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Natural and Synthetic Mosquito Repellents: Efficacy, Safety, Formulation Challenges and Future Directions

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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Review Article

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Abstract

Aims: to reveal effective plant-based mosquito repellent products as personal protection.
Discussion: Mosquitoes are among the most annoying hematophagy insects affecting human population. Mosquitoes are key vectors for severe diseases like malaria, dengue, lymphatic filariasis, yellow fever, and Japanese encephalitis, which represent significant global public health challenges, particularly as climate change expands their habitats. Personal protection through mosquito repellents is essential in integrated vector management strategies. This review compiles current scientific findings on both synthetic and plant-based mosquito repellents, focusing on their mechanisms, effectiveness, safety, environmental impact, and formulation methods.
Synthetic repellents such as DEET, picaridin, and IR3535 are known for their long-lasting efficacy; however, concerns regarding toxicity and environmental persistence, as well as shifting consumer preferences, have sparked renewed interest in natural alternatives. Essential oils and botanical

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extracts are biodegradable options but face limitations due to their shorter effectiveness, volatility, and instability in formulations.
Recent advancements in formulation science, such as nano-encapsulation, lipid-based carriers, and controlled-release systems, show promise in enhancing the stability, effectiveness, and consumer acceptance of natural repellents. This review identifies existing knowledge gaps and emphasizes the need for standardized evaluation methods, improved delivery systems, and collaborative research to promote the development of safe, cost-effective, and sustainable mosquito repellent solutions
Conclusion: The effort to establish a robust scientific basis for plant-based insect repellents is a significant and ongoing area of research, driven by a desire for safer, more sustainable alternatives to hazardous synthetic chemicals. These effort, however, need further work to validate reliability.

Keywords: Vector; control; biodegradable; environmentally friendly; safety; natural; chemical.

1. Introduction

Mosquitoes as significant threat to the public health, globally (Abbasi, 2025) and regionally (Barçante & Cherem., 2024) and their expanding existence in combination with global warming (Nair et al., 2025) shows potency of borderless in geographical perspective (Barçante & Cherem., 2024). It represented by the genera Aedes spp. (Abbasi, 2025), Anopheles spp. (Djihinto et al., 2022), and Culex spp. (Madhav et al., 2024) are an as they are known vectors for various protozoans, viruses, and bacteria which result in many life threatening diseases like malaria, filariasis, yellow fever, Japanese encephalitis, chikungunya, and dengue; a group of disease sometime classified as mosquito borne diseases (Lee et al., 2018). These diseases have been considered as a major obstacle to and severely hinder socioeconomic, environment and human development of developing countries particularly in the tropical region (Alqassim 2024). For the case of lymphatic filariasis, in 2024, global progress continued towards eliminating Lymphatic Filariasis (LF), with 21 countries finally validated as having eliminated it as a public health problem, including Brazil and Timor-Leste, though 657 million people in 39 countries still needed preventive treatment, particularly India (highest burden) and parts of Africa/Asia (Jabir & Rahi, 2025; World Bank, 2024).

Notwithstanding substantial attempts in recent decades to control and eliminate vector-borne diseases, malaria alone, as WHO estimates, still responsible for 263 million malaria cases (95% CI 238 million to 294 million) occurred globally in 2023 (Venkatesan, 2025). While global dengue epidemiology in 2024 noticeable a historic peak, which never happen before, where around the globe >14 million cases of morbidity and 10,000+ mortality reported, more than doubling the cases of previous year, determined mostly by an exceptional outbreak in the Americas region which exceed >13 million cases (Venkatesan, 2024). Other common vector borne disease named Lymphatic Filariasis (LF), just in the year 2024, have showed continuous global progress towards eliminating, with 21 countries validated as having eliminated LF as a public health problem, including Brazil and Timor-Leste, though 657 million people in 39 countries still needed preventive treatment, particularly India (highest burden) and parts of Africa/Asia (Jabir & Rahi, 2025). The global economic burden of malaria alone is colossal, with costs including lost productivity, healthcare spending, and reduced GDP, estimated in the tens of billions of dollars annually, impacting households (losing 2-6% income) and national economies, with one estimate suggesting tackling it could boost Africa's GDP by $16 billion a year, though specific total figures vary by study and timeframe.

Due to the potential upward trend previously mentioned, combined with the massive economic burden, integrated vector control and management, especially in this review is by the prevention of mosquitoes to feed on human (Singhamahapatra et al., 2020) could be better and wiser option than the cure of vector-borne disease (Tiffin et al., 2025). Principally, mosquito-borne diseases can be minimized by avoiding direct contact of human beings with mosquitoes (Onen et al., 2023). The application of mosquito repellents on potentially exposed skin area of vulnerable individuals living in areas where mosquito still a potential hazard is strongly recommended. Mosquito repellents emerge out as the best possible alternative in this regard, and this become the aim of study of this minireview, including its development and improvement.

2. Principles of Repellent

Repellents are chemicals that deter mosquitoes from host-seeking and biting (Meier et al., 2025). Insect repellents usually work by providing a vapor barrier dissuasive the arthropod from nearing into proximity with the skin surface (da Silva & Ricci-Júnior, 2020). These repellents create an effective virtual chemical based barrier between human beings and mosquitoes (Frances & Wirtz, 2005); reduce the biting of mosquitoes (Noguera-Gahona et al., 2025), thus diminish the probability of numerous mosquito borne diseases (Norris & Coats, 2017). Spatial repellents target the mosquito chemosensory systems of the mosquito's olfactory system function (Ray, 2015). How the virtual barriers works is as follows: The process involves interfering with the mosquito's highly sophisticated sensory systems (Wooding et al., 2020, Riffell, 2019). This complex olfactory system facilitate mosquito to track vulnerable human host primarily through the carbon dioxide -Carbon dioxide (CO_2) is one of the prominent sensory cues used by mosquitoes to find hosts for blood-feeding (Goyal et al., 2023)- which perceived during normal inhale-exhale respiratory process and the various chemical cues such as 1-Octen-3-ol, a key human body odor, emitted from human skin (Bello & Cardé, 2022).

Actually, to navigate the environment and search for hosts, mosquitoes utilize multiple sensory cues including carbon dioxide (CO_2), olfactory, visual and even humidity signals which act as a cross modal integration during its flight (Kato-Namba et al., 2025; Coutinho-Abreu, et al., 2022). CO_2 significantly enhances the sensitivity of mosquitoes to visual and olfactory signals by way of: (1) CO_2 urges stimulus to track and follow moving objects, (2) CO_2 empower mosquitoes to rapidly follow rousing and even low-contrast objects, (3) CO_2 enhances attraction to pleasant odors and avoidance of unpleasant odors. (Kato-Namba et al., 2025). Rather than forming a clear physical barrier, repellents primarily work by interfering with the mosquito's ability to locate its host (Meier et al., 2025, da Silva & Ricci-Júnior, 2020, Norris & Coats, 2017, Ray, 2015). Most of the commercial mosquito repellents are prepared using nonbiodegradable, synthetic chemicals like N, N-diethyl-3-methylbenzmide (DEET), dimethyl phthalate (DMP), and allethrin, which may lead to their higher exposure to the environment and, hence, the unacceptable health risks. This will be briefly discussed in the following section.

2.1 Synthetic Chemical Repellent

Synthetic chemical repellents are man-made compounds like N,N-dietil-meta-toluamida (DEET) (DeGennaro, 2015), Picaridin (Icaridin) (Shiau et al., 2022), and ethyl butylacetylaminopropionate or IR3535 (Moreau et al., 2020), aimed to protect against insects (mosquitoes, ticks) by primarily involves a twofold approach: they disrupt mosquito olfactory receptors directly (Riffell, 2019, Benelli & Pavela, 2018) and chemically mask human scent by reducing the volatility of human odorants on the skin (Liyanage & Perera, 2025, Afify et al., 2019). These chemical based repellent actually offers long-lasting, effective protection for personal use, e.g., skin or clothing (Luan et al., 2021). Furthermore, repellent already used spatially as an area treatment, which generally referred to as spatial repellents or emanators (Achee et al., 2022), which efficacy have been reported for control of Aedes-borne virus transmission in Peru and also malaria in Indonesia (Syafruddin et al., 2020).

Chemical repellent actually represents an incredibly important and evolving frontier in public health and vector control. though some (like Permethrin) are insecticides that kill on contact and are not aimed for dermatological use (Sharma et al., 2024).

Basically, chemical repellent work by interfering with insect receptors, and until recently, DEET considered being the gold standard not just for mosquito (Leal, 2014) but also for tick (Zheng et al., 2025). Picaridin is considered as effective as DEET but is often preferred for its less greasy feel and milder odor (Goodyer & Schofield, 2018). It also provides longer-lasting protection compared to DEET and is less likely to irritate the skin (Tavassoli et al., 2015). While ethyl butylacetylaminopropionate or IR3535 is generally considered a safe and effective insect repellent (Lo et al., 2018), suitable for all ages including children and pregnant women (MotherToBaby, 2024), with a good safety profile established over decades of use and endorsed by the WHO as low-risk. Even though according to Thavara et al in Thailand, its superior efficacy for use as a topical treatment against a wide range of mosquito species belonging to several genera (Thavara et al., 2001) but Colombo & Souza reported that, disinfection by-products

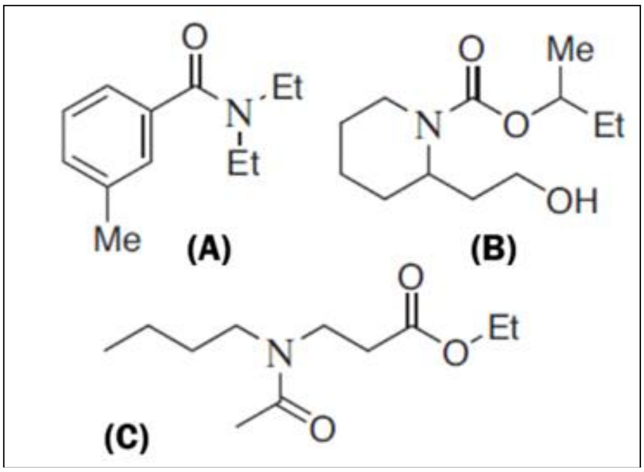

Fig. 1. Chemical structure of (A) N,N-dietil-meta-toluamida (DEET), (B) Picaridin (Icaridin), and (C) ethyl butylacetylaminopropionate or IR3535

(DBPs) from IR3535 presented predicted mutagenic and carcinogenic properties (Colombo & Souza, 2021). It must be acknowledged that variability between studies is very likely to occur and further discussions strongly advisable as new emerging research, due the dynamicity of this synthetic substance in the environment, rather than settled conclusions.

The synthetic repellent market is a growing global sector driven by vector-borne diseases, dominated by major global companies, utilizing key ingredients like DEET, picaridin, and permethrin. The market size is valued in the billions, with projections to reach over $11 billion by 2035, growing steadily ~ 5.6% Compound Annual Growth Rate or CAGR (Mosin-Abdul, 2023). Various product types consist of sprays, creams, lotions, vaporizers, coils, and wearable devices. In Brazil, synthetic repellents are produced on an industrial scale, with DEET, IR3535, and picaridin being the most commonly used (Noguera-gahona et al., 2025).

Due to their synthetic chemical composition, their environmental sustainability become the major threat and risk for its widespread use (Dubey & Mostafavi, 2023). It is very important that the authority establish a clear risks of synthetic repellents to better distinguish regulated use from misuse (when used as regulated it is safe and vice-versa). With an increasing awareness on public and environmental safety, a renewed interest on the use of natural products of plant origin is become more evident. The increasing desire and escalating demand for natural products as alternatives to their synthetic chemical counterparts, particularly in applications like insect repellents, is a truly significant modern trend. Consumers actually prefer “natural” more for preventatives than for curatives (Scott et al., 2020). Natural repellent products in general are considered effective, environment friendly (Abolade et al., 2024), biodegradable (Shen et al., 2024), low cost or affordable (Mng'ong'o et al., 2011), and readily available, e.g., repellent compounds derived from coconut oil (Zhu et al., 2018).

2.2 Natural Repellent

A natural mosquito or other insect repellent uses plant-based ingredients (Isman, 2020; Benelli & Pavela, 2018; Maia & Moore, 2011) like essential oils (Setyaningsih et al., 2020) extracted from basil (Lopes et al., 2016) lemon or citrus (Oshaghi et al., 2003), peppermint (Ansari et al., 2000), eucalyptus (Sheikh et al., 2021), citronella (Yadav et al., 2014), lavender and geranium (Sanei-Dehkordi, et al., 2023), clove of olive and coconut (Sritabutra & Soonwera, 2013) or extracts derived from neem (Chatterjee et al., 2023), soybean (Sansabhilla et al., 2020), and even celery (Kumar et al., 2014) to keep mosquitoes away. From those plant based extract or essential oil, Limonene, 1,8-cineole, geraniol, eugenol and citronellal are the most extensive studied active compounds that mostly appear in the essential oils of plants with repellent activity (da Silva & Ricci-Júnior, 2020, Isman, 2020).

This natural repellent often mixed with carrier oils (Alonso Leite Dos Santos et al., 2024) or other kind of natural binder (Das et al., 2021) and even nowadays with engineered nanostructured lipid carriers (Kechagia et al., 2024). These approach basically fulfill the wishes of many people by offering a chemical-free way to protect skin or create aromatic barriers, ancient compounds explained and supported by evidence based modern science (Isman, 2020, Vaughn et al., 2018). Even though its effectiveness varies and needs reapplication more often than DEET, and this will briefly discuss in the following section.

3. Advancement in Formulation

Once again, as a reminder, primary ingredients of natural repellent include lemon eucalyptus oil (PMD), citronella, catnip, lemongrass, peppermint, and neem oil, working by masking scents or emitting repellent odors. The basic formulation chemistry of mosquito repellents focuses on:

1. Optimizing the delivery (Abrantes et al., 2021). Optimizing drug delivery is an absolute necessity in modern medicine because it ensures that medications provide their maximum therapeutic benefit while simultaneously minimizing harmful side effects, thereby significantly improving patient outcomes and overall quality of life which basically revolutionizing healthcare (El-Tanani et al., 2025, Ezike et al., 2023, Meyers, 2023). Conventional drug administration often results in non-specific distribution, leading to suboptimal drug levels at the target site and unnecessary exposure of healthy tissues to the medication (Adepu & Ramakhrisna, 2021). The use of natural repellents has gained significant public (Ivanove et al., 2025) and market (Sumangala Bhat & Aravind, 2021) attention due to their perceived safety and eco-friendly profile, but it is crucial to understand that these products come with several inherent limitations that impact their effectiveness, particularly in high-risk environments (Almeida et al., 2023, Abrantes et al., 2021). The primary limitation centers on their inherent shorter duration of protection (Almeida et al., 2023) due to their rapid evaporation rate which determined by their air permeability (Mapossa et al., 2020) and due to those previous reasons mentioned, then obligating its users for frequent reapplication which brings serious implication for its effectiveness (Abrantes et al., 2021, Gryseels et al., 2015), and their variable efficacy compared to synthetic counterparts like DEET or (Noguere-Gahona et al., 2025). Perhaps, these difference based partially on mechanism of action where DEET affected proteins related to the insect's synapses and ATP production, whereas natural-based repellents increased transport, signaling, and detoxification proteins (Portilla Pulido et al., 2022).
2. Stability. Stability is a foundational pillar of drug delivery, and its importance cannot be overstated. Ensuring that a certain medication stays stable from the moment it is manufactured until the patient uses the very last dose (Wu et al., 2018) is absolutely critical for safeguarding patient safety, guaranteeing therapeutic efficacy, and ensuring regulatory compliance. An unstable drug is a true hazard to patients and also the public health, potentially leading to treatment failures or even toxic consequences. In the context of natural repellent, the mechanism of action of its plant based essential oils relies on the binding capacity of their chemical compounds to odorant-binding proteins (OBPs) at insect antennae, eliciting repellent effects (Fuentes-Lopez et al., 2024). The stability of these active ingredients is a critical factor, as it must keep effective under discrepant environmental conditions, particularly temperature and humidity (Kechagia et al., 2024; Mapossa et al., 2019)). Unlike many synthetic repellents which are continually engineered for robust persistence (Norris & Coats, 2017), natural active ingredients (often as essential oils or their isolated bioactive components like eucalyptus oil, citronella oil, and catnip oil) are inherently susceptible to degradation (Lopez et al., 2025). This vulnerability stems from their chemical structures, commonly in the form of terpenoid (Siddiqui et al., 2024) phenylpropanoid and sesquiterpenes (Li et al., 2024) chemical structures that dominate their composition. This chemical structure evolved in nature to be biodegradable (Nabi et al., 2025) rather than indefinitely stable, Essential oils are proven to have antimicrobial properties (Mangalagiri et al., 2021), which now used widely, e.g., for food preservation (Nabi et al., 2025, Sharma et al., 2020). Generally, its biodegradability properties as natural plant extracts occurred in its chemical composition breaking down via diverse microbial communities action into simpler substances like water and CO_2 (Silme &

Baysal, 2016), but differentiated by their complex composition (terpenes, esters, etc.) means degradation rates vary significantly (Ganosi et al., 2023), influenced by factors like oxygen through oxidative process (Jenner et al., 2011), light (Park et al., 2022), thermal and storage condition (Ganosi et al., 2023, Park et al., 2022), and specific microbial environments, e.g., sludge composting process (Wei et al., 2024), wastewater (Naz et al., 2025) and soil (Mena-Rodríguez et al., 2018). Unfortunately, several factors limit the development of plant-based repellent products, primarily including reduced efficacy duration at equivalent dosages (Yoon, 2025) combined with high volatility rate which causes them to easily evaporated (Sadgrove et al., 2022). From numerous study regarding topical drug delivery systems, various solvents and carriers, such as nanolipidic formulation (Javed et al., 2024), natural macromolecules (Dajic Stevanovic, et al., 2020), alcohol (Raab et al., 2025) or cyclomethicone (Johnson et al., 2011), are often included to improve solubility, promotes uniform distribution, and ameliorate skin absorption without causing irritation (Javed et al., 2024, Barnes et al., 2021, Dajic Stevanovic, et al., 2020). Furthermore, advancement in topical drug delivery also included emulsifiers (Mohd Narawi et al., 2020) and stabilizers like liposomal formulation (Hazarika, 2018) are used to create uniform mixtures, especially in water-based formulations, improving consistency and ease of application.

3. Efficacy of active repellent ingredients varies widely in efficacy (Sheikh et al., 2021, Maia & Moore, 2011), with synthetics like DEET (Zheng et al., 2025, DeGennaro, 2015) and Picaridin (Shiau et al., 2022, Goodyer & Schofield, 2018) generally offering longer protection. On the other hand, natural oils with anti-mosquito activities such as Lemon Eucalyptus, Citronella, Peppermint, Cinnamon, provide shorter, but effective, repellency, requiring frequent reapplication due to quick evaporation and volatility (Mapossa et al., 2020). This bring consequences to strategically deal with effectiveness (Webb & Russell, 2009) depending on concentration, mosquito species, and the repellent's mode of action (olfactory vs. contact).

Emulsions, aerosols, lotions, gels, and sprays are among the most common formulations (Drapeau et al., 2009), each type demanding different chemical considerations to ensure efficiency and effective release and prolonged action of the active compounds, such as DEET and essential oils (Meyers, 2023, Asadollahi et al., 2019). Encapsulation techniques, such as microencapsulation and nano-emulsion, have also been explored to provide controlled release of repellents over time, increasing the duration of mosquito protection while minimizing the evaporation of volatile components like essential oils. Data collected from recent scientific articles and patents show that micro particles are the most widely used extended release systems nowadays for natural repellent (da Silva & Ricci-Júnior, 2020) Such advanced formulation strategies (Meyers et al., 2023) help in balancing potency, longevity, and user comfort, making repellents more convenient and effective for consumers.

Additionally, distinguishing laboratory-scale formulation advances from commercially validated products is a very different things. The future prospect for natural repellents is challenging but promising, driven by consumer demand and increased awareness regarding eco-friendly, chemical-free options due to health/environmental concerns and rising morbidity and mortality due to mosquito-borne diseases, with significant market growth expected. Key innovations involve developing sustained-release nano-encapsulation technologies, exploring new botanical sources, and creating spatial repellents, while overcoming challenges like short action times and temperature sensitivity through advanced formulation science.

4. Conclusion

There were considerable efforts made to promote and improve the use of environmentally friendly and biodegradable, essential oils based natural repellents, particularly from botanical sources in order to change or at least minimize the unwanted effect from synthetic chemical based ant mosquito. However, limited period of effect and other variability is the major drawback of these products. There is an urge in need for formulation improvement, specifically to accommodate a safe, cost effective and highly efficient carriers/absorbent composition of matter that provides for a controlled time release of an aromatic substance, such as an essential oil or a combination of essential oils.

Disclaimer (Artificial Intelligent)

Author(s) hereby declare that no generative ai technologies such as large language models (chatgpt, copilot, etc.) And text-to-image generators have been used during writing or editing of this manuscript.

Competing Interests

Author has declared that no competing interests exist.

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