (Verbanaceae) flowers against *Aedes* mosquitoes have also been reported [16]. Most of the plant based insect repellents currently on the market contain essential oils from one or more of the following plants: citronella (*Cymbopogon nardus*), cedar (*Juniper virginiana*), eucalyptus (*Eucalyptus maculata*), geranium (*Pelargonium reniforme*), lemon-grass (*Cymbopogon excavatus*), peppermint (*Mentha piperita*), neem (*Azadirachta indica*) and soybean (*Neonotonia wightii*) [17].

Typically these oils are liquid at room temperature and get easily transformed from liquid to gaseous state at room or slightly higher temperature without undergoing decomposition. The aromatic characteristics of essential oils provide various functions for the plants including attracting or repelling insects, protecting themselves from heat or cold and utilizing chemical constituents in the oil as defence materials. The concept of "Green Pesticides" refers to all types of nature-oriented and beneficial pest control materials that can contribute to reduce the pest population. They are safe, ecofriendly and are more compatible with the environmental components than synthetic pesticides. The purified terpenoid constituents of essential oils are moderately toxic to mammals but with few exceptions, the oils themselves or products based on oils are mostly nontoxic to mammals, birds and fish thereby, justifying their placement under "green pesticides" [5].

Table 4: Mammalian toxicity of some essential oil compounds

Compound	Animal tested	Route	LD ₅₀ (mg/kg)
1,8 Cineole	Rat	Oral	2480
Cinnamaldehyde	Guinea pig	Oral	1160
Citral	Rat	Oral	4960
Eugenol	Rat	Oral	2680
d-limonene	Rat	Oral	4600
Linalool	Rat	Oral	>1000
Myrcene	Rat	Oral	5000
Thujone	Mice	Subcutaneous	87.5
Thymol	Rat, Mice	Oral	980,1800
(+) Carvone	Rat	Oral	1640

The promising herbal medicines should be subjected to phytochemical analysis and identification of active ingredients and clinical trials to confirm their efficacy and safety (Table: 4), and also to determine the recommended doses in line with WHO guidelines [18].

Mode of action of essential oils:

Essential oils being complex mixtures of volatile organic compounds are generally produced as secondary metabolites in plants. They are constituted by hydrocarbons (terpenes and sesquiterpenes) and oxygenated compounds (alcohols, esters, ethers, aldehydes, ketones, lactones and phenols). Essential oils extracted from different families have shown high repellency against arthropod species. Literature has documented that essential oils and extracts from genus *Eucalyptus* and *Cymbopogon* have been traditionally used as effective repellents. The metabolites like the monoterpenes such as α -pinene, cineole, eugenol, limonene, terpinolene, citronellol, citronellal, camphor and thymol are the common constituents in a number of essential oils presenting mosquito repellent activity. Generally the monoterpenoids and sesquiterpenes are associated with repellent properties of several essential oils [19]. Amongst the monoterpenes, a majority of them are cytotoxic to plants and animal tissue causing a dramatic reduction in the number of intact mitochondria and golgi bodies thereby impairing respiration, photosynthesis and decreasing the cell membrane permeability. Being volatile in nature so they also act as chemical messengers for insects and other animals, serving as a signal of relatively short duration and alarm the pheromones. Literature cites that hairs on the mosquito antennae are temperature and moisturesensitive. The repellent molecules thus interacts with the female mosquito olfactory receptors thereby blocking the sense of smell which therefore comes as an hurdle in the recognition of host by the mosquitoes (Fig:1) [4].

Studies have indicated that terpenoids containing two functional groups are biologically active as mosquito repellents. The repellent activities of 20 synthesized terpenoids with two functional groups, one being negatively charged end containing either ester/ether bonds or an ethanol hydroxyl group and the other positively charged end containing alkane groups were assessed. It was revealed that the positive end is more favorable for receptor

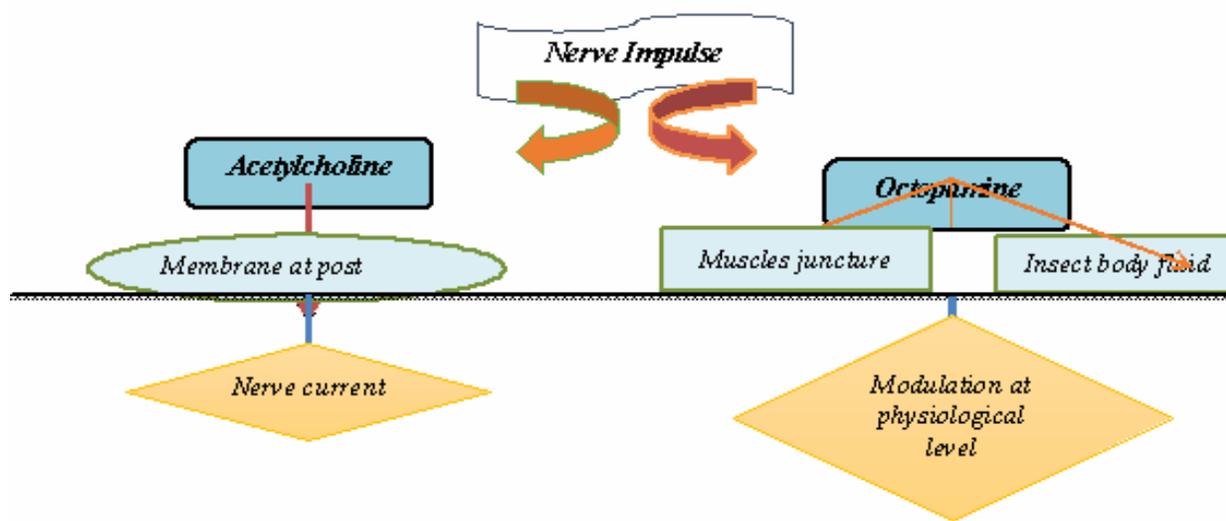
interactions and its magnitude characterizes the electrophilic nature of the group, consequently the repellent-receptor interactions are most likely to be related to electrophilic interactions. Also it was shown that molecular descriptors such as dipole moment and boiling point are closely related to repellent activity. Generally the dipole moment is related to lipophilicity or specific electrostatic interactions with receptor whereas boiling point/vapor pressure might determine duration of contact with olfactory chemosensilla of mosquitoes [20]. Although repellent activity of essential oils are generally attributed to some particular compounds but if a synergistic phenomenon is established among these metabolites then it may result in an increased bioactivity compared to isolated components. Also this synergistic effect is showed with mixture of oils. The minor constituents found in low percentages may also act as synergists enhancing the effectiveness of the major constituents through a variety of mechanisms [21]. Essential oils act at a vapor phase and are generally effective when freshly applied as they usually dissipate quickly within a short period of time due to their high volatility. However this property can be improved through the development of formulations that would keep the active ingredients onto the skin for a longer period of time. The product composition basically determines the increase in repellency property of essential oils [22].

Formulation based on creams, polymer mixtures or microcapsules results in increase in repellency duration through controlled release. An example is the successful microencapsulation of *Zanthoxylum limonella* oil in glutaraldehyde crosslinked gelatin in order to improve mosquito repellent properties. Development of new formulations, fixative additives and the production of combined repellents are the possibilities that add up for the effectiveness and greater economic value to repellents obtained from essential oils [23].

CONCLUSION

Plants as alternative source of repellent agent reported in numerous ethnobotanical evaluation. They have been used traditionally in many parts of the world. The repellent properties of plant essential oils to mosquitoes and insects were well known before the advent of synthetic chemicals. Plant-derived repellents usually do not pose hazards of toxicity to humans and domestic animals and are easily biodegraded. Compared to synthetic compounds, natural products are presumed to be safer for human use. Moreover, in contrast with synthetic repellents which pose environmental threat, lethal effects on nontarget organisms and the resistance of mosquitoes to insecticides have increased during the last five decades, the natural products

Fig 1: Target sites in insects as possible neurotransmitter mediated action of essential oils.



are usually simple, cost effective and accessible to communities with minimal external input. These problems have demanded the necessity for developing alternative strategies. Due to the easy availability, low budget and less adverse environmental impact the interest in developing plant origin insecticides as an alternative to chemical insecticides has attracted great attention. Although there is widespread use of plants as repellents, scientific understanding of these plants is, however, largely unexplored and therefore there is a need to collect ethnobotanical information on these plants as a first step prior to evaluation of their efficacy and safety as repellents.

Novel drug delivery system of plant based active substances are need of the time. Recent technological developments in isolation and standardization of herbal drugs motivating research in novel sustained and controlled delivery device taking phytoconstituents. But pharmaceutical research in mosquito repellent products yet to gear up. Novel mosquito repellent device of essential oils have greater scope in lieu of the fact that in twenty first century also mosquito borne diseases are affecting a large population worldwide. Essential oils because of their volatility act for a short duration. Polymeric slow release device containing essential oils can be one option for making them long acting. Also multiple emulsion with essential oil core may be a smart delivery system. Such topically applicable formulations will be convenient for people to apply and terminate. Essential oils abundant in nature and apart from its medicinal and flavor value, its use in repelling mosquito can be considered as sustainable and biocompatible delivery device as green alternative.

REFERENCES

1. Siriyasatien P, Thavara U. (2006). Genetically Modified Mosquitoes: A New Strategy to Control Mosquito Borne Diseases. *Thai Journal of Veterinary Medicine*; 36(4): 9-19.
2. Kumar R, Hwang JS. (2006). Larvicidal Efficiency of Aquatic Predators: A Perspective for Mosquito Biocontrol. *Zoological Studies*; 45(4): 447-466.
3. Shaalan EAS, Canyon DV. (2009). Aquatic insect predators and mosquito control. *Tropical Biomedicine*; 26(3): 223-261.
4. Tripathi AK, Upadhyay S, Bhuiyan M, Bhattacharya PR. (2009). A review on prospects of essential oils as biopesticide in insect-pest management. *Journal of Pharmacognosy and Phytotherapy*; 1(5): 52-63.

5. Koul O, Walia S, Dhaliwal GS. (2008). Essential oils as green pesticides: Potential and Constraints. *Biopesticide International*; 4(1): 63-84.
6. Vishwanathan AS, Basavaraju R. (2010). A Review on *Vitex negundo* L. - A Medicinally Important Plant. *European Journal of Biological Sciences*; 3(1): 30-42.
7. Patel EK, Gupta A, Oswal RJ. (2012). A review on: Mosquito Repellent Methods. *International Journal of Pharmaceutical, Chemical and Biological Sciences*; 2(3): 310-317.
8. Tolle MA. (2009). Mosquito-borne diseases. *Curr Probl Pediatr Adolesc Health Care*; 39(4): 97-140.
9. Michel K, Kafatos FC. (2005). Mosquito immunity against *Plasmodium*. *Insect Biochemistry and Molecular Biology*; 35(7): 677-689.
10. Publication of World Health Organization, India, available at www.who.int/entity/gho/malaria/en/
11. Adams M, Althera W, Kessler M, Kluge M, Hamburger M. (2011). Malaria in the renaissance: Remedies from European herbals from the 16th and 17th century. *Journal of Ethnopharmacology*; 133(2): 278-288.
12. Gurugama P, Garg P, Perera J, Wijewickrama A, Seneviratne SL. (2010). Dengue viral infections. *Indian Journal of Dermatology*; 55(1): 68-78.
13. Kumar A, Kumar R, Kaur J. (2012). Japanese encephalitis: medical emergency in India. *Asian Journal of Pharmaceutical and Clinical Research*; 5(3): 9-12.
14. Sritabutra D, Soonwera M, Sirirat S, Pongjai S. (2011). Evaluation of herbal essential oil as repellents against *Aedes aegypti*(L.) and *Anopheles dirus* Peyton & Harrion. *Asian Pacific Journal of Tropical Biomedicine*; 1(1): 124-128.
15. Bakkali F, Averbeck S, Averbeck D, Idaomar M. (2008). Biological effects of essential oils-a review. *Food and Chemical Toxicology*; 46(2): 446-475.
16. Das NG, Baruah I, Talukdar PK, Das SC. (2003). Evaluation of botanicals as repellents against mosquitoes. *Journal of Vector Borne Diseases*; 40(1-2): 49-53.
17. Choochote W, Chaithong U, Kamsuk K, Jitpakdi A, Tippawangkosol P, Tuetun B, Champakaew D, Pitasawat B. (2007). Repellent activity of selected essential oils against *Aedes aegypti*. *Fitoterapia*; 78(5): 359-364.
18. Kazembe T, Chaibva M, Nkomo S. (2012). Evaluation of mosquito repellence of *Ocimum americanum* and *Blumea alata* plants. *Journal of Scientific Research in Pharmacy*; 1(2): 55-57.
19. Nerio LS, Olivero-Verbel J, Stashenko E. (2010). Repellent activity of essential oils: A review. *Bioresource Technology*; 101(1): 372-378.
20. Wang Z, Song J, Chen J, Song Z, Shang S, Jiang Z, Han Z. (2008). QSAR study of mosquito repellents

- from terpenoid with a six-member-ring. *Bioorganic & Medicinal Chemistry Letters*; 18(9): 2854-2859.
21. Omolo MO, Okinyo D, Ndiege IO, Lwande W, Hassanali A. (2004). Repellency of essential oils of some Kenyan plants against *Anopheles gambiae*. *Phytochemistry*; 65(20): 2797-2802.
 22. Trongtokit Y, Rongsriyam Y, Komalamisra N, Apiwathnasorn C. (2005). Comparative repellency of 38 essential oils against mosquito bites. *Phytotherapy Research*; 19(4): 303-309.
 23. Maji T, Baruah I, Dube S, Hussain MR. (2007). Microencapsulation of *Zanthoxylum limonella* oil (ZLO) in glutaraldehyde crosslinked gelatin for mosquito repellent application. *Bioresource Technology*; 98(4): 840-844.

How to cite this article:

Kalita B., Somi Bora S., Sharma A.K., "Plant essential oils as mosquito repellent-A Review" *Int. J. Res. Dev. Pharm. L. Sci.*, 2013, 3(1), pp. 741-747.