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A REVIEW ON UNVEILING THE EFFICACY OF HERBAL BASED APPROACH TO MOSQUITO REPELLENCY

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Abstract
This review examines the efficacy of herbal-based approaches to mosquito repellency, highlighting the growing interest in natural alternatives to conventional chemical repellents. With the increasing concern over the adverse effects of synthetic repellents on human health and the environment, there is a growing need to explore safer and more sustainable alternatives. Herbal-based repellents offer a promising solution, utilizing plant-derived ingredients known for their insect-repelling properties. This paper provides an overview of the various herbal ingredients commonly used in mosquito repellent formulations, along with their effectiveness in repelling mosquitoes. Additionally, it discusses the mechanisms of action underlying the repellent properties of these herbal ingredients, shedding light on their potential advantages over synthetic alternatives. Overall, this review underscores the potential of herbal-based approaches as effective and environmentally friendly alternatives for mosquito repellency, while also highlighting the need for further research to optimize their efficacy and address existing limitations.
Keywords: Mosquito-borne-diseases, Repellents, herb-based approaches.

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INTRODUCTION:

Mosquito-borne diseases, such as malaria, dengue fever, Zika virus, and chikungunya, continue to pose significant threats to public health globally, particularly in regions with tropical and subtropical climates.[1] These diseases exact a heavy toll on human populations, causing millions of illnesses and deaths each year. Traditional methods of mosquito control, including the use of chemical insecticides and repellents, have played a crucial role in combating mosquito-borne illnesses.[2] However, the widespread use of synthetic chemicals in mosquito control efforts has raised concerns about their potential adverse effects on human health and the environment.

The growing awareness of the ecological and health risks associated with synthetic pesticides and repellents has led to a shift in focus towards exploring safer and more sustainable alternatives. [3-4] In recent years, there has been a surge of interest in herbal-based approaches to mosquito repellency. Herbal repellents utilize plant-derived ingredients, such as essential oils and extracts, which are known for their natural insect-repelling properties. [5] These botanical ingredients have been used for centuries in traditional medicine and folk remedies to ward off mosquitoes and other biting insects.

The appeal of herbal-based repellents lies in their perceived safety and environmental friendliness compared to synthetic chemicals. Unlike conventional insecticides, which often contain potentially harmful synthetic compounds, herbal repellents rely on natural ingredients that are biodegradable and pose minimal risks to non-target organisms.[4] Additionally, many herbal ingredients used in mosquito repellents are readily available, making them accessible to communities in resource-limited settings where mosquito-borne diseases are endemic. This review aims to provide a thorough understanding of their potential as safe and sustainable mosquito control methods. Through a systematic analysis of the effectiveness, mechanisms of action, and practical considerations related to herbal-based repellents.

Mosquitoes

Mosquitoes are small flies belonging to the Culicidae family. Mosquito is a Spanish word that primarily refers to "little fly."[6] Mosquitoes are the primary vectors for the spread of a variety of tropical and subtropical diseases that can be fatal to humans. Malaria, yellow fever, filariasis, schistosomiasis, and Japanese encephalitis are the most common dreadful diseases spread by mosquitos.[7] Mosquitoes eject saliva into the host's blood, causing an immune response due to the binding of IgG and IgE antibodies to antigens.[8] The reactions cause irritation, itching, redness, and, in some cases, bumps. Mosquitoes alone transmit diseases to over 700 million people, with over one million deaths reported each year around the world. Mosquitoes have a set of sensors that can detect their target presence (Fig.1), which include [9] :

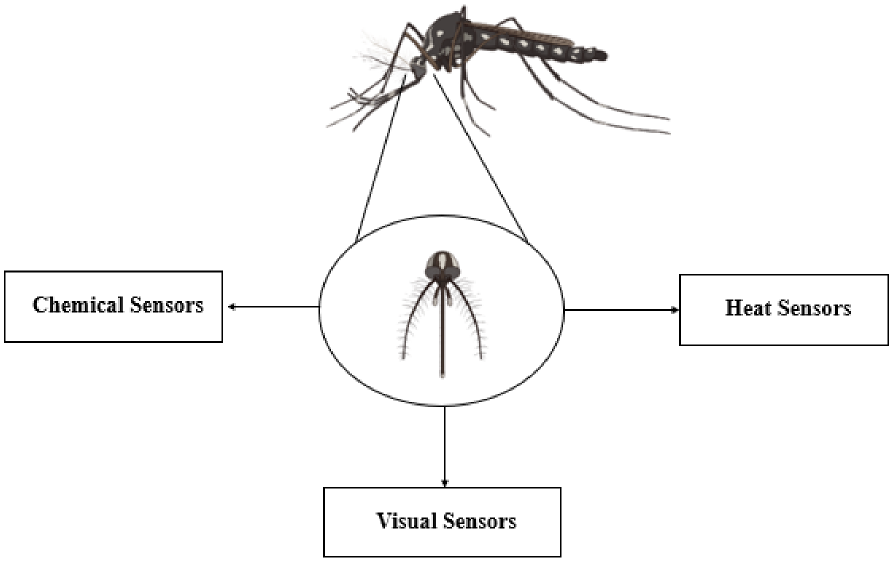

Figure 1: Various Sensors present in different Mosquitoes

A. Chemical Sensors: Mosquitos can detect lactic acid, carbon dioxide, and propen-3-ol from up to several yards away. Humans and animals release these compounds through respiration or perspiration. A person who sweats more becomes the species' target, while someone who sweats less receives fewer bites.

B. Heat Sensors: Mosquitoes can detect heat as well, allowing them to target warm-blooded animals quickly once they get close.

C. Visual Sensors: Mosquitoes are known to be intelligent insects because they can detect targets by looking clothing, which contrasts with the background.

Mosquito-Borne Human Diseases
Vector-borne diseases are illnesses spread by vectors such as mosquitoes, ticks, and fleas. These vectors can transport infectious pathogens like viruses, bacteria, and protozoa from one host (carrier) to another (Table.1)

Table 1: Major mosquito-borne diseases

Sl.no	Vector Mosquito (es)	Pathogen involved	Diease	Refernces
1	*Anopheles* spp *Culex* spp	*Plasmodium falciparum P. malariae, P. ovale,* and *P. vivax*	Malaria	[10]
2	*Culex* spp., *Aedes* spp., *Mansonia* spp. (Asia-Pacific); *Anopheles* spp. (Americas); *Ochlerotatus* spp	*Wuchereria bancrofti Brugia malayi* *B. timori*	Filariasis	[11-14]
3	*Aedes aegypti* and *Ae. albopictus*	Dengue virus serotypes DEN-1, DEN-2, DEN3, DEN-4 and DEN-5	Dengue	[15-16]
4	*Ae. aegypti, Ae. albopictus*	Chikungunya virus (CHIKV)	Chikungunya	[15]
5	*Aedes* spp. *Haemogogus* spp, *Sabethes* spp.	Yellow fever virus	Yellow fever	[15]
6	*Culex* spp., *Mansonia* spp., *Aedes curtipes*, *Anopheles* spp	JE virus	Japanese Encephalitis	[17]
7	*Ae. aegypti*, *Ae. albopictus*	Zika virus	Zika	[18]

Mode of action of Mosquito repellents
Mosquito repellents work through various mechanisms to prevent mosquitoes from landing on or biting humans. Here are some common modes of action for mosquito repellents:

Chemical Repellents: Most mosquito repellents contain active ingredients that interfere with the mosquito's ability to detect and locate humans. These chemicals disrupt the mosquito's olfactory receptors, making it difficult for them to sense the presence of humans or other prey. Common chemical repellents include DEET (N,N-diethyl-meta-toluamide), Picaridin, and IR3535.[19]

Masking Odors: Some repellents work by masking the scent of carbon dioxide and lactic acid, which are chemicals emitted by humans and attract mosquitoes. By masking these odors, repellents make it harder for mosquitoes to locate their human hosts.[20]

Spatial Repellents: These repellents create a barrier between humans and mosquitoes by releasing volatile compounds into the air. These compounds deter mosquitoes from entering the protected area or disrupt their ability to locate and feed on humans.[2]

Physical Barriers: Certain repellents, such as mosquito nets and clothing treated with insecticides, act as physical barriers that prevent mosquitoes from encountering human skin.

Natural Repellents: Some natural substances, such as citronella oil, lemon eucalyptus oil, and lavender oil, have been found to repel mosquitoes to some extent. These natural repellents often work by emitting strong odors that mosquitoes find unpleasant or by interfering with their ability to detect humans. [21]

Table-2: Mosquito repellent plants and their activities against various mosquito species

S.No	Plant Name	Common Name	Plant Parts Used	Phytoconstituents	Tested Mosquito Species	Author / References
1	*Azadirachta indica*	Neem	Leaves and seed oil	Azadirachtin, salanin, gedunin and deacetylnimbin	*An. Stephensi*	[37]
2	*Calendula officinalis*	Marigold	Aerial parts	β-carotene containing α-carotene, γ-carotene, lutein, luteoxanthin, flavoxanthin, rubixanthin, and other carotenoids	*An. stephensi*	[38]
3	*Carica papaya*	Papaya	Leaves	Papain, cystatin, chymopapain, tocopherol, phenolic acids, cyanogenic glucosides, glucosinolates and vitamin C	*Aedes. Spp*	[39]
4	*Cinnamomum zeylanicum*	Ceylon cinnamon	Leaves and Barks	Cinnamaldehyde	*Cx. quinquefasciatus, An. tessellatus* and *Ae. aegypti*	[40]
5	*Citrus aurantifolia*	Key lime	Stems and leaves	Geijerene, limonene and germacerene D	*Ae. aegypti, An. stephensi*	[41]
6	*Citrus reticulate*	Mandarin orange	Fruit peel	D-limonene and γ-terpinene	*Ae. aegypt*	[42]
7	*Citrus sinensis*	sweet orange	Fruit peel	Limonene	*Cx. Pipiens*	[43]
8	*Cymbopogon citartus*	Lemongrass	Leaves	Citral, neral and β-myrcene	*Ae. aegypti*	[44]
9	*Eucalyptus globulus*	Blue gum	Leaf	1,8-Cineol, α-pinene	*An. stephensi*	[45]
10	*Lantana camara*	Sage	Leaves, flower	Caryophyllene, eucalyptol and bicyclogermacerene	*Ae. aegypti*	[46]
11	*Mentha piperita*	Peppermint	Leaves	Diterpenes, Steroids, tannin, flavonoids, cardial glycosides, alkaloids, phenols, coumarin and saponin	*Ae. aegypti*	[47]
12	*Ocimum americum*	Lime basil	Leaf	6-methyl cinnamate	*Ae. aegypti*	[48]
13	*Ocimum basilicum*	Sweet basil, common basil	Leaf	Linalool and methyleuganol	*Ae. albopictus, Cx. triaeniorhynchus*	[49]
14	*Olea europaea*	Common olive	Leaves	Betulinic acid, uvaol ursolic acid, and maslinic acid	*An. arabiensis*	[50]
15	*Pelargonium*	Rose	Leaves	Geraniol, citronellol	*Ae. aegypti*	[51]

	graveolens	geranium				
16	*Piper longum*	Long pepper	Fruits	Pipernonaline	*Cx. pipiens pallens*	[52]
17	*Piper nigrum*	Black pepper	Fruits	Piperine	*An. arabiensis, An.coluzzii, An. funestus, An. gambiae* and *An. quadriannulatus*	[53]
18	*Rosmarinus officinalis*	Rosemary	Leaves	α-pinene, 1,8-Cineole, 1-Verbenon, Borneol, Geraniol	*Ae. Aegypti*	[54]
19	*Solanum lycopersicum*	Tomato	Leaves	carotenoids, lycopene	*Ae. Aegypti*	[55]
20	*Syzygium aromaticum*	Clove	Flower bud	Essential oil such as 2- methoxy-3-(2-propenyl)	*An. Stephensi*	[56]
21	*Zingiber offincinale*	Ginger	Rhizome	Zingiberene, kaemferol and zingibberol	*Ae. Aegypti*	[57]

Overall, mosquito repellents function by either masking the cues that attract mosquitoes to humans or by directly repelling mosquitoes through chemical or physical means (Fig.2).

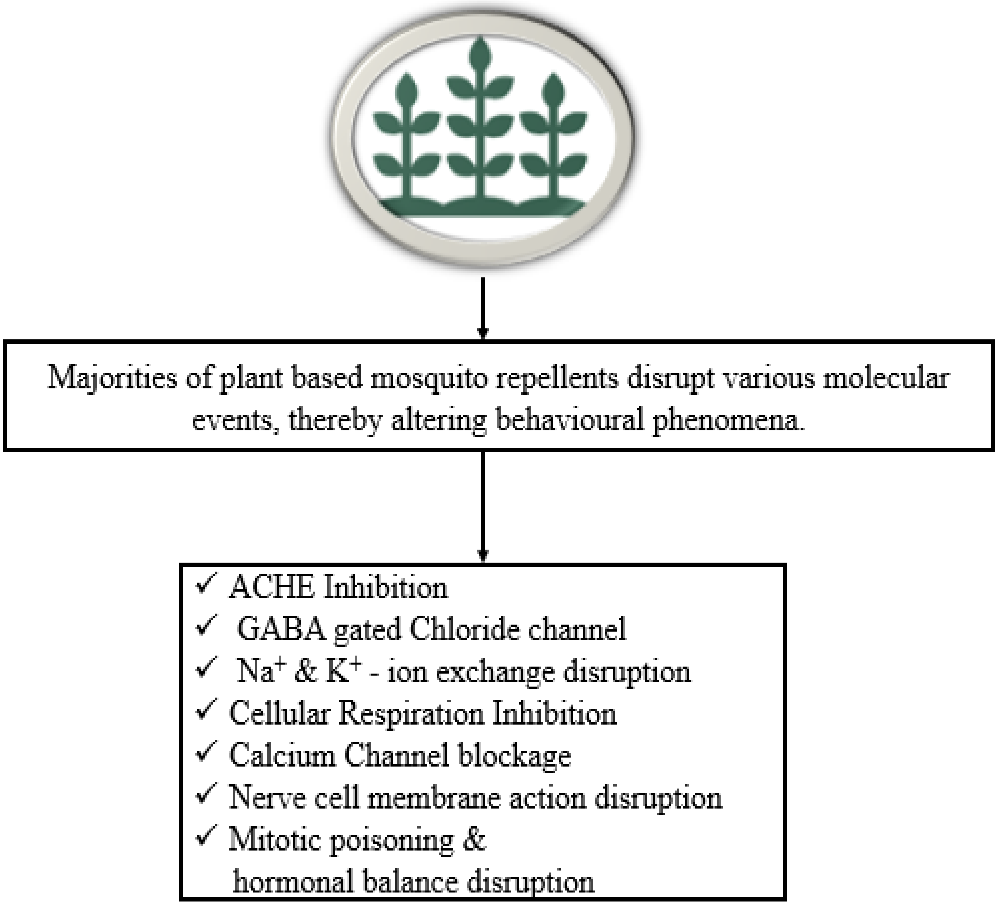

Figure 2: Mode of action of Mosquito Repellents

Mosquito repellent methods

Mosquitoes have been identified as an important insect vector for the spread of diseases in humans. Mosquito repellents are an effective preventive measure against vector-borne diseases. There is a wide range of insect/mosquito repellent products on the market. However, the effectiveness of these repellents in keeping mosquitos away from the skin is entirely dependent on their chemical composition. There are several methods for evaluating mosquito repellent against various mosquito species. The most used techniques such as Arm-In-Cage, Cone Bioassay test, Excito Chamber, Fabric test and Flammability test. [22-23]

Arm-In-Cage method:

The arm-in-cage test is the most common way to assess the efficacy of mosquito repellent formulations. The arm in cage test method is designed to evaluate the effectiveness of mosquito repellent formulations (40 x 40 x 40 cm). This mosquito repellent test includes topical repellents (such as lotions, cremes, and spray formulations) as well as impregnated textiles. The test cage contains 200 host-seeking female mosquitos. Repellent is applied to the volunteers' forearms and exposed to mosquitos every 30 minutes. The test can be performed for up to eight hours after application, or until the insect repellent becomes ineffective. [24-25] The effectiveness of a repellent compound is determined by calculating the total complete protection time (CPT) of the test mosquito repellent when compared to reference material.[26] CPT is defined as the time between repellent application and the first confirmed bite. The repellents become more effective as the CPT time increases.

The modified arm-in-cage test is a modification of the conventional arm-in-cage test procedure that follows the American Environmental Protection Agency's (EPA) guidelines. A modified arm-in-cage test, like the traditional arm-in-cage method, is used to assess the efficacy of topical repellents (creams, lotions, and spray formulations) and impregnated textiles. The test cage contains 30 host-seeking female mosquitos. Repellents are applied to the volunteers' forearms and exposed to mosquitoes every 30 minutes. Textiles involves wrapping the fabric around the forearms of four volunteers (two male and two female). The test can be conducted for up to eight hours after application, or until the insect repellent becomes ineffective (Fig.3). A comparison of the modified arm-in-cage test and the traditional arm-in-cage test using a standard repellent revealed that the modified setup provided longer protection times. Insect repellent formulations are designed to protect against insect-borne diseases and irritating insect bites.[27] Some of the studies demonstrated the use of cage tests in their study for mosquito repellent action. [28-30]

The percentage of repellency or protection time was calculated using the formula.

% Mosquito protection: $(U-T)/U \times 100$

Where U corresponds to the number of mosquitoes on untreated samples or control samples and T represents the number of mosquitoes on treated samples.

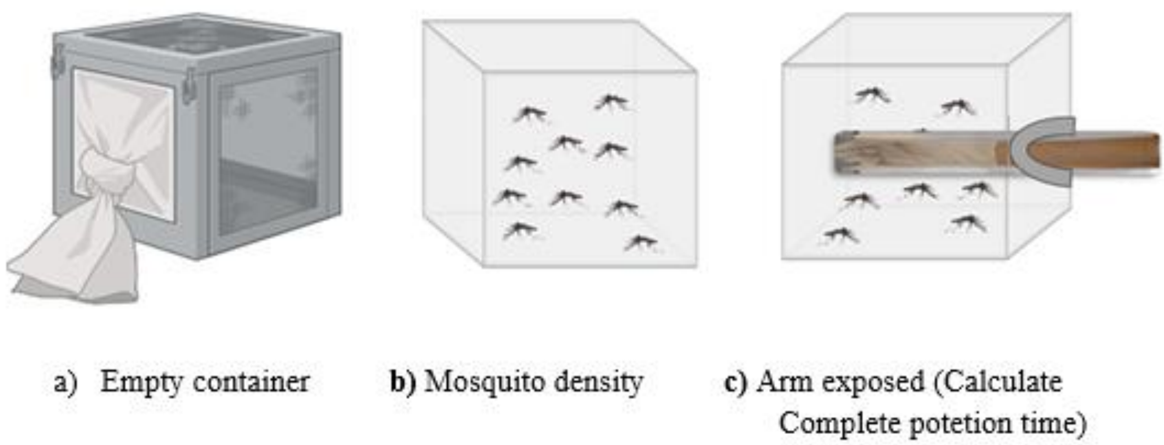

Figure 3: Modified Arm-In-Cage Method (Modified)

Cone test

The cone test was previously used to evaluate the toxicity of insecticide-treated bed nets against malaria (Fig. 2), and it can also investigate the toxicity of other impregnated (textile) surfaces. The fabric was treated and evaluated using the WHO cone test in accordance with the standard procedure described in WHO 1998: test procedures for insecticide resistance monitoring in malaria vectors, bioefficacy and persistance of insecticides on treated surfaces (WHO 1996). This test does not use human participants as bait to attract mosquitos to fabric, which is one of the benefits of this method. Because of this factor, researchers are less likely to use this method to conduct mosquito repellent tests on clothing. [31-32]

The use of artificial blood or animal blood as bait to attract host-seeking mosquitoes in this cone test may aid future studies in better assessing the efficacy of treated clothing. During the three-minute exposure, mosquitos may spend more time resting on the cone than on the treated surface. The 3-minute exposure test was carried out at a temperature of 27°C. The standard WHO plastic cone was placed on top of the treated surface of the sample and secured with masking tape.

Five to ten female mosquitoes were blown into the cone with an aspirator, and they were exposed to the treated surface. The low mosquito density used in this method allowed for easy observation of mosquito behaviour. The number of mosquitos resting on the treated samples was counted after a 3-minute exposure. After the exposition, the mosquitos were transferred to plastic cones for further observation. The plastic cup was kept in an insecticide-free environment and filled with 10% sucrose solution. The number of immobilized, knocked-down test mosquitos was counted one hour after exposure, and the mortality rate was calculated 24 hours later. [33-34]

The percentage mosquito repellency was calculated using the following formula:

% Mosquito mortality: (MR-MC)/(100-C) x 100

where MR represents the mosquito's mortality in test replicate while the MC corresponds to the mosquitoes mortality in control samples.

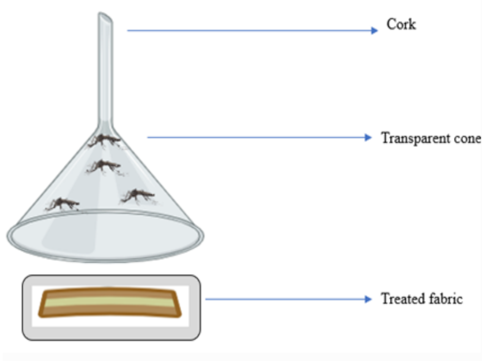

Figure 4: Cone Method

Excito Chamber test

The excito chamber method is a modified custom method for observing mosquito behavior changes (Fig. 3) as they move from treated to untreated fabric. This method, like the Cone test method, does not require the human subject to trap the mosquito. The box has one front and one exit panel, each with a single escape portal. The structure consists of a screened inner chamber, a glass holding frame, and a door cover. The mosquito was starved overnight or for at least 4 hours prior to the test. The behaviour of mosquitos was observed in terms of the number of mosquitoes that escaped to another space and the number of mosquitoes that remained inside the chamber filled with treated product. The observation is taken after 10- and 30-minute exposures. [35-36] The test was conducted in daylight and repeated four times. The percentage of mosquito repellency was calculated using the following formula:

% Mosquito repellency = (NES + NDE/NEX) x100

Where NES corresponds to the number of mosquitoes escaped, while the NDE refer to the number of mosquitoes dead and last is NEX represents the number of mosquitoes exposed.

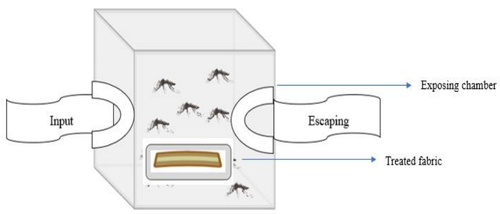

Figure 5: Excito Chamber

CONCLUSION:

In conclusion, the current review has provided valuable insights into the effectiveness and importance of mosquito repellents in safeguarding against mosquito-borne diseases, mode of action of various repellent types and their application methods. Moreover, continued research and adoption of suitable repellent strategies are crucial for minimizing the risks associated with mosquito bites and promoting public health.

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Conflict of interest

The authors have no conflict of interest.

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