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## Human health risks to the use of chemical mosquito repellents: A review

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### Abstract

Mosquitoes are the main carriers of diseases and pests. Millions of deaths each year due to Mosquito-borne diseases. Using insect repellent reduces the risk of mosquito bites. To protect from mosquitoes and mosquito-related diseases, various types of mosquito repellents have been widely used, including liquid vaporizers, coils, and mats. The current use of synthetic pesticides to control insects and other arthropods causes several health problems for both humans and the environment. Because the health risks arising from complications of mosquito bites can become life-threatening, it is necessary to explore alternative methods to control them. As a result, there is increasing interest in alternative strategies, such as the use of plant-based mosquito repellents. This review will provide information on the potential side effects of uncontrolled use of insect repellents and alternative safe control suggested for mosquitoes.

**Keywords:** Diseases, mosquito repellents, potential toxicity, health hazards, strategies, humans

### Introduction

Worldwide, insect-borne illnesses are a concern to public health, particularly in tropical and subtropical regions. Numerous illnesses, such as yellow fever, dengue hemorrhagic fever, malaria, encephalitis in various forms, West Nile virus, and filariasis, are spread by mosquitoes<sup>[1]</sup>.

A report released by the World Health Organization (WHO) revealed that malaria caused 247 million cases and 619,000 deaths in 2021, and there is no significant progress in current malaria control<sup>[2]</sup>. Mosquito-borne diseases pose a threat to over 40% of the world's population and are becoming a more serious global health challenge<sup>[3]</sup>. Dengue has become much more commonplace worldwide, and there are now many documented epidemic areas<sup>[4]</sup>. Furthermore, several significant outbreaks affecting 89 countries and territories have recently been brought on by Zika, a recently discovered mosquito-borne illness linked to neurological complications<sup>[5]</sup>. Moreover, there are currently no effective medications or vaccines for diseases like dengue and Zika that are accessible to the general public, and conventional insecticide-based methods continue to be the mainstay of vector control<sup>[6]</sup>.

According to a recent study, mosquito species are expected to continue spreading across the globe in the ensuing decades, putting roughly 50% of the world's population at risk of contracting a virus through mosquito-borne disease by 2050<sup>[7]</sup>.

To reduce the number of mosquitoes, particularly in residential areas, people use chemical insecticides in a variety of forms, such as creams, coils, vaporizers, and mats. In recent years, insecticide resistance has become widespread in mosquito populations<sup>[8, 9]</sup>. Insecticides were heavily used in mosquito control, which polluted the environment and had an impact on organisms<sup>[10]</sup>.

In India, most of the population resides in an area where malaria is a concern. Comparably, dengue fever, which is endemic in about 112 countries worldwide and primarily affects tropical and subtropical urban areas, is on the rise. Approximately 3.5 billion people are at risk of contracting the virus including Indian metropolitan areas.

Other diseases carried by vectors, like Japanese encephalitis, lymphatic filariasis, and chikungunya, are a major concern in some parts of India<sup>[11-17]</sup>.

India's climate makes it a mosquito breeding ground. Mosquitoes cannot be completely eradicated from the nation. This is the situation in which insect repellents become useful. India's market for insect repellent is thought to be worth more than Rs 4 billion. The use of personal insect repellent is common among families with young children. Mosquito repellents come in a variety of forms, including oils, patches, and sprays as well as creams. Long-term inhalation of smoke and odor can have dangerous health effects on people, even though the severity of diseases caused by mosquito repellent use may not be immediately apparent.

Mosquito-borne diseases not only cause physical suffering and death, but also result in substantial economic losses, loss of productivity and decreased quality of life [18]. Mosquitoes not only carry diseases that afflict humans, they also transmit several diseases and parasites to which dogs and horses are very susceptible [19].

Epidemic of these diseases can lead to fear resulting in a loss of employment and productivity due to illness, disability and death [20].

Mosquito control research is now focusing on understanding the resistance of mosquitoes against synthetic insecticides as well as developing new strategies to overcome these resistance issues. Natural compounds are increasingly being explored as more effective and toxic alternatives to synthetic ones. Bioinsecticides composed of botanically or plant-derived compounds have been an ideal alternative due to their low level of toxicity to human health and the environment. This review provides current knowledge on the synthetic insecticides currently being used in mosquito control, how they influence the prevalence of insecticides resistance in mosquitoes, major plant-based insecticides, how they work, and the research on their potential mosquito-compatibility. It also provides an in-depth understanding on how biochemical compounds can be beneficial to synthetic ones as well as how we can overcome insecticide resistance issues in the fight against the transmission of mosquito diseases.

### Chemical Mosquito Repellents

**Table 1:** Most commonly used residential repellents are available in the form of creams, coils, mats and vaporizers [21]

S.No.	Repellent	Description
1.	Mat	Pads that have a volatile repellent imbedded in them that must be heated on a tiny electric heating plate in order to evaporate.
2.	Vaporizer(Dispensers)	A fluid-repellent reservoir bottle with a porous wick that allows an electric heater to evaporate the contents.
3.	Coil	Combination of flammable filler, coil-shaped binder, and repellent powder. When it burns, repellent is released into the air.
4.	Cream	Skin oil or cream with an added repellent.

Repellents can't completely stop mosquito bites but can make people less appealing to mosquitoes [22]. The effects of repellents can linger for 6–8 hours, whereas liquid mosquito incense typically lasts for 60 days [23]. People use repellents on a daily basis without understanding the ingredients or safety precautions [24]. One mosquito coil emits fine particulate matter equivalent to 75–137 cigarettes [25].

The burning of mosquito repellents can release harmful pollutants such as particulate matter, CO, VOCs, SO<sub>2</sub>, and NO<sub>2</sub> [26-29]. Acute respiratory infections such as colds, asthma attacks, and pneumonia are brought on by the constant or extended use of various repellents (at least 8–10 hours per day) [30]. Numerous research on diseases spread by mosquitoes and the health risks associated with using repellents have been conducted [31-35].

Mosquitoes serve as vectors for a range of human illnesses caused by protozoa, helminthes, and viruses [36-37]. Mosquito-borne diseases pose a significant risk to more than 80% of the global population, making them the primary contributor to the burden of human vector-borne diseases.

Transmission occurs primarily through mosquito bites, which play a pivotal role in the spread of these diseases [38-39]. Collectively, vector borne diseases account for more than 17% of all infectious diseases globally and are responsible for more than 700, 000 deaths annually. Among these diseases, malaria and dengue alone contribute to nearly 450,000 fatalities [40].

In 2017, the "Global Vector Control Response" (GVCR) 2017–2030 was approved by the World Health Assembly.

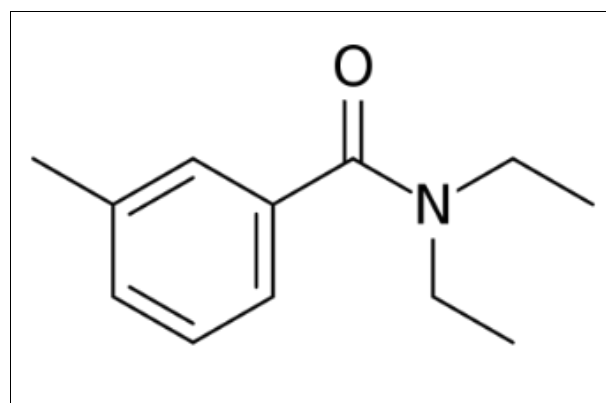
This initiative emphasizes the critical need to strengthen vector control as a key strategy for disease prevention and outbreak response, offering strategic advice to nations and

development partners. It asks for reorganizing vector control initiatives, bolstering infrastructure, increasing technical capability, fortifying monitoring and surveillance systems, and organizing the community. The goal of the GVCR is to support the attainment of national and international goals related to specific diseases, as well as the Sustainable Development Goals and Universal Health Coverage, by putting into practice a comprehensive approach to vector control. India is presently making efforts to eradicate these illnesses by 2030 [41].

### 2.1 Active Ingredients in Mosquito Repellents

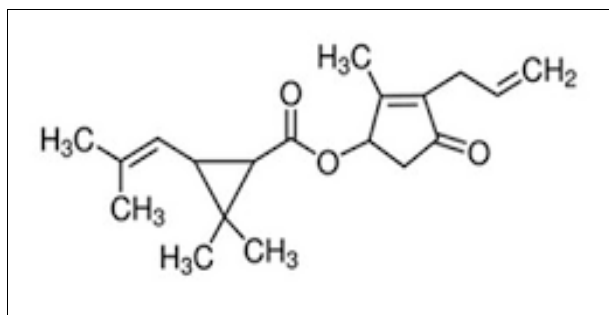
#### DEET (N,N-diethyl-meta-toluamide)

The primary active component of most topical insect repellents, N,N-diethyl-m-toluamide (DEET), was initially created by the US Department of Agriculture in 1946 as a military protection measure and was approved for use by the general public in 1957 [42, 43].



### Deet(N,N-diethyl-meta-toluamide) Allethrin (d-trans-ALLETHRIN)

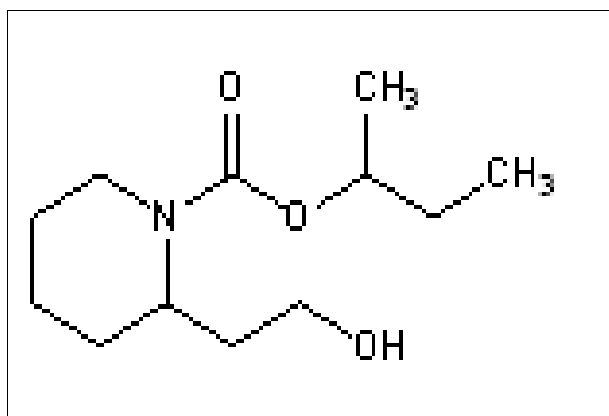
It is a Pyrethroid insecticide, widely used as a coil mosquito repellent, and is credited with being the first commercially synthesized product in 1949. Allethrin is widely used in a variety of products, including coils, mats, aerosol sprays, and liquid lotions [44].



### Allethrin (d-trans-ALLETHRIN)

#### 1. Picaridin (KBR 3023)

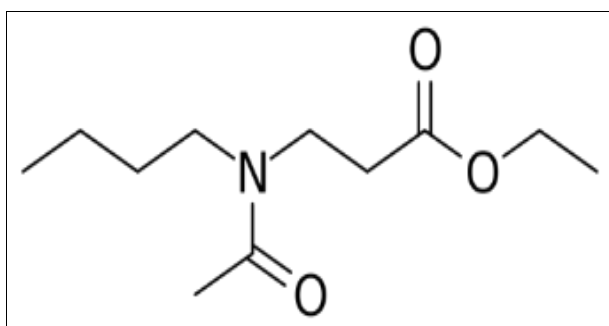
Icaridin, sometimes referred to as picaridin, is a topical insect repellent that works well on skin and clothing. It is a synthetic substance that was created in the 1980s. Among the trade names are Saltidin and Bayrepel. It was designed to resemble piperine, a naturally occurring compound found in the family of plants used to make black pepper. Applied to human skin or clothing, picaridin effectively deters ticks, fleas, chiggers, mosquitoes, and biting flies. These goods could be wipes, aerosols, liquids, or pump sprays.



### Picaridin (KBR 3023)

#### 2. Ethyl 3-[acetyl (butyl) amino] propanoate (IR3535)

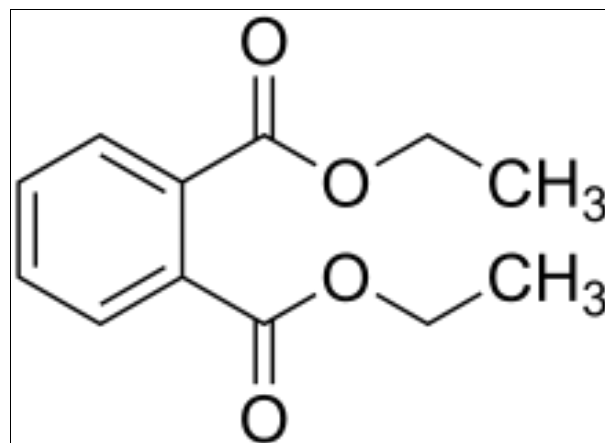
Ethyl 3-[acetyl (butyl) amino] propanoate (IR3535), an insect repellent, was created by Merck and Company. Back in 1975. When applied topically or orally, IR3535 causes less irritation and toxicity in mammals than DEET [45, 46].



### Ethyl 3-[acetyl (butyl) amino] propanoate (IR3535)

#### 3. Diethyl phthalate (DEP)

Sulfuric acid, phthalic anhydride, and ethanol react to form diethyl phthalate, a colorless liquid used in industry. Not only is diethyl phthalate a component of insecticide sprays and mosquito repellents, but it is also utilized in skin care products and makeup [47].



### Diethyl phthalate (DEP)

Due to pyrethroid and DDT resistance issues worldwide, they have been used as alternative insecticides in IRS, but they have a shorter residual effectiveness, high toxicity to mammals, and are more costly compared to the others that limit their persistent long-term usage.

### Adverse effect of Mosquito Repellents

Skin reactions, neurological, and cardiovascular disorders are the most common adverse effects of overexposure to DEET that have been reported [48-54]. Human self-poisoning through ingestion or excessive dermal application has been observed to cause neurological effects, such as encephalopathy and seizures [55-58]. Studies on human nasal mucosal cells [59], Hodgkin lymphoma, and soft tissue sarcomas [60] have observed that DEET may have carcinogenic effects.

The most toxic structural form of allethrin that is used to control parasites in animal systems is allethrin d-trans isomer [61-64]. It can be neurotoxic because it alters the permeability of the membrane to Na<sup>+</sup> and K<sup>+</sup> ions, stimulating neurons in the process [65-66]. The main cause of skin and respiratory allergies is overexposure to allethrin [67-68]. Although it takes time, anyone who works with chemicals or sprayers frequently runs the risk of this. Ingestion is extremely rare and unintentional, but it can result in potentially fatal symptoms such as vomiting, nausea, sore throat, stomach pain, oral ulcers, increased secretions and/or dysphagia, coma, and convulsions [69-70]. Pregnant women, small children, and infants are particularly vulnerable to it. Eye irritation brought on by IR3535 overuse [71].

Researchers have discovered that the vapor phase of mosquito repellents contains carbonyl compounds, such as formaldehyde and acetaldehyde, which have a potent irritating effect on the upper respiratory tract [72-73]. Pyrethroids cause oxidative stress and lower antioxidant levels [74-75]. The smoke and vapors from mosquito repellents contain volatile organic compounds and free radicals, which are major causes of DNA and tissue damage. They may induce apoptosis, necrosis, inflammation, and carcinogenesis.

These repellents are primarily applied at night, particularly in

Asian nations, where the vapors released or burned during the night can have toxic effects on the body as a whole [76]. When a mosquito coil is burned overnight, heavy metals, aldehyde, and carbon particles are released. When these substances are inhaled, the lungs' tissues sustain cellular damage and the mucous membrane is destroyed [77]. As an insecticide, pyrethrins and allethrins are present in the majority of mosquito repellents [78]. Since pyrethrum-based insecticides have a fast metabolism and almost no accumulation, they are relatively low-risk toxins for mammals. However, long-term exposure to these highly toxic repellents can have serious negative health effects because they are packed with toxic chemicals. Additionally, burning or spraying these repellents releases a large amount of toxic particulate matter, which mixes with indoor air and eventually pollutes the air [79]. Pesticides are essential tools in controlling insect pests that affect both agriculture and public health; their indiscriminate use can lead to adverse consequences [80].

### Conclusions and Safe alternatives to chemical mosquito repellents

The main objective of this study was to learn more about the use of Mosquito repellents and their potential health risks to humans. Recent research has shown that exposure to different types of mosquito repellent may be detrimental to one's health. It is important to find a balance between effective pest control and minimizing the negative effects of pesticides on the environment and on human health. Appropriate regulation and sustainable practices are essential for achieving this. There is a growing need to find new ways to prevent and treat mosquito-borne illnesses such as Zika virus, dengue virus, Japanese encephalitis, and other diseases [81]. Biological control agents are an important alternative to chemical insecticides, as they are sustainable, cost-effective, safe for humans, and do not create any pollution of the environment. As a result, researchers are increasingly looking for plant-based mosquito repellents as alternatives [82]. Natural plant extracts with pesticidal properties have been confirmed in more recent studies [83-85].

Before synthetic chemicals were developed, it was known that some essential oils from plants had insect- and mosquito-fighting properties. Repellents made from plants usually do not present any toxicity risks to humans or pets, and are easy to degrade in the environment. Generally, natural products are considered safer for human consumption than manufactured chemicals. New areas of interest for the design of new mosquito-repellent formulations are natural polymers, which are derived from natural sources [86]. In recent years, many institutions and researchers have started to create natural active ingredients, with a particular emphasis on plant-based ingredients [87]. Still research is going on eco-friendly and non-toxic compounds as insecticide.

In addition, public health campaigns should inform people about the adverse effects of using mosquito repellents, and encourage them to reduce their use of chemical-based repellents and increase the use of natural alternatives.

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