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Natural extracts as a sustainable alternative for the control of *Aedes aegypti*: an updated review

Extratos naturais como alternativa sustentável para o controle do Aedes aegypti: uma revisão atualizada

Oscar H. Pardo Cuervo*(0000-0003-4357-404X), Laura Valentina Barrera Martínez (ORCID 0009-0000-5143-8764), Ingrid Dayana Jiménez Camacho (ORCID 0000-0002-3425-6448), Andrea Camila Martínez Gordon (ORCID 0009-0005-9322-9852), Edwin Alejandro Figueredo López (ORCID 0009-0007-7881-3801), Nidya Alexandra Segura Guerrero (ORCID 0000-0001-5810-4847)

Facultad de Ciencias Básicas, Universidad Pedagógica y Tecnológica de Colombia, Tunja, Boyacá, Colombia. *Author for correspondence: oscarhernando.pardo@uptc.edu.co

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ABSTRACT

Aedes aegypti is the primary vector of viruses that cause diseases such as dengue, yellow fever, Zika, and Chikungunya, leading to high rates of morbidity and mortality in humans and substantial healthcare costs. The most common method for mosquito control involves the use of synthetic insecticides; however, continuous use of these substances leads to species resistance and environmental contamination. In response to these challenges, natural extracts have emerged as a promising alternative for vector control as they contain components potentially toxic to mosquitoes. The aim of this review is to present the current state of the use of natural extracts as a strategy for controlling both larval and adult *Ae. aegypti*. By means of information retrieval from databases, considering original articles published from 2018 to 2023, we sought information related to the plant part used for extract obtainment, extraction methods, and solvents used. A total of 676 articles were found, of which 35 met the established criteria. In these publications, 38 families, 69 genera, and 87 species of plants were identified, with a particular emphasis on the Asteraceae, Anacardiaceae, Myrtaceae, and Lamiaceae families due to their higher number of species used in research. On the other hand, the most commonly used methods for obtaining extracts included maceration with subsequent filtration, as well as Soxhlet extraction. Meanwhile, the preferred solvents for extract obtainment were ethanol and water. In conclusion, there is widespread use of plant extracts as insecticides, with extraordinary potential to control vector populations such as *Ae. aegypti* and, in turn, contribute to the reduction of arbovirus transmission by this mosquito.

KEYWORDS: *Aedes aegypti*; arboviruses; natural extracts; vector control; insecticide.

RESUMO

O *Aedes aegypti* é o principal vetor de vírus que causam doenças como dengue, febre amarela, Zika e Chikungunya, levando a altas taxas de morbidade e mortalidade em humanos e a custos substanciais de saúde. O método mais comum de controle do mosquito envolve o uso de inseticidas sintéticos; entretanto, o uso contínuo dessas substâncias leva à resistência das espécies e à contaminação ambiental. Em resposta a estes desafios, os extratos naturais surgiram como uma alternativa promissora para o controle de vetores, pois contêm componentes potencialmente tóxicos para os mosquitos. O objetivo desta revisão é apresentar o estado atual do uso de extratos naturais como estratégia de controle tanto larval quanto adulto de *Ae. aegypti.* Por meio da recuperação de informações em bases de dados, considerando artigos originais publicados de 2018 a 2023, buscamos informações relacionadas à parte da planta utilizada para obtenção do extrato, métodos de extração e solventes utilizados. Foram encontrados 676 artigos, dos quais 35 atenderam aos critérios estabelecidos. Nessas publicações foram identificadas 38 famílias, 69 gêneros e 87 espécies de plantas, com destaque especial para as famílias Asteraceae, Anacardiaceae, Myrtaceae e Lamiaceae devido ao maior número de espécies utilizadas em pesquisas. Por outro lado, os métodos mais utilizados para obtenção de extratos incluíram maceração com posterior filtração, bem como extração Soxhlet. Enquanto isso, os solventes preferidos para obtenção do extrato foram etanol e água. Concluindo, existe um uso generalizado de extratos de plantas como inseticidas, com potencial extraordinário para controlar populações de vetores como *Ae. aegypti* e, por sua vez, contribuir para a redução da transmissão de arbovírus por esse mosquito.

PALAVRAS-CHAVE: *Aedes aegypti,* arbovírus, extratos naturais, controle vetorial, inseticida.

INTRODUCTION

Aedes aegypti (Linnaeus, 1762) (Diptera: Culicidae) is a cosmopolitan species found in tropical and subtropical regions worldwide, with its reproduction favored by climate and environmental conditions (REINHOLD et al. 2018, PANDEY et al. 2021). The species originates from the tropical belt of Africa, where two subspecies are found: *Ae. aegypti queenslandensis* and *Ae. aegypti formosus*, a darker and smaller wild mosquito (NELSON 1986). *Ae. aegypti* in its typical form is distributed in the Americas and is believed to have been transported to the New World in water barrels on ships during early European explorations and colonizations (NELSON 1986, SANTOS et al. 2022).

Ae. aegypti is the most extensively studied mosquito species as it is the primary vector of arboviruses causing diseases such as dengue (DENV), Zika (ZIKV), yellow fever (YFV), and Chikungunya (CHIKV), which pose significant public health concerns (BRAACK et al. 2018). Currently, there are no specific medications to treat these diseases, and there are no vaccines or antiviral strategies against zika and chikungunya viruses. In contrast, yellow fever can be prevented by the YF-VAX® vaccine, considered effective and safe, which has been used for over 60 years for active immunization of children and adults against YFV infection (PAHO 2023). However, although there is a vaccine against DENV, there is no consensus on the efficacy of the licensed dengue CYDTDV vaccine (Dengvaxia®) because it does not provide the same level of protection against all four viral serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), and specific criteria for its use in humans are required, including being between nine and 45 years old, having antibodies against DENV before immunization, and residing in high-endemic areas (FLASCHE et al. 2019, THOMAS 2023, PINTADO & FERNANDEZ-SESMA 2023, WHO 2009 2019 2022 2023).

Considering the high risk associated with mosquito proliferation and viral transmission, the main strategy has been the control of the vector through the use of synthetic organophosphates and pyrethroid insecticides, which reduce its population density (ANOOPKUMAR & ANEESH 2022). However, the increasing use of chemical insecticides and their mismanagement have led to changes in the vital functions and behavior of *Ae. aegypti*, resulting in resistance to commercially used insecticides and, in turn, a reproductive advantage for resistant mosquitoes over their susceptible counterparts, promoting an increased risk of arbovirus transmission. Furthermore, the use of these chemicals affects water, soil, plant life, as well as other species of wildlife and beneficial insects that maintain ecosystem balance (AMELIA et al. 2018, ROMERO 2018, WALSH 2021, REZENDE et al. 2022).

Natural extracts are an alternative vector control method against *Ae. aegypti* due to their effectiveness, rapid biodegradation, and minimal negative effects on the environment and non-target species (AL-ZAHRANI et al. 2019, ALYAHYA et al. 2021, SILVÉRIO et al. 2020). These substances are known to contain a wide range of chemical components used as insecticides for mosquito control in general, in addition to having antibacterial, antifungal, and repellent activities (BOSLY 2022). Moreover, the effects of these substances interfere with feeding, oviposition, and disruption of insect growth and development processes, making them a safer option for the environment and human health (MARTIANASARI & HAMID 2019, LUZ et al. 2020).

Unlike commercial chemical insecticides, plant-derived insecticides consist of mixtures of chemical compounds that act on the physiological and behavioral processes of the target population (RODRIGUES et al. 2019, LUZ et al. 2020). Therefore, the probability of mosquitoes developing resistance to these substances is minimal (FALKOWSKI et al. 2020, QIE et al. 2022).

Plant families such as Solanaceae, Asteraceae, Cladophoraceae, Labiaceae, Miliaceae, Oocystaceae, and Rutaceae are among the most known for their larvicidal, adulticidal, or repellent activity against different mosquito species (SHAJAHAN et al. 2022). It should be noted that differences in insecticidal bioactivity of plant-derived extracts may occur because the efficacy of phytochemicals can vary depending on the plant species, parts used, plant age, even the target vector species and the region it inhabits, as it has been reported that for the same mosquito species, resistance can vary by location (FALKOWSKI et al. 2020, ALYAHYA et al. 2021, QIE et al. 2022). Additionally, another important factor is that the extraction of active biochemical compounds from plants depends on the polarity of the solvents used, as they can affect the potency of the extracted compounds (FALKOWSKI et al. 2020, QIE et al. 2022).

Taking into consideration the aforementioned, the fundamental objective of this study is to provide a comprehensive analysis of the current state of using natural extracts as a control strategy for both larvae and adults of *Ae. aegypti*. This analysis is based on a thorough review of scientific databases, aiming to provide a comprehensive overview of the plant species most commonly used for obtaining natural extracts with insecticidal properties. Furthermore, it addresses the topic of solvents and methods used for the extraction of these compounds and evaluates their effectiveness in combating the vector mosquito.

METHODOLOGY

This literature review was conducted by using various electronic databases, including ScienceDirect, Google Scholar, Elsevier, Jstor, Scielo, SpringerLink, and Pubmed. Both English and Spanish keywords such as "*Aedes aegypti*", "natural extracts", "insecticides", "adulticide", and "larvicide" were employed. Studies published between *February 2018 to March 2023* were selected if they addressed the use of natural extracts against the *Ae. aegypti* mosquito and described insecticidal bioactivity in both its adult and larval forms. Furthermore, studies focusing solely on ovicidal and pupicidal effects, those lacking information about the plant part used or the extraction method, as well as those indicating the commercial acquisition of the extract, were excluded. Studies that did not fall within the specified time frame were also excluded. Additionally, research presented in the format of academic theses was not considered as part of this review.

PLANTS WITH POTENTIAL INSECTICIDAL EFFECT AGAINST *AE. AEGYPTI*

The search conducted in the electronic databases yielded a total of 676 articles, of which 35 were selected for analysis and inclusion in this review after applying information exclusion criteria. We identified 87 plant species belonging to 38 families, with Asteraceae being the most representative with 25 species. AGUIRRE et al. 2018 stated that natural extracts from the Asteraceae family exhibited high larvicidal activity against *Ae. aegypti*, and the best results in terms of mortality rate were obtained when evaluating leaf extracts of species such as *Jaegeria hirta* (97%), *Helicopsis oppositifolia* (94%), and *Austroeupatorium inulaefolium* (90%). In contrast, species with the lowest mortality rates in this family included *Bidens pilosa* (6%), *Tagetes erecta* (4%), *Artemisia vulgaris*, *Acmella ciliata* (2%), *Baccharis trinervis*, *Bunchosia nitida* (1%), and *Clibadium surinamense*, where no mortality was observed (AGUIRRE et al. 2018).

Species from the Myrtaceaea family have not shown such favorable results, as in the case of *Melaleuca leucadendra*, which reached a mortality rate of 47% at a concentration of 40000 ppm. These results indicate differences in the insecticidal potential that can exist among species of the same family (GHOSH et al. 2012, PINEDA et al. 2019). On the other hand, the larvicidal activity of *Croton nepetaefolius* from the Euphorbiaceae family has been evaluated, obtaining a lethal concentration fifty (LC50) of 81.7 ppm (RODRIGUES et al. 2019).

It is important to continue conducting studies related to insecticidal activity because most of the families found during the information review only had one species studied, and the lethality values in *Ae. aegypti* varied greatly (Table 1).

Table 1. Families and species studied with insecticidal potential against *Ae. aegypti.*

Family	Species	References
Asteraceae (25 sp)	*Jaegeria hirta, Helicopsis oppsitifolia, Austroeupatorium inulaefolium, Conyza bonariensis, Hypochoeris radicata, Acmella mutisii, Galinsoga quadriradiata, Camellia japonica, Taraxacum officinale, Ambrosia cumanensis, Echeveria coccinea, Camptotheca acuminata, Fleischmannia microstemon, Ageratum conyzoides, Celtis caudata, Schistocarpha eupatorioides, Bidens pilosa, Tagetes erecta, Acmella ciliata, Baccharis trinervis, Bunchosia nitida*	AGUIRRE et al. 2018
	Artemisia vulgaris	AGUIRRE et al. 2018 NINDITYA et al. 2020
	Saussurea costus	ALI & VENKATESALU 2020
	Clibadium surinamense	AGUIRRE et al. 2018 CRUZ et al. 2022
	Acmella oleracea	ARAÚJO et al. 2020
Anacardiaceae (6sp)	*Mangifera laurina, Mangifera casturi,*	MAHDI et al. 2022

	Mangifera indica, Mangifera odorata, Mangifera caesia, Mangifera foetida	
Myrtaceae (4 sp)	*Melaleuca leucadendra*	PORUSIA & SEPTIYANA 2021
	Syzygium aromaticum	RODRIGUES et al. 2019
	Myrrhinium atropurpureum, Neomitranthes obscura	CARNEIRO et al. 2020
Fabaceae (4 sp)	*Saraca asoca*	SHARMA et al. 2019
	Cassia alata	MUANGMOON et al. 2018
	Cassia fístula	RAJASHEKARA et al. 2021
	Acacia farnesiana	GRANADOS et al. 2021
Solanaceae (3 sp)	*Lycium barbarum*	MUANGMOON et al. 2018
	Solanum indicum	RAJASHEKARA et al. 2021
	Solanum mammosum	PILAQUINGA et al. 2019
Euphorbiaceae (3 sp)	*Vernicia fordi*	MUANGMOON et al. 2018
	Croton nepetaefolius	RODRIGUES et al. 2019
	Acalypha fruticosa	ALYAHYA et al. 2021
Annonaceae (3 sp)	*Annona squamosa L, Annona cherimolia L*	OLIVEROS et al. 2022
	Annona muricata	PRADA et al. 2021
		BOBADILLA & REYES 2020
Malvaceae (2 sp)	*Waltheria viscosissima*	FERREIRA et al. 2019
	Helicteres velutina K. Schum	FERNANDES et al. 2021
Bignoniaceae (2 sp)	*Tecoma stans*	HARI & MATHEW 2018
	Tabebuia heptaphylla	BORGES et al. 2019
Lamiaceae (4 sp)	*Leonurus japonicus*	MUANGMOON et al. 2018
	Hyptis suaveolens	
	Origanum vulgare	HARI & MATHEW 2018
	Thymus vulgaris	DE OLIVEIRA et al. 2021
Apocynaceae (2 sp)	*Nerium oleander*	
	Tabernaemontana cymosa Jacq	OLIVEROS et al. 2022
Piperaceae (2 sp)	*Piper ovatum*	KANIS et al. 2018
	Piper solmsianum	MACEDO et al. 2018
Lauraceae (2 sp)	*Litsea petiolata*	MUANGMOON et al. 2018
	Persea americana	LOUIS et al. 2020
Moraceae (2 sp)	*Artocarpus altilis*	MUANGMOON et al. 2018
	Artocarpus blancoi	PINEDA et al. 2019
Amaryllidaceae (2 sp)	*Crinum asiaticum*	MUANGMOON et al. 2018
	Allium sativum	PRADA et al. 2021
Rubiaceae (2 sp)	*Pavetta tomentosa, Tarenna asiatica*	PRATHEEBA et al. 2019
Zingiberaceae (2 sp)	*Alpinia conchigera*	MUANGMOON et al. 2018
	Curcuma amada	RAJASHEKARA et al. 2021
Brassicaceae (2 sp)	*Brassica pekinensis, Brassica juncea*	MUANGMOON et al. 2018
Cucurbitaceae (1 sp)	*Momordica charantia*	MUANGMOON et al. 2018 MITUIASSU et al. 2021
Moringaceae (1 sp)	*Moringa oleifera*	MUANGMOON et al. 2018 DE SANTANA et al. 2019
Boraginaceae (1 sp)	*Trichodesma indicum*	CHELLAPPANDIAN et al. 2019
Verbenaceae (1 sp)	*Lantana camara*	HARI & MATHEW 2018
Caryocaraceae (1 sp)	*Caryocar brasiliense*	MORAIS et al. 2020
Calophyllaceae (1 sp)	*Mammea americana L.*	OLIVEROS et al. 2022
Sapotaceae (1 sp)	*Manilkara zapota*	RAJASHEKARA et al. 2021
Asparagaceae (1 sp)	*Sansevieria trifasciata*	
Araceae (1 sp)	*Homalomena aromatica*	MUANGMOON et al. 2018
Ebenaceae (1 sp)	*Diospyros rhodcalyx*	
Irvinggiaceae (1 sp)	*Irvingia malayana*	
Menispermaceae (1 sp)	*Cissampelos pareira*	
Primulaceae (1 sp)	*Ardisia polycephala*	
Smilacaceae (1 sp)	*Smilax peguana*	

Dioscoreaceae (1 sp)	*Tacca chantrieri*	
Nyctaginaceae (1 sp)	*Bougainvillea spectabilis*	SHARMA et al. 2019
Amaranthaceae (1 sp)	*Chenopodium album*	
Chorellaceae (1 sp)	*Chlorella sp*	SIGAMANI et al. 2020
Celastraceae (1 sp)	*Maytenus guianensis*	MARTINS et al. 2021
Cornaceae (1 sp)	*Alangium salvifolium*	THANIGAIVEL et al. 2018
Meliaceae (1 sp)	*Swietenia mahagon*	VASANTHA et al. 2021

Furthermore, Figure 1 represents the parts of plants used to obtain extracts with potential insecticidal power, with leaves being the most used with 40.3%, of which 80.6% of the studies found evaluated the larvicidal activity, and 19.4% evaluated the adulticidal activity in *Ae. aegypti*. Some studies that assessed leaf extracts showed good results against both larvae and adult mosquitoes. For example, extracts obtained from *Pavetta tomentos*a and *Tarenna asiatica* exhibited 90% larval mortality after 24 hours of exposure at concentrations of 1223 ppm and 1992 ppm, respectively. For adults, concentrations of 4100 µg/ml for *P. tomentosa* and 11852 µg/ml for *T. asiatica* were required to achieve 90% mortality one hour post-exposure (PRATHEEBA et al. 2019). 12.7% corresponds to natural extracts obtained from fruit peels; in this case, all studies evaluated the larvicidal effect. For example, extracts obtained from *Acacia farnesiana* showed a mortality rate of 95.2%, although the extract concentration used was not reported in the article (GRANADOS et al. 2021). Similarly, natural extracts of *Persea americana* isolated through methanol maceration resulted in a 90% mortality rate at a concentration of 86.59 ppm (LOUIS et al. 2020). Another species with larvicidal potential is *Momordica charantia*, which exhibited 87% larval mortality at a concentration of 100 µg/ml (MITUIASSU et al. 2021). Regarding the parts of the plant least used to obtain extracts, 10.9% corresponded to seeds, 9.1% roots and stems, 5.5% flowers and traces of wood and only 1.8% used the entire plant.

Finally, in one study, extracts from *Chlorella sp*. algae cells were used against *Ae. aegypti* larvae, resulting in a 50% mortality rate at concentrations of 116.82 ppm and 159.20 ppm using chloroform as a solvent, and 445.16 ppm and 703.49 ppm using methanol as a solvent. These results highlight the importance of continuing research by using different parts of plants to specifically assess the larvicidal potential of each. Additionally, it is crucial to expand the number of studies focusing on the adult stage of the vector, as most of the research is concentrated on larvicidal activity. However, it is important to combine control measures at different stages of development to achieve better results in the control of Ae. aegypti and, consequently, in the control of arboviruses and the diseases they cause.

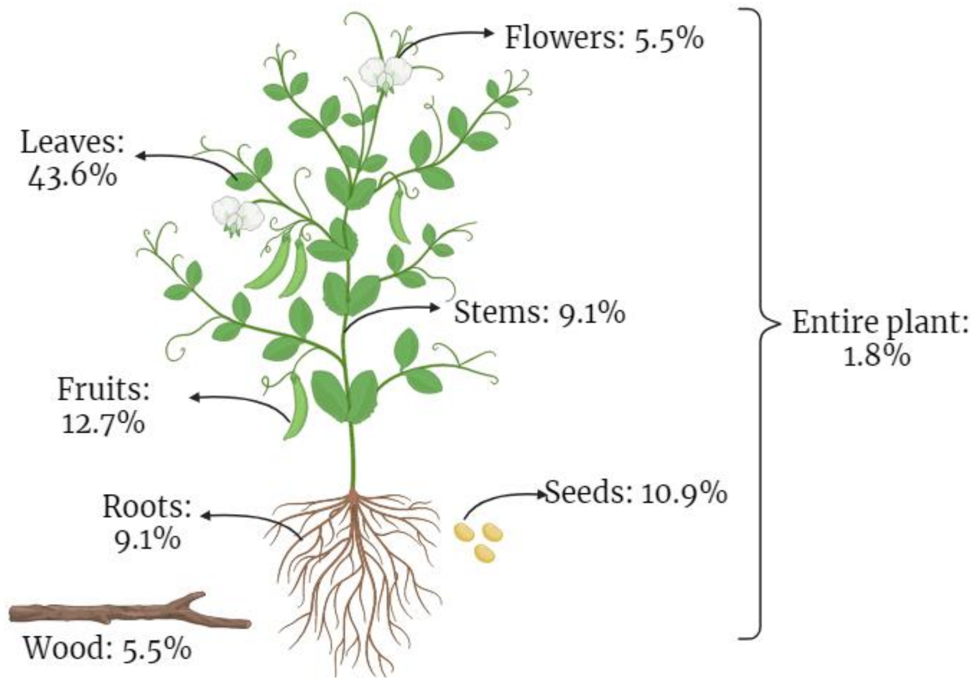

Figure 1. Percentage of usage of different plant structures employed for the extraction of natural extracts with insecticidal activity against *Ae. aegypti.*

EXTRACTION METHODS FOR THE PRODUCTION OF PLANT-BASED INSECTICIDES

The supplementary information includes a table that shows the analyzed papers that include some type of control, phytochemical analysis, types of active compounds, regional distribution, as well as bioassay methodologies conducted. Seven extraction methods were identified for the production of plant-based insecticides with activity against *Ae. aegypti*. The most commonly employed extraction method was maceration with subsequent filtration, with a total of 20 studies, followed by Soxhlet extraction with eight, simple extraction with two, and finally, hydrodistillation (Clevenger) and liquid-liquid extraction, each with one study (Figure 2). However, it is important to note that none of the studies compared different extraction methods to establish potential differences when evaluating *Ae. aegypti* mortality.

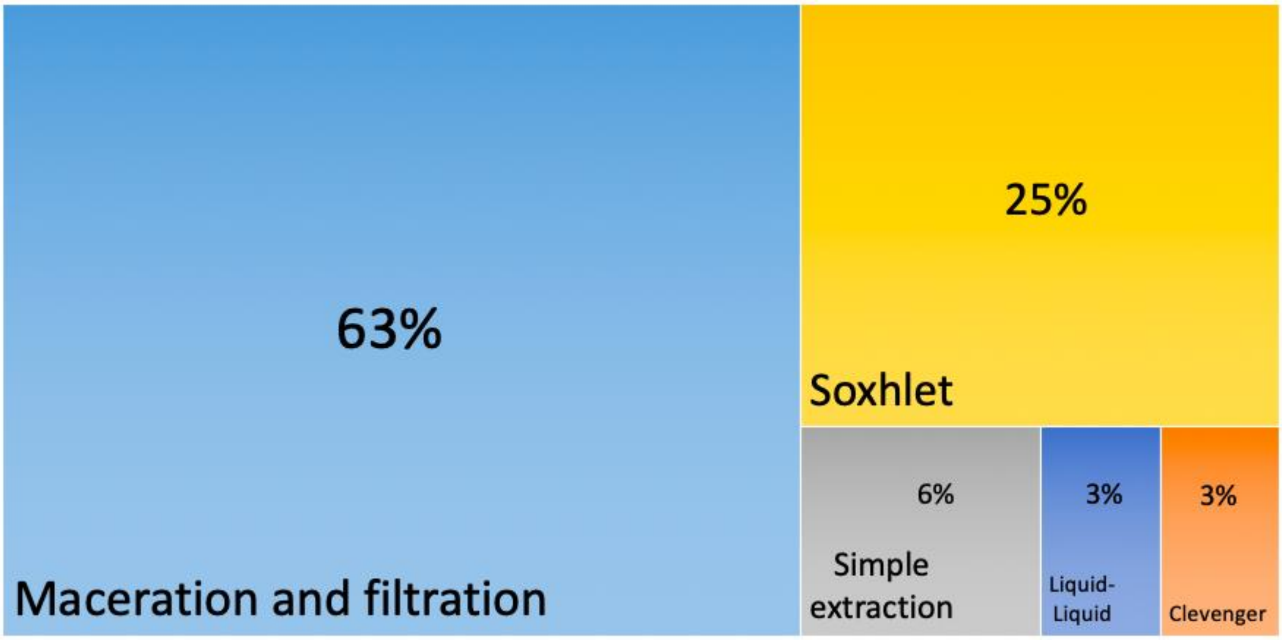

Figure 2. Most commonly employed extraction methods in the control of larvicidal and adulticidal activity against *Ae. aegypti.*

Regarding the solvents used for obtaining extracts with insecticidal activity against *Ae. aegypti*, nine solvents were reported, being ethanol the most common, it was reported in 19 studies. Among these, five used 70% ethanol, two used 95%, two used 96%, and two used 100% while the remaining six studies did not specify the concentration used for extraction. Methanol was the second most commonly solvent used, with a total of eight studies, followed by hexane with six, while chloroform, petroleum ether, and water were reported in four studies each, and ethyl acetate in three. The least commonly used solvents were acetone, a mixture of ethanol-dimethyl sulfoxide (DMSO) (1:1) (BOBADILLA & REYES 2020), and dichloromethane (DCM) (FERNANDES et al. 2021) (Figure 3).

It's worth noting that out of the 35 articles reviewed, only seven evaluated variations in solvents and/or concentrations used as insecticides against the *Ae. aegypti* vector. According to a study conducted by HARI & MATHEW in 2018, where extracts were obtained from leaves of the species *Hyptis suaveolens*, *Lantana camara, Nerium oleander*, and *Tecoma stans* by using the Soxhlet method and employing the organic solvents methanol, chloroform, and petroleum ether, it was observed that the extract with the best results was obtained with petroleum ether. For the species *T. stans,* it showed an LC50 of 55.41 mg/L, followed by *H. suaveolens* with an LC50 of 64.49 mg/L. Finally, *L. camara* presented an LC50 of 74.93 mg/L. The second solvent evaluated was methanol, where the extract of *N. oleander* had an LC50 of 84.09. These results suggest the potential use of petroleum ether as an efficient solvent for obtaining plant extracts with ecological larvicidal effects against *Ae. aegypti* when using the species *T. stans*, *H. suaveolens*, and *L. camara.*

BORGES et al. (2019) conducted a study comparing chloroform and hexane for the extraction of compounds from wood residues of the species *Tabebuia heptaphylla*. The extract with chloroform showed greater larvicidal effect. However, when using the LC95, which corresponds to 172 µg/ml for chloroform and 388.7 µg/ml for hexane, residual larvicidal activity remained above 80% for up to 144 hours for the hexane extract, whereas for the chloroform extract, it dropped below this value after 48 hours of exposure. Additionally, mortality caused by the chloroform extract reduced by 50% after 120 hours. Therefore, it is suggested that the most effective extract in this case would be hexane, thanks to the prolonged effect it exhibits.

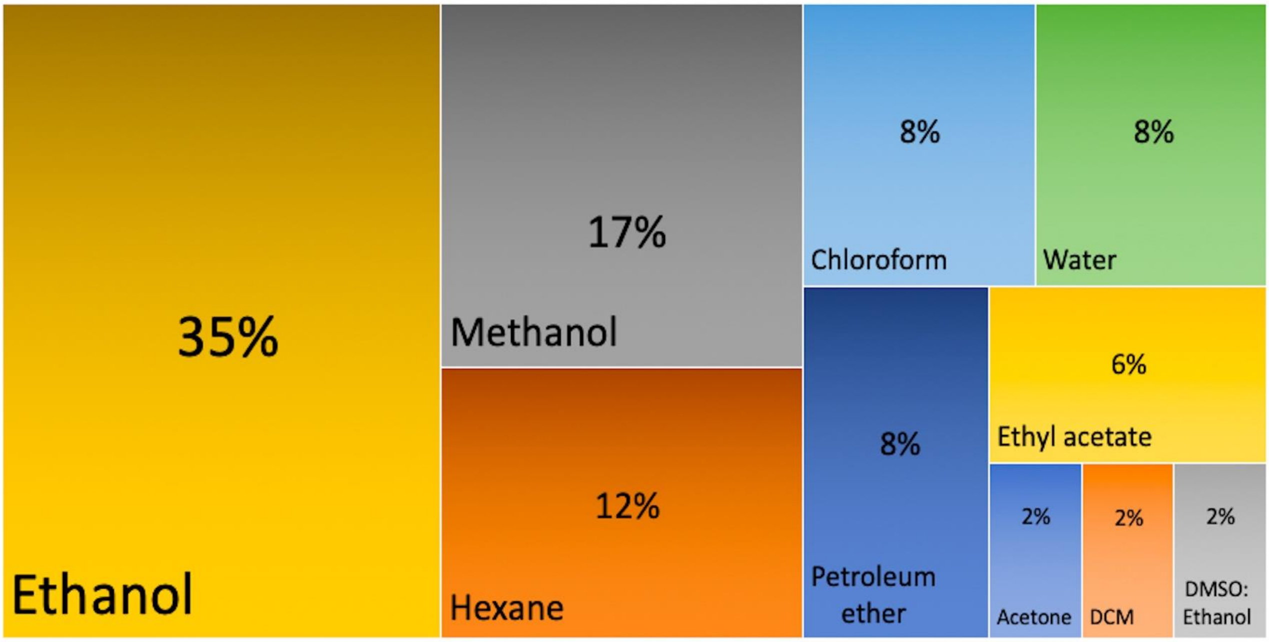

Figure 3. Types of solvents used in the control of larvae and adults of the vector mosquito *Ae. aegypti.*

Recently, MITUIASSU et al. (2021) employed ethanol, ethyl acetate, and hexane for obtaining extracts from *Mordica charantia*, which showed significant differences in effectiveness. The extract obtained with ethyl acetate at concentrations of 100 µg/ml and 200 µg/ml demonstrated the highest efficiency, with mortality rates of 97% and 87%, respectively. Ethanol also showed good results with a mortality rate of 78%. On the other hand, the extracts obtained with hexane did not show insecticidal activity and only achieved a mortality rate of 1.7%.

Based on the aforementioned, it is possible to affirm that the insecticidal power of an extract relies on the polarity of the solvents used for extractions, and that the solvent efficiency is contingent upon the plant species intended for extract procurement among other factors. Additionally, it is crucial to assess the residual effect of solvents to choose the most suitable one for obtaining extracts and conducting tests for their efficacy as insecticides.

BIOACTIVITY OF NATURAL EXTRACTS

Among the articles analyzed during this review, 25 of them employed negative controls, which included: water (16), a mixture of water and extraction solvent (15), and solely extraction solvent (8). As positive controls, OLIVEROS et al. (2022) and NINDITYA et al. (2020) used Temephos; ARAÚJO et al. (2020) and FERREIRA et al. (2019) employed 0.02% Imiprothrin, 0.05% Permethrin, 0.1% Esbiotrin, while GRANADOS et al. (2021), MAHDI et al. (2022) and PINEDA et al. (2019) used the larvicide Abate. Three investigations did not carry out any type of control.

Phytochemical studies

It is important to highlight that in addition to the bioassays conducted to assess *Ae. aegypti* mortality using natural extracts, 14 out of the 35 analyzed articles conducted phytochemical studies, either qualitative (9) or quantitative (4). For instance, a study conducted by MARTINS et al. (2021) separated compounds present in the hexane extract of *M. guianensis* using silica gel column chromatography with n-hexane as the mobile phase, followed by a mixture of *n*-hexane:$CHCl_3$, thereby isolating the compound tingenone B (22β-hydroxytingenone). Subsequently, for larvicidal tests, the crude extract was dissolved in DMSO (1%), and tingenone B was dissolved in ethanol (1%). Five different concentrations of the crude extract of *M. guianensis* (30, 22, 18, 16, and 14 ppm) and the isolated substance from *M. guianensis* (30, 25, 20, 15, and

10 ppm) were used to calculate lethality. As a result, the LC50 of the crude extract was 11.3 ppm, which caused larval gut ejection, and the LC50 of tingenone B was 14.8 ppm.

Larvicidal activity

According Phytochemical Studies to the conducted review, among the botanical families with the highest insecticidal potential for the control of *Ae. aegypti* there is the Asteraceae family (Table 1), which comprises approximately 25000 vascular plants (AGUIRRE et al. 2018). In this family, the phytochemical components present correspond to flavonoids, which are attributed to larvicidal and adulticidal activity against *Ae. aegypti*. They act on the neuroendocrine system, interfering with metamorphic processes, and are also able to inhibit feeding activities (SPINOZZI et al. 2023).

Natural extracts have been extensively researched as an alternative for controlling the vector at the larval stage. According to SIGAMANI et al. (2020), natural extracts from *Chlorella* sp. microalgae obtained with chloroform and methanol exhibited larval mortalities of 91.2% and 50.1%, with LC50 values ranging from 116.82 to 159.20 ppm and 445.16 to 703.49 ppm, respectively. Furthermore, histopathology conducted on the larvae showed severe damage to the midgut and hindgut, brush border, epithelial cells, and food bolus due to the action of the extracts.

In a study conducted by AGUIRRE et al. (2018), larvicidal activity against *Ae. aegypti* was evaluated in 23 species belonging to the Asteraceae family. It was found that three species exhibited mortality rates exceeding 95% (*Jaegeria hirta*, *Helicopsis oppositifolia*, and *Austroeupatorium inulaefolium*); four species showed values ranging from 52% to 72% (*Conyza bonariensis*, *Hypochoeris radicata*, *Acmella mutisii*, *Galinsoga quadriradiata*); six displayed mortality rates ranging from 17% to 42% (*Camellia japonica*, *Taraxacum officinale*, *Echeveria coccinea*, *Camptotheca acuminata*, *Fleischmannia microstemon*, *Ageratum conyzoides*), whereas eight species had the lowest mortality rates, ranging from 0% to 10% (*Celtis caudata*, *Schistocarpha eupatorioides*, *Bidens pilosa*, *Tagetes erecta*, *Artemisia vulgaris*, *Acmella ciliata*, *Baccharis trinervis*, *Clibadium surinamense*). Additionally, phytochemical analysis allowed for the identification of tannins, quinones, flavonoids, sterols, coumarins, and alkaloids as active compounds.

On the other hand, when comparing methanolic extracts obtained from the leaves of *Eugenia astringens*, *Myrrhinium atropurpureum*, and *Neomitranthes obscura*, it was observed that at 25 µl/ml, the extracts of *M. atropurpureum* caused mortality rates exceeding 50% and 100%, whereas for *E. astringens*, it was 50% and 63.33% after 24 hours and 48 hours post-exposure, and *N. obscura* induced a maximum mortality of 46.66% in *A. aegypti l*arvae after 48 hours (CARNEIRO et al. 2020).

It is important to mention that the type of phytochemical also varies depending on the plant part from which the extraction is performed. This was observed in a study conducted by RAJASHEKARA et al. (2021), where they tested ethanolic extracts from different parts of *Cassia fistula*, *Curcuma amada*, *Manilkara zapota, Momordica charantia*, *Sansevieria trifasciata*, and *Solanum indicum*. In this study, *C. amada* and *M. zapota* extracts showed 100% mortality on the larvae, whereas the other species exhibited values ranging from 50.33% to 96%. However, this study does not specify from which part of the plant the extracts were obtained. In contrast, aqueous extracts of *Bougainvillea spectabilis*, *Saraca asoca*, and *Chenopodium album* showed very low efficiency in controlling *Ae. aegypti* larvae. These plant species had LC50 values of 0.22%, 0.26%, and 0%, respectively, after 24 hours (SHARMA et al. 2019).

Similarly, among the 18 plants analyzed by MUANGMOON et al. (2018) a selective dose (200 mg/l) prepared from the ethanolic extract of each plant species was individually analyzed to detect larvicidal activity against the fourth larval stage of *Ae. aegypti*, resulting in two plant extracts with larvicidal potential. In this case, *Cissampelos pareira* showed a mortality rate of 63% at LC50 of 157.77, LC95 of 274.45, and LC99 of 248.61. *Litsea petiolata* exhibited a mortality of 42% at LC50 of 187.6, LC95 of 274, 30 and LC99 of 310.21. The species *Vernicia fordii, Leonorus japonicus* and *Alpinia conchigera* presented mortality percentages of 22%, 16% and 12%, respectively. They were followed by *Brassica pekinensis, Crinum asiaticum, Brassica juncea, Diospyros rhodocalyx, Ardisia polycephala, Smilax peguana, Lycium barbarum, Artocarpus altilis, Irvingia malayana, Homalomena aromatica, Cassia alata* and *Tacca chantrieri,* which showed mortality percentages that ranged between 0% and 3%. However, for the 16 plants mentioned above, the concentration used to achieve their mortality percentages was not specified and no positive control was used throughout the study.

Adulticidal Activity

Another important activity provided by natural extracts derived from plants is their control as adulticides (HIKAL et al. 2017). These substances exhibit interference with the nervous axons and synapses, respiration, hormonal balance, growth, and behavior of insects (BEKELE 2018). However, despite their favorable use and impact, and despite understanding the mechanisms of action on vectors, adulticidal activity has not been studied extensively.

During the review, only five of the 35 selected articles, assessed the effectiveness of natural extracts on adults. However, when comprehensive studies on the adulticidal activity of natural extracts against *Ae. aegypti* are conducted, good results can be found. For example, in a study conducted with methanolic extracts of *Alangium salvifolium*, it was found that the adulticidal activity was dose-dependent. In this case, the extract at a concentration of 400 ppm achieved a mortality rate of over 98% in adults 30 minutes post-exposure. Similarly, concentrations of 300 and 200 ppm showed a mortality rate of 97% in both cases, but they occurred at different exposure times, with the first being at 45 minutes and the second at 60 minutes (THANIGAIVEL et al. 2018).

Also, PRATHEEBA et al. (2019) demonstrated that the adulticidal activity of extracts from *Pavetta tomentosa* and *Tarenna asiatica*, using acetone as a solvent and evaluated at 60-minute intervals, as results L50 and L90 values of 32.105 and 41.001 μg/ml, and 09.012 and 11.854 μg/ml were obtained for each plant species. Meanwhile, CHELLAPPANDIAN et al. (2019) evaluated ethanolic extracts of *Trichodesma indicum* and found that at concentrations of 400 ppm, 500 ppm, and 600 ppm, mortality reached 100%. Additionally, it was observed that the extract at concentrations of 100 ppm and 200 ppm significantly reduced female fecundity.

We also found that NINDITYA et al. (2020) analyzed the adulticidal activity of ethanolic extracts of *Artemisia vulgaris* against *Ae. aegypti* mosquitoes and determined that at values of 11.35 mg, 9.63 mg, and 6.46 mg, mortality rates of 50% were observed.

On another note, in Brazil, through the evaluation of extracts obtained from the leaves and stems of *Helicteres velutina*, it was established that at the same concentration of 1.0 mg/mL, the dichloromethane fraction achieved a mortality rate of 58.3%, whereas the hexane fraction showed a mortality rate of 8.33% after 48 hours of exposure. Additionally, during the tests, it was observed that both leaf and stem extracts altered the behavior of the vector mosquito, as they exhibited lethargic movements, indicating a lack of energy and agility. These changes became more evident as the extract doses increased (FERNANDES et al. 2021).

Finally, it is possible to suggest further research on the mechanisms of action of natural extracts on adults of this species, as arbovirus transmission to humans occurs during this stage of the life cycle. Therefore, greater vector control over adults is necessary to prevent or reduce their population spread, thus reducing infections that lead to severe health and social problems in vulnerable populations.

CONCLUSION

The use of natural plant extracts as insecticides has great potential in the fight against mosquito vectors such as Ae. *aegypti*, responsible for transmitting viruses such as DENV, ZKV, CHIKV and FAV. This is due to the chemical variability that depends on the plant species, the plant part used, and its geographical location. These factors work together to reduce the likelihood of insects developing resistance. Furthermore, because of their natural origin, these insecticides biodegrade more rapidly compared to chemicals, thus minimizing risks to non-target species, including humans. This makes them a safer and more sustainable option.

However, it is crucial to recognize that the effectiveness of these natural insecticides can vary significantly due to biological factors such as the plant species and structure used, as well as vector-related factors like species, population origin, and developmental stage. Additionally, chemical factors such as extraction methods and solvents used can also impact their efficacy. Therefore, not all of them exhibit the same level of effectiveness in controlling species like the *Ae. aegypti* mosquito.

It is important to emphasize that further research should be conducted to evaluate the effectiveness of these natural extracts as adulticides. In the present review, only five studies were conducted on adults. This is important because during this life stage, the spread of viruses responsible for human diseases occurs, as well as an increase in the population size of the species. However, ongoing and meticulous research is required to maximize their efficacy and fully understand their potential in vector control and the prevention of insect-borne diseases.

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