REVIEW PAPER

A Comprehensive Review on Diverse aspects of Natural and Synthetic Mosquito Repellents

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ABSTRACT

The present review was based on the diverse aspects of natural and synthetic mosquito repellents. Every year, 2.5 million cases of dengue & chikungunya are caused by the Aedes aegypti mosquito. Avoiding direct human-mosquito contact is the primary way to reduce mosquitoborne illnesses. It is highly advised that susceptible people who live in places where mosquitoes are still a possible threat apply insect repellents to all exposed skin areas. Warm-blooded animal's sweat contains lactic acid and CO2, which are attractive chemicals to mosquitoes. Essential oils, which are utilized as natural repellents, are mostly derived from plants. For instance, citronella oil, clove, eucalyptus, rosemary, peppermint, and lemon grass can deter mosquitoes. The most powerful synthetic repellent is N, N-diethyl-meta-toluamide (DEET), a toxic chemical that may produce carbon monoxide and a natural odor that resembles that of the human body. Moreover, 3-[N Butyl-N-acetyl]-amino propionic acid (IR3535) is the best mosquito repellent which is more effective than DEET for longer time. In conclusion, natural and synthetic mosquito repellents are effective in managing the insect's spread diseases. However, other methods including physical methods i.e., mosquito net, medicated net, non-medicated net, mosquito trap and mechanical methods i.e., electric zipper and mosquito's magnet are promising as strong mosquito repellent without any side effects to the host cell/body....

Keywords: Malaria, Natural mosquito repellents, synthetic mosquito repellents, DEET, R3535..

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INTRODUCTION

With an estimated 3,500 species, mosquitoes could survive in a broad range of temperatures and geographical areas worldwide. Approximately 700,000 deaths annually and more than 17% of all infectious diseases are caused by diseases transferred by vectors, however other species are only an irritation due to their biting tendencies [1]. Mosquitoborne diseases are the leading cause of vector-borne infections, affecting 80% of population globally [2]. Malaria affects approx. 219 million people annually, with over 40,000 deaths and an anticipated 627,000 deaths in 2020 [3].

Every year, 2.5 million cases of dengue and chikungunya are caused by the Aedes aegypti mosquito [4][5]. The primary causes of the dengue fever outbreak include increased urbanization, rapid population growth, ineffective mosquito control strategies, and an increase in Aedes mosquito breeding grounds [6]. Numerous dangerous diseases are spread by mosquitoes i.e., Aedes aegypti, Anopheles species, Culex quinqueflasciatus, It is essential to develop a new, safe, and effective mosquito repellent chemical composition [7].

Prompt intervention is necessary to prevent mosquito-borne infections. There are several techniques to protect oneself against mosquito bites. When working outside, it is advised to wear full-sleeved shirts and pants with socks [8]. Additionally, while we are indoors, we should use bed nets, and live in air-conditioned locations [9]. By applying insect repellents and emptying standing water, you can stop mosquitoes from breeding [10]. In the mid-1900s, the first contemporary insecticides were introduced for use in pest control [11].

In the modern world, controlling mosquito populations is becoming more and more important as the number of diseases caused by insects or mosquitoes gradually rise [12]. Human activity is at blame for both of these problems. Applying insect repellents is essential for preventing mosquitoes [13].

Mosquito Repellent

Mosquito repellent refers such material which inhibits the attractions and biting of mosquitoes at living surfaces [14]. Furthermore, diverse mosquito repellents are available in the market that use high frequency sounds and are based on ultrasonic [15].

Additionally, to lessen the quantity of mosquitoes in their surroundings, ancient people burned bay, cumin, and oregano. Burning plants or plant parts to create smoke is one of the oldest ways to keep mosquitoes away [16][17]. Fogging is a short-term method of controlling pests,

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although it is mostly necessary for outdoor movements where these pests are undesirable and when there is a substantial risk to human health from insect inhabitants [18]. One strategy for controlling mosquitoes is fogging. Each gallon comprises a combination of pyrethrins at a concentration of 0.5% and piperonyl butoxide (5%), and thermal fogging is mostly used. Additionally, a technique called transdermal technology involves injecting repellents into the circulation to shield the body from mosquito bites [19].

Given the aforementioned possible rising tendency and the enormous financial burden, comprehensive vector control and management-particularly in the beginning by preventing mosquitoes from feeding on humans-may be a better and more prudent course of action than treating vector-borne illnesses [20][21]. Avoiding direct human-mosquito contact is the primary way to reduce mosquitoborne illnesses. It is highly advised that susceptible people who live in places where mosquitoes are still a possible threat apply insect repellents to all exposed skin areas [22].

Mechanism of action of Mosquito Repellent

The repelling effect is often caused by physiological or biochemical mechanisms. The repellent action of DEET is based on a receptor's site inhibition [23].

Warm-blooded animal's sweat contains lactic acid and CO_2, which are attractive chemicals to mosquitoes. The olfactory pulp detects the amount of carbon dioxide, whereas the antennae's olfactory receptor detects the host's odor. The person is able to detect the smell thanks to the antennae, which include chemoreceptors.

For instance, *Anopheles* and *Anopheles albimanus* mosquitoes are 7 times less sensitive than *Culex* & *Pipiens* mosquitoes. The molecular weight range of an efficient insect repellent is between 150 and 250. When evaluating the efficacy of a mosquito repellent, the vapor pressure is thought to be the most crucial factor [24].

The expression of several energy-producing proteins, including ubiquinone synthetase, acetyl-CoA synthetase, glyceraldehyde 3-phosphate dehydrogenase, and ATP synthase (subunits α & β) was down-regulated. Enzyme fructose 1,6-bisphosphatase was also discovered to be increased for this therapy. Thus, it is established that the gluconeogenesis pathway is activated by adversely regulating the glycolysis process [25].

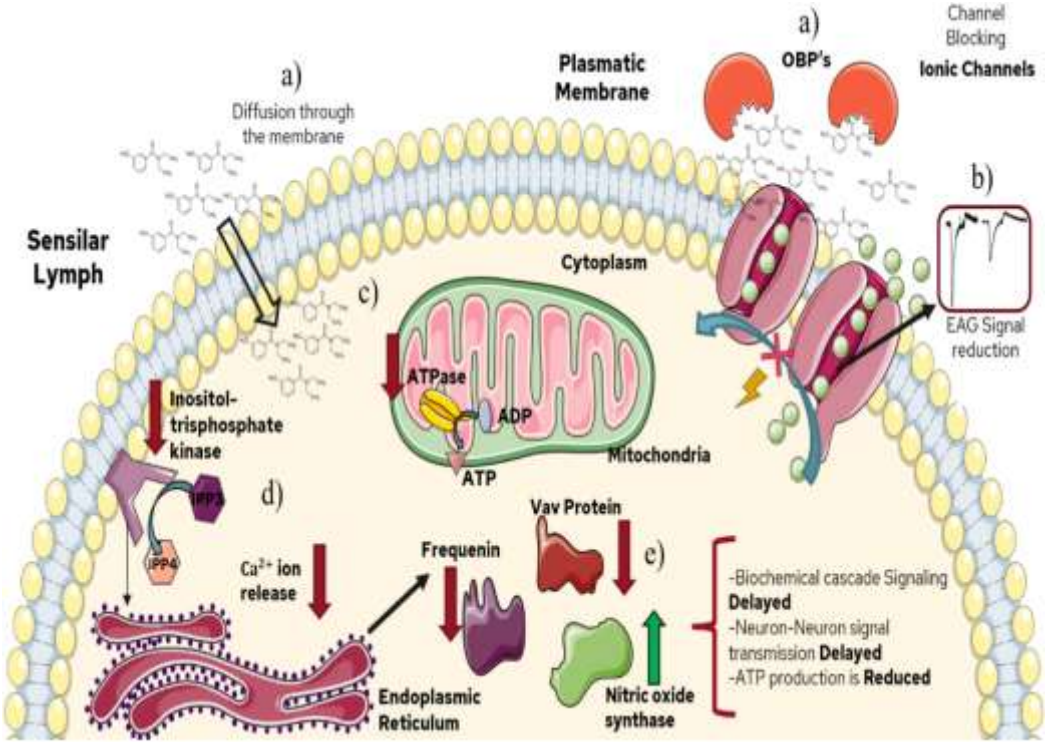


Fig 1. Possible mosquito repellent action of DEET [27]

The neuron axon contains the dynactin proteins. These protein's overexpression implies that the neuron boosts transport activity prior to exposure to combination 1 repellent. This action is also associated with other upregulated proteins, such as LIM Mlp84b, which, with the help of actin proteins, provide cytoskeletal integrity and control the efficacy of cell movement [26][27].

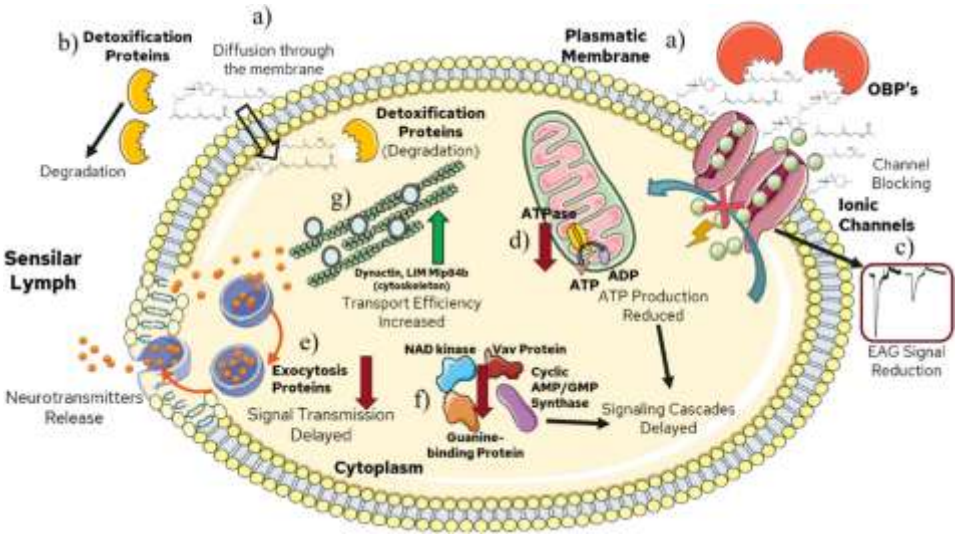


Fig 2. Possible mosquito repellent action of a mixture of geranyl acetate, α-bisabolol, and nerolidol [27]

Natural repellents

Essential oils are volatile compounds that are present in many odoriferous plants. The concentrated hydrophobic liquid is made from several plant parts and smells volatile [28]. Essential oils can be extracted through hydro distillation, solvent extraction, steam distillation, and others. Essential oils are kept in plant parts including leaves, flowers, fruits, and roots. People use essential oils to ward off mosquitoes and other hemophagous insects. Numerous research have demonstrated that essential oil compounds and derivatives can be a useful substitute for traditional mosquito control techniques. Essential oils must be reapplied often to maintain their effectiveness due to their extremely volatile qualities [29]. They are not long-lasting enough to offer complete protection, thus their effectiveness is diminished. Plant-based essential oils are recognized to have a number of advantageous properties. Plant repellents including lemon grass, citronella oil, lavender, eucalyptus, tulsi, clove and castor etc [30].

Cedar oil works well against mosquitoes and moths.

Mosquito repellency is 86% when rosewood and lutes are combined in 1:1 ratio at 10% conc. Essential oils that have demonstrated operative effects can be used to create insect repellents [31].

C. aurantifolia is the strongest repellent against diverse mosquitoes [32].

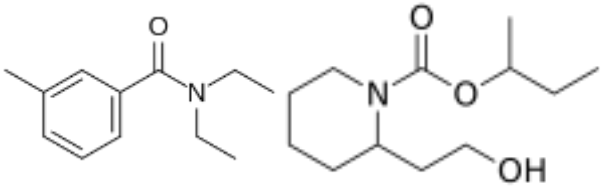
The oviposition deterrent and ovicidal actions in *Cx. Aedes aegypti*, and *Quinquefasciatus* [33].

To battle the Aedes aegypti mosquito, *Cassia fistula* leaf extract is used for its ovicidal, repellent, and larvicidal properties.

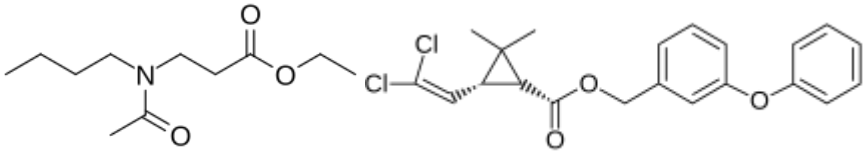
One harmless and possibly successful method of keeping insects away is to extract the oil from catnip plants. The nepetalactone molecule is present in this oil in two distinct forms [34].

Chemical-Based Repellent

Among the several insect repellents used to combat mosquitoes are chemicals, and aromatic oils. Although chemical insect repellents have a remarkable protective profile, they are hazardous to the skin and neurological system. The most powerful synthetic repellant is N, N-diethyl-meta-toluamide (DEET), a toxic chemical that may produce CO and a natural smell that resembles that of the human body [35].



N, N-diethyl-meta toluamide (DEET) **Picaridin**



IR3535 **Permethrin**

Fig 3. Chemical structure of some chemical-based repellents

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In contrast DEET, IR3535 **(**3-[N Butyl-N-acetyl]-amino propionic acid) has the longest action and efficacy as mosquito repellent. Another useful source of relief is plant-based repellents. Essential oils are not particularly effective because of their short duration of action and rapid dissipation. DEET (N, N-diethyl-meta toluamide) and picaridin are the most effective and widely available alternative to permethrin for treating bog myrtle; nonetheless, it has certain potentially harmful side effects [36].

The chemical molecule known as acaridan is commonly referred to as hydroxyethyl isobutyl piperidine carboxylate. It is a useful weapon in the fight against insects because of its neutral color and scent. It is utilized as an insecticide due to its lack of color and odor [33]. Although there are no harmful effects on the skin or eyes, swallowing it might be a little risky. Even the most sensitive skin won't usually be irritated by it. Picaridin is a mild chemical that disappears quickly and does not build up. Combining it with other substances can reduce its toxicity [37].

Its powerful actions eradicate both mosquitoes and ticks. Permethrin-treated clothing is completely safe for people to use on clothing, but you shouldn't put it on your skin. Spraying fabric is the suggested technique of application. After application, it keeps working for six hours. It offers even more protection when used with DEET. Permethrin offers 97.7% bug protection when applied on a lightweight uniform [38].

Other methods for mosquito repellents

Physical Methods

The water in the rain barrels, fountains, pools, and bird baths should not be changed for at least a week. It is necessary to wear full-sleeved clothing in the early morning and late evening. Screening windows and doors is another important precaution to take against mosquito attacks [39].

Mosquito's net

They are more effective than coils or other repellents because using them has no negative health impacts. Sleeping under netting is another way to protect oneself from mosquito attacks. The two types of nets that are differentiated from each other are medicated & non-medicated net [40].

Medicated net

They are medicated with 25% deltamethrin to increase their effectiveness. The net is first mixed with one pill and one liter of water, immersed in the mixture for ten minutes, and then dried in a cold atmosphere. This net will remain effective and keep mosquitoes away for six months. The World Health Organization has shown that medicated nets are more effective than coils or liquidators [41].

Non medicated net

There are many different types of mosquito netting that may be made from cotton, polyester, and polyamide, among other materials. There are more shapes and sizes available. The kind of net is crucial when it comes to preventing mosquito bites. An efficient way to naturally keep mosquitoes away is to use mosquito netting [42].

Mosquito Trap

It chiefly attracts and gathers female mosquito. It mimics the many elements in the surroundings that draw mosquitoes, including body temp. and inhaled CO_2. It is electricity operated, thus employing them carries little danger [43][44].

Mechanical Methods

Electric zipper

This device uses UV light to effectively capture mosquitoes. When the mosquitoes later come into touch with the dangerous electric charge, they are killed [32].

Mosquito's magnet

Its basic idea is to mimic the traits of animals, including the release of carbon dioxide, heat, and moisture. The apparatus attracts the mosquito, and when it gets near enough, it abruptly dies. This magnet can be used in conjunction with octenol to eradicate sand flies, black flies, midges, and mosquitoes [45].

Different repellents have different modes of action, and different mosquito species react differently to the same repellent. These plants may be used to manufacture a range of pharmaceuticals, have promise for value-added products, and are helpful in creating natural plant-based repellents. The results of our review research show that the development of natural or plant-based insect repellents will reduce the adverse effects or side effects of synthetic repellents and may be utilized as an economical, safe, and eco-friendly alternative to synthetic repellents.

Toxicity of mosquito repellents

The detoxification of ammonia from dietary protein catabolism is found reduced after the systemic intake of DEET. Ornithine transcarbamylase deficiency is characterized by hyperammonemia and metabolic hepatic encephalopathy in infancy. The use of DEET is prohibited in people with urea cycle disturbances i.e., OTD. It is fatal as DEET toxicity in children with OTD [46].

Formaldehyde, are used to make mosquito coils. When the coils are fired, they will smolder and smoke for hours, inhibiting mosquito bites but polluting the air with volatile chemicals and particulates. Lung disease, including lung cancer, may be significantly increased by repeated exposure to smoke from mosquito coils [47]. For a few hours, burning a variety of plant's oil-based candles may lessen mosquito and fly bites [48].

Non-chemical protocols for the prevention of arthropod-borne infectious diseases

The CDC advises wearing long sleeves, long pants, helmets, and boots or covered shoes rather than sandals to reduce mosquito bites when outdoors. Webster and colleagues showed that human skin scents and slight increases above ambient CO_2 levels caused synergistic effects that boosted mosquito landings in human landing trials using the malaria vector, Anopheles gambiae [49].

People should sleep indoors in air-conditioned or screened spaces, or in lodgings with insufficient air conditioning or screening, under bed nets impregnated with permethrin. Dawn and evening are the best times to avoid being bitten by the Anopheline mosquitoes that spread malaria. Nonetheless, the Culicine mosquitoes that spread dengue, and chikingunyabite violently all day long, which makes it wise to use insect repellents when outside [50].

Fig. 4. A) A female Aedes aegypti mosquito that bites people during the day becomes engorged with blood. B) *Aedes albopictus,* a strong vector of dengue and chikungunya as *A aegypti* [50].

Attachment sites may be invisible or obscured by hair, and the majority of patients do not remember painless tick bites, particularly those caused by tiny nymphs. In the event that tick avoidance strategies are unsuccessful and attached ticks are found, they should be removed as quickly as possible-ideally within a day-for expert identification, if one is available. Instead of being burned with spent matches or painted with adhesives, solvents, nail polishes or removers, should be removed in close proximity to their feeding mouthparts [51].

CONCLUSION

Many ethnobotanical analyses demonstrate the effectiveness of plants as repellents. Natural repellents can fast biodegrade and pose no threat to people or domestic animals. Furthermore, they don't pose any new environmental dangers. Natural products are safer for human consumption than produced ones. The use of synthetic repellents causes mosquitoes to become resistant to pesticides, negatively affects animals that are not the intended targets, and endangers the ecosystem. Due to their lower environmental effect and lower cost, it got the customer attention.

To alter or at least lessen the negative effects of synthetic chemical-based ant mosquito repellents, significant efforts were made to promote and enhance the use of natural repellents based on essential oils that are biodegradable and ecologically safe, especially those derived from botanical sources. However, the main disadvantage of these products is their short duration of impact and other unpredictability. Formulation improvement is urgently needed, particularly to accommodate a safe, economical, and highly effective carrier/absorbent composition of matter that allows for a regulated temporal release of an aromatic material, such an essential oil or a blend of essential oils.

In conclusion, natural and synthetic mosquito repellents are effective in managing the insect's spread diseases. However, other methods including physical methods i.e., mosquito net, medicated net, non-medicated net, mosquito trap and mechanical methods i.e., electric zipper and mosquito's magnet are promising as strong mosquito repellent without any side effects to the host cell/body.

CONFLICT OF INTEREST

Authors declare for none conflict of interest..

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