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A systematic review of Datura stramonium as a potential biocide for mosquito control

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Abstract

Global burden of malaria reduction has been significantly slowed down by malaria vectors developing resistance to conventional chemical pesticides currently in use. Anopheles mosquitoes, which are malaria vectors, have over time developed coping mechanisms which can enable them to detoxify poisonous chemical pesticides meant to kill them consequently threatening the effectiveness of such control measures. Coupled with the danger of the chemical pesticides on the environment, attention is shifting to natural products that would successfully control malaria vectors particularly those that have developed bacteria-mediated resistance to conventional pesticides currently in use. A web-based literature search using scientific databases was explored to find data on the insecticidal and antibacterial properties of Datura stramonium. This was prompted by a dearth of information on alternative bio-pesticides that are cost-effective, eco-friendly, and with high toxicity on vectors. This review evaluated the potential of extracts of D. stramonium in different solvents as a biocide. A lot of research on D. stramonium extracts has focused more on its potential as a medicinal plant rather than as a biocide. This review outlines research evidence that D. stramonium has phytochemicals and bio-active compounds which are antibacterial, insecticidal, and anti-malarial. Not much studies have been done with Anopheles gambiae of confirmed resistance and its inhibition effect on mosquito bacterial community is not fully understood.

Key words: Biocide, *Datura stramonium*, Resistant Malaria Vectors.

INTRODUCTION

Malaria, an infectious disease spread by *Plasmodium*-infected female *Anopheles* mosquito, continues to remain a public health concern globally and in Kenya where seventy percent are at risk of the infection with children under five years as the most vulnerable (WHO, 2023; Bonizzoni *et al*., 2012). In 2023, WHO reported global data of 500 million people affected by malaria, 2 million cases reported in hospitals, and over 600,000 deaths. Climate change is reported to also cause unprecedented weather changes that favour malaria vectors and causes a humanitarian crisis that increases the exposure of vulnerable people to the vector. Invasive species such as *Anopheles stephensi have* been described in places new places such as Kenya (Ochomo *et al*., 2023). Annually, the world spends USD 12 billion on malaria control, Africa alone spends $4.1 billion, while Kenya spends Ksh 53.7 million on control (WHO, 2023). This translates to a 1.3% gross domestic product (GDP) annual loss making malaria a socio-economic threat. Major strategies put in place to reduce morbidity and mortality due to malaria have focused on timely diagnosis and treatment, prevention through prophylaxis, and vector control. Vector control methods currently put in place include majorly chemical pesticides and an integrated vector control strategy that may include biological control (using *Gambusia*, *Toxorychnchites*, *Bt. Mettarizium*, viruses, *Wolbachia*). Insect sterile technique (males are taken through radiation to produce sterile sperms), cultural practices, environmental engineering, and botanicals. Biological control and botanical though slow-acting and require periodic repeated application, are very eco-friendly.

Major malaria vector control mechanisms are designed to aim at reducing human and vector contact. They include insecticide-treated nets (ITNs), internal residual spraying (IRS), larval source management, and environmental engineering (WHO, 2023). These approaches have weaknesses. IRS and ITNs only control indoor biting mosquitoes. Moreover, ITNs have not only been fully embraced by communities but also wear out after some time. Human activities create new habitats for vectors and make larval source management ineffective. Tools such as traps, indocides such as ivermectin and spacial repellents have not fully been embraced.

The success of malaria control, therefore, is currently under serious challenges. Malaria parasite is increasingly developing resistance to antimalarial drugs while malaria vectors have recorded increased resistance to insecticides (Bonizzoni *et al*., 2012 Ochomo *et al*., 2023; Omoke *et al*., 2021; Mathias *et al.*, 2011). 78 countries have so far reported confirmed resistance of malaria vectors to insecticides (WHO, 2023). Mosquito vectors' avoidance behavior of insecticide-treated surfaces and human behavior has caused residual malaria challenges (Ondeto *et al*., 2017; Ochomo *et al*., 2023; Omoke *et al*., 2021; Abongo *et al.*, 2018).

In the earlier years, malaria vector research has concentrated more on chemical control of indoor biting mosquitoes in endemic areas than exophagic (outdoor biting) ones (WHO, 2023). This has resulted in a vicious circle of transmission of malaria by outdoor biting vector species. A multi-sectoral malaria control approach through integrated vector management has been advocated for by researchers with an emphasis on the need for novel malaria control methods that would complement current malaria control measures while at the same time minimizing the resistance menace (Ondeto *et al*., 2017; WHO, 2023, Ochomo *et al*., 2023). The pressure to quickly reduce morbidity and mortality due to malaria resulted in the excessive use of popular fast-acting but environment-unfriendly chemical pesticides (Ondeto *et al*., 2017; Ochomo *et al.*, 2015; Kirar *et al*., 2023). The current progressive development of the ability of malaria vectors and parasite *Plasmodium* to cope with the chemical insecticides is a threat to effective control and its elimination. Botanical biocides are promising control methods because of their multiple mode of action that makes it difficult for insects to develop resistance to them. There is a dearth of information on the effectiveness of novel eco-friendly alternative pesticides that can be considered for malaria vector control and which would reduce the adverse consequences of the overuse of chemical pesticides (Ochomo *et al.*, 2015; Kirar *et al*., 2023, Ullah *et al*., 2018). Currently, there is a research shift with a greater interest in novel biocides that would complement existing malaria vector control tools while at the same time controlling resistance issues.

Using insecticides with various modes of action, either individually or in combination, significantly lowers the likelihood of resistance development (Ochomo *et al*., 2023; Ondeto *et al*., 2017). *D. stramonium* though highly poisonous may be a potential botanical for control of malaria-spreading mosquitoes. A web search using online tools was done on *D. stramonium,* a noxious weed in Kenya, which has gained research interest as a promising botanical both for antimalarial drug development and as a potential botanical bio-insecticide (Satish *et al*., 2018; Al-Snafi *et al.,* (2017); Mukherjee *et al*., 2013, Mohamed *et al*., 2022). A web-based literature search using scientific databases was explored to find data on the insecticidal and antibacterial properties of *D. stramonium*. This was prompted by a dearth of information on alternative potential bio-pesticides that are cost-effective, eco-friendly, and with high toxicity on vectors.

This review evaluated the potential of extracts of *D. stramonium* in different solvents as a biocide for different life stages of mosquitoes. The review was to answer the following research questions. The general and main research question being: What is the effectiveness of *D. stramonium* extracts on mosquitoes? Specific research questions were four: 1. Which solvents have been extensively used on *D. stramonium* extractions studies as bio-insecticide? 2. Which mosquito developmental stages are susceptible to *D. stramonium* extracts? 3. Which parts of *D. stramonium* has been used in experiments to test in bio-insecticidal properties? 4. Do extracts of *D. stramonium* have an inhibitory effect on bacteria that have been associated with resistant mosquitoes?

MATERIALS AND METHODS

In this systematic review, a web-based search for English publications and patents was done through electronic databases such as PubMed, Google Scholar, and Web of Science for years between 2010 and 2024. The search in this review was done using key statements such as "mosquitocidal properties of *D. stramonium*". "*D. stramonium* extracts for controlling mosquitoes" and "Insecticidal properties of *D. stramonium*". References from selected and downloaded articles used here were also screened for relevant data.

To incorporate the social aspect of this study, a discussion was done with people some of whom consider this weed as poisonous and good for nothing, and another cohort who believed the weed is medicinal and has been used to cure bhang addiction. From the discussions, it is clear that a significant number of members of the community in Eldoret Kenya know *D. stramonium* majorly as a poisonous plant and noxious weed. Very few members of the community are aware of the potential benefits of this weed. The web search was done to ascertain which disciplines have researched extracts of *D. stramonium*. The disciplines considered were medicine, pharmacology, biotechnology, chemistry, phytology, environmental, and entomology with a focus on vector control. This makes this review not fully systematic because it did not precisely follow all the specifications for a systematic review.

A publication was considered eligible if it was full text, written in English, experimented on mosquitoes spreading malaria using extracts of *D. stramonium,* and reported the solvent and/ or compounds used and their concentrations including protection time for repellency tests. References of the selected papers reporting microbial inhibitory data were also considered to answer research question number four; do extracts of *D. stramonium* have an inhibitory effect on bacteria that have been associated with resistant mosquitoes? Any article and abstracts which had inadequate data and those which did not meet the criteria described above were excluded. Two investigators did the screening of titles and only eligible and agreed on publications were selected.

Data Screening

A standardized form was used to screen for articles and to collect data from selected publications to ensure accurate and succinct data. Purposive sampling was agreed on by all the reviewers to use full texts, original and review papers were to be uploaded and used. All the authors acknowledged any weaknesses that may be tagged to this. Arguments about articles to include were sorted by an arbitrator. Inclusion of articles was done using data form which included the first author's name, name of the country where the study was done, journal details, year of publication (2010-2024), part of *D. stramonium* used, malaria vector species, study type (field or laboratory), solvent used, effective dosage, and the discipline within which the research was done.

The exclusion was done if an article was published before 2010, not published in English, letters, editorial articles, conference papers, thesis, not reporting concentrations used. We did not reach out to authors concerning published data but all used data and information from authors have been cited and authors acknowledged in text and references. Figure 1 below was modified by Asadollahi and others in 2019 and summarizes the procedure used to extrapolate data.

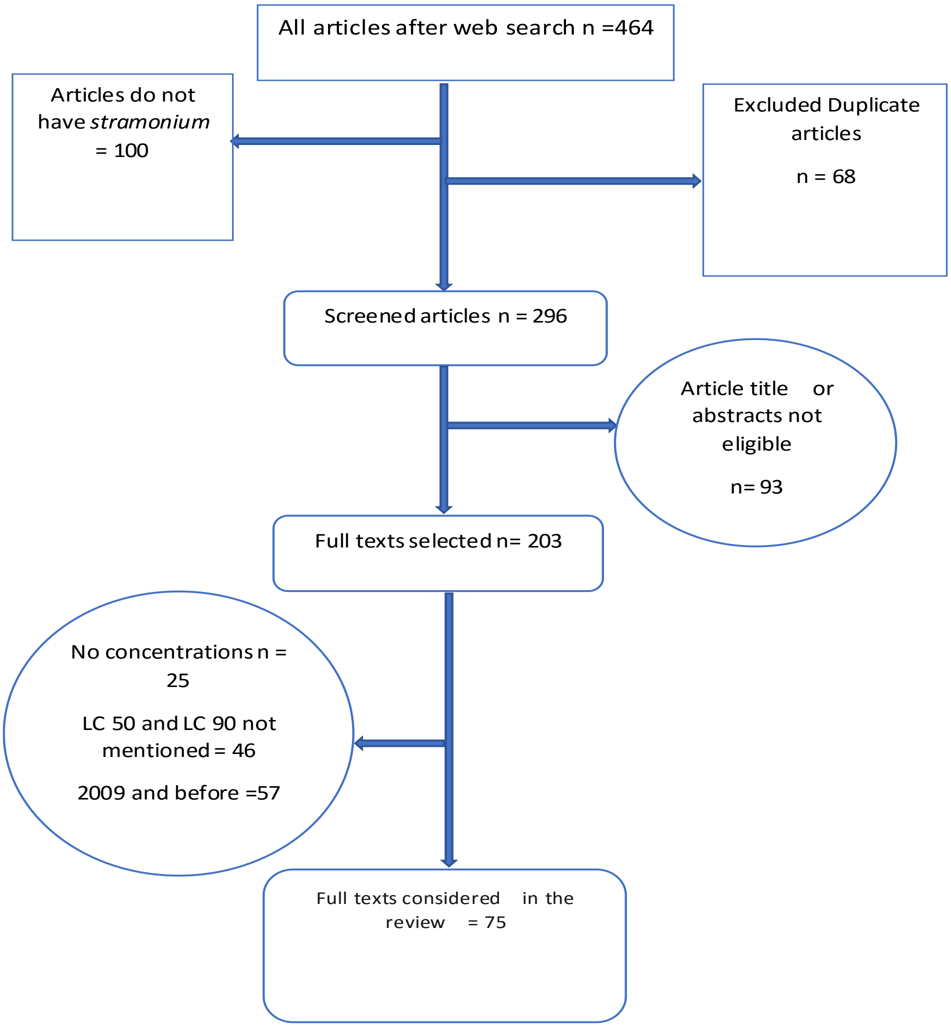

Figure 1: Article extrapolation procedure in a flow chart.

Data Extraction.

The form used in screening was also used to extract and record data. The data was extracted by one, checked by another author and disputes were sorted by the arbiter. 464 articles were retrieved from the online web search engine. All the duplicate publications were identified and excluded as well as articles that were not reporting on *D. stramonium*. 296 articles were screened and 93 of the articles and titles which were not reporting on mosquitoes were excluded. 203

articles were then selected both reviews and experimental research articles and further consideration was done leaving out 25 articles that did have a mention of the extract concentrations used. Another 46 which did not report LC 50 and LC 90 of the concentrations, and 57 wpublished before 2010 were left out. Only 75 articles were considered in this study and results were reported and authors cited and listed in the references.

Data analysis and synthesis

Selected 75 articles were studied to answer the major research questions which was: What is the effectiveness of *D. stramonium* extracts on mosquitoes? and the four specific research questions: 1. Which solvents have been extensively used on *D. stramonium* extractions studies as bio-insecticide? 2. Which mosquito developmental stages are susceptible to *D. stramonium* extracts? 3. Which parts of *D. stramonium* has been used in experiments to test in bio-insecticidal properties?4. Do extracts of *D. stramonium* have an inhibitory effect on bacteria associated with resistant mosquitoes?

Data was recorded in an Excel sheet. The Excel sheet form captured country, place of research (field or laboratory), developmental stage of mosquito, mosquito species, part of plant used and solvent, first author name and year of publication (2010-2024), web-search engine, journal details, and the discipline within which the research was done. SPSS was used to analyze data and report in percentages.

RESULTS AND DISCUSSION

Results

PubMed being one of the most extensive web databases reporting articles of all disciplines, had only three articles published two were excluded because of the year of publication and the other relevance. Most of the articles reported in this review were from the Google Scholar web search engine. From the articles selected as in Table 1, most studies done with *D. stramonium* extracts on mosquitoes were in India (Kirar *et al*., 2022; Asrar *et al*., 2023; Borah *et al*., 2012; Swathi, 2012, Srivastava *et al*., 2023), three in Pakistan (Elhaj *et al*., 202; Ahmed *et al*., 2019; Ullah *et al*., 2018); four in Nigeria (Olajide *et al*., 2018; Afolabi *et al*., 2018; Owoeye *et al*., 2016; Olofintoye *et al*., 2011) and only one done in Sudan (Mohamed *et al*., 2022). Of all the experiments, all used larvae, three used adults (Olajide *et al*., 2018; Owoeye *et al*., 2016; Srivastava *et al*., 2023), and 1 each used eggs and pupae (Owoeye *et al*., 2016). Based on parts of the plants, Leaves have been extensively studied in all experiments except three on flowers (Swathi *et al*., 2012; Mohamed *et al*., 2022), three on seeds (Asrar *et al*., 2023; Elhaj *et al*., 2021; Afolabi *et al*., 2018) and one on roots (Olofintoye *et al*., 2011) stem (Kirar *et al*., 2022) and fruit one study (Ahmed *et al*., 2019).

Articles where researchers used adult mosquitoes reported repellency. Olajide and others documented 120 minutes of protection time for ethanolic seed extracts from *An. gambiae* (Olajide *et al*., 2018). Srivastava *et al*., 2023 reported Ovicidal and oviposition deterrence of *A. aegypti* petroleum ether extracts of *D. stramonium.* From the search results, most excluded articles had data on pharmacological properties followed by data on insects of agricultural importance some of which have been mentioned in the review as they existed in selected review articles. Table 1 gives a summary of the data collected.

Table 1: Uses of *D. stramonium E*xtracts on Different Developmental Stages of Mosquitoes in Different Countries

Country	Age	Species	Solvent used	Part of Plant	Reference
Ethiopia	Larva	*An. arabiensis*	Water	Leaves	Jemberi *et al.*, 2016
India	Larva	*quinquefasciatus*	Petroleum ether	Leaves	Borah *et al.*, 2012
India	Larva	*A. aegypti*	Petroleum ether	Leaves	Srivastava *et al.*, 2022
India	Eggs	*A. aegypti*	Petroleum ether	Leaves	Srivastava *et al.*, 2022
India	Adult	*A. aegypti*	Petroleum ether	Leaves	Srivastava *et al.*, 2022
India	Larva	*An. stephensi*	Ethanol	Leaves	Swathi, 2012
India	Larva	*A. aegypti*	Ethanol	Leaves	Swathi, 2012
India	Larva	*A. aegypti*	Ethanol	Leaves	Asrar *et al.*, 2023
India	Larva	*C. quinquefasciatus*	Ethanol	Leaves	Asrar *et al.*, 2023
India	Larva	*An. Stephensi*	Crude Protein	Stem	Kirar *et al.*, 2022
India	Larva	*A. aegypti*	Petroleum ether, chloroform, water	Leaves	Rajesekaran *et al.*, 2012
Nigeria	Larva	*An. gambiae*	Ethanol	Seed	Afolabi *et al.*, 2018
Nigeria	Adult	*An. gambiae*	Ethanol	Seed	Afolabi *et al.*, 2018
Nigeria	Larva	*An. arabiensis*	Methanol, Ethanol	Leaves	Eukubay *et al.*, 2021
Nigeria	Adult	*An. gambiae*	Petroleum Ether	Leaves	Olajide *et al.*, 2018
Nigeria	Larva	*An. gambiae*	Water	Leaf, root	Olofintoye *et al.*, 2011
Nigeria	Larva	*An. gambiae*	Petroleum ether, hexane, ethanol	Leaves	Owoeye *et al.*, 2016
Nigeria	Pupae	*An. gambiae*	Petroleum ether, hexane, ethanol	Leaves	Owoeye *et al.*, 2016
Nigeria	Adult	*An. gambiae*	Petroleum ether, hexane, ethanol	Leaves	Owoeye *et al.*, 2016
Pakistan	Larva	*aegypti*	Petroleum ether	Fruit	Ahmed *et al.*, 2019
Pakistan	Larva	*C.quinquefasciatus*	Acetone	Leaves	Ullah *et al.*, 2018
Sudan	Larva	*aegypti*	Ethanol	Leaves, flowers	Mohamed *et al.*, 2022
Sudan	Larva	*C. quinquefasciatus*	Ethanol	Leaves. flowers	Mohamed *et al.*, 2022
Sudan	Larva	*An. arabiensis*	Ethanol	Leaves, flowers	Mohamed *et al.*, 2022
Sudan	Larva	*C. quinquefasciatus*	Ethanol	Leaves, flowers	Swathi, 2012
Turkey	Larva	*C. quinquefasciatus*	Water	Leaves	Iqbal *et al.*, 2018
Yemen	Larva	*A. aegypti*	Methanol Water	Leaves	Aj-jami *et al.*, 2021

The search results in Table 2, indicates that the majority of studies on the potential of *D. stramonium* extracts as a biocide were based in India (46%), followed by Nigeria 38%). Pakistan and Sudan both had 16% of the total articles, and Ethiopia, Yemen, and Turkey each had 7% the articles reporting experiments with mosquitoes. Table 1(b) gives a summary of countries in which extracts of *D. stramonium* has been tested as a biocide for mosquito control.

Table 1(b): Countries where *D. stramonium E*xtracts has been Tested as Mosquito Biocide (n=18)

Country	Articles	% Articles	References
Ethiopia	1	7%	Jemberi *et al*., 2016
India	6	46%	Srivastava *et al*., 2023; Borah *et al*., 2012; Swathi, 2012; Kirar *et al*., 2022; Rajasekaran *et al*., 2021, Asrar *et al*., 2022
Nigeria	5	38%	Olofintoye *et al*., 2011; Owoeye *et al*., 2016; Olajide *et al*., 2018, Afolabi *et al*., 2018, Eukubuy *et al*.,2021
Pakistan	2	15%	Ullah *et al*., 2018, Ahmed *et al*., 2019,
Sudan	3	15%	Mohamed *et al*., 2022, Swathi, 2012. Elhaj *et al*., 2023.
Turkey	1	7%	Iqbal *et al*., 2018
Yemen	1	7%	Aj-jami *et al*., 2021

The most reported mosquito species was 37% *A. aegypti* in seven different articles, followed by 3 articles reporting 26% of the experiments on *An. gambiae*, then 6 articles reporting 19% of the experiments with *C. quinquefasciatus* and *An. arabiensis reported* in three articles with (16%) of the experiments and only two articles reporting 11% experiments with *An. stephensi.* Table 1(c) provides a summary of the mosquito species that have been tested with *D. stramonium* extracts. Considering that it is the female adult *Anopheles* mosquitoes that spread the malaria parasite *P. falciparum*, there is a need for more studies on female *Anopheles* species of known resistance status.

Table 1(c): Summary of Different Mosquito Species Used in the Experiments in the Selected Studies. (n=13)

Mosquito Species	Experiments (Exp.)	% Exp.	References
C. quinquefasciatus	5	19%	Srivastava *et al*., 2023; Ullah *et al*., 2018, Borah *et al*., 2012; Swathi, 2012; Mohamed *et al*., 2022
An. stephensi	2	11%	Kirar *et al*., 2022, Swathi, 2012.
A. aegypti	10	37%	Asrar *et al*., 2023; Rajesekaran *et al*., 2021; Ahmed *et al*., 2012; Swathi *et al*., 2012, Aj-jami *et al*., 2021, Mohamed *et al*., 2022, Srivastava *et al*., 2022
An. gambiae	7	26%	Olofintoye *et al*., 2011; Owoeye *et al*., 2016' Olajide *et al*., 2018
An. arabiensis	3	11%	Eukubuy *et al*., 2021, Mohamed *et al*., 2022. Jemberi *et al*., 2016

To answer question one: Which solvents have been extensively used on *D. stramonium* extractions studies as bio-insecticide? a search results revealed that all the studies were laboratory-based reporting toxicity of different concentrations of crude extracts of *D. stramonium* on mosquitoes and bacteria which have been associated with them in a variety of solvents. Only in one study done by Kirar *et al.,* 2021, did isolation of crude protein compounds from *D. stramonium* stem. Most experiments in the studies used ethanol (39%), followed by petroleum ether (26%), water (13%) and hexane (8%) to extract phytochemicals and bio-active compounds of *D. stramonium*. Very few studies used methanol, and acetone, and none used ethyl acetate as is summarized in Details in table 2.

Table 2: Summary of Type of Solvents Used in the Experiments (Exp). (n=27)

Solvent Used	Experiments (Exp.)	% Exp.	References
Aqueous	5	13%	Rajasekaran *et al.*, 2012; Olofintoye *et al.*, 2011.
Chloroform	1	3%	Rajasekaran *et al.*, 2012
Methanol	2	5%	Eukubay *et al.*, 2021, Aj-jami *et al.*, 2021
Chloroform	1	3%	Rajesekaran *et al.*, 2012
Hexane	3	8%	Owoeye *et al.*, 2016
Crude protein	1	3%	Kirar *et al.*, 2022
Acetone	1	3%	Ullah *et al.*, 2018
Ethanol	14	39%	Mohamed et al., 2022; Swathi, 2012; Olajide et al., 2018; Asrar et al., 2023.
Petroleum Ether	10	26%	Rajasekaran *et al.*, 2012; Borah *et al.*, 2019; Ahmed *et al.*, 2019; Srivastava *et al.*, 2023; Olajide *et al.*, 2018; Owoeye *et* al., 2016.

Results for question two: Which mosquito developmental stages are susceptible to *Datura stramonium* extracts? showed that most experiments in the selected studies used larvae (77%), then adult mosquitoes experiments which were 14% and lastly experiments with eggs and pupa were 12% as summarized in Table 3.

Table 3: Summary of Experiments in the Selected Articles Reporting the Developmental Stage Used (n=27)

Stage	Expreiments (Exp.)	% Exp.	References
Egg	1	4%	Srivastava *et al.*, 2023; Owoeye *et al.*, 2016;Olajide *et al.*, 2018
Larvae	21	77%%	Srivastava *et al.*, 2023; Ullah *et al.*, 2018, Borah *et al.*, 2012; Swath, 2012; Kirar *et al.*, 2022; Olofintoye *et al.*, 2011; Mohamed *et al.*, 2022, Owoeye *et al.*, 2016; Olajide *et al.*, 2018.
Pupa	1	4%	Srivastava *et al.*, 2023; Owoeye *et al.*, 2016; Olajide *et al.*, 2018
Adult	4	14%	Srivastava *et al.*, 2023; Owoeye *et al.*, 2016; Olajide *et al.*, 2018

To answer question three: Which parts of *D. stramonium* has been used in experiments to test in bio-insecticidal properties? the parts of the plant used (see Table 4) in the experiments were considered in each of the articles. Results shows that most of the experiments in the selected studies were done with *D. stramonium* leaves (66%), followed by flowers (15%), stem, seed, and fruits were the least used in the experiments each with a proportion of 4%.

Table 4: Summary Results for Parts of *D. stramonium P*lant Used in the Experiments Reported in the Selected Articles. (n=27)

Part of plant	Number of Experiments	% Exp.	References
Stem	1	4%	Kirar *et* al., 2022
Flower	4	15%	Mohamed *et al*., 2022, Swathi, 2012
Seed	2	7%	Olajide *et al*., 2018
Leaves	18	66%	Srivastava *et al*., 2023; Ullah *et al*., 2018, Borah *et al*., 2012; Swath, 2012; Kirar *et al*., 2022; Olofintoye *et al*., 2011; Mohamed *et al*., 2022, Owoeye *et al*., 2016; Olajide *et al*., 2018; ; Asrar *et al*., 2023, Rajasekaran *et al*., 2021.
Fruit	1	4%	Ahmed *et al*., 2019

To answer question four: Do extracts of *D. stramonium* have an inhibitory effect on bacteria that have been associated with resistant mosquitoes? Search results showed that 22 genus of gram positive bacteria have been associated with resistant *Anopheles* mosquitoes. Inhibitory effects of D. stramonium seeds and leaves extracts on five bacteria have been reported. *Pseudomona* is the most reported in 12 different articles, followed by *Klebsiella* in 11 studies, then *Escherichia* in in 7 articles, *Bacillus* and *Enterobacter* each were reported in 4 studies and *Staphylococcus* was reported in three studies. The inhibitory effects of the other 17 different genus of the bacteria were not established from the selected articles. Table five gives a detailed data on microbiota associated with resistant mosquito and their inhibitory response to *D. stramonium* extracts.

Table 5: Data on Microbiota Associated with Resistant *Anopheles M*osquitoes and their Inhibitory Response to *D. stramonium* Extracts

Gram-positive Bacteria genus	**Inhibitory effect of *D. stramoniun* extracts**	**References associating the bacteria genus to *Anopheles* mosquito.**
Klebsiella	inhibited	Diamini *et al*., 2020, Dada *et al*.,2018 and 2019, Wu *et al*., 2006, Gendrin *et al*., 2013, Wong *et al*., 2020, Al-Snafi ,2017, Rehman *et al*., 2022, Bhakta *et al*., 2013, Arruda et al., 2021
Staphylococcus	inhibited	Saab *et al*., 2020, Gupta *et al*., 2021, Sharma *et al*., 2021
Serratia	Unknown	Bahia *et al*., 2014, Cirimotich *et al*., 2011, Diamini *et al*., 2020, Pelloquin *et al*., 2021, Wu

		et al., 2006, Gendrin *et al*., 2013, Wong *et al*., 2020.
Escherichia	inhibited	Takhi and Quinten, 2011, Soni *et al*., 2012, Feng *et al*., 2021, Dada *et al*., 2018 and 2019, Arruda *et al*., 2021
Gram-positive Bacteria genus	**Inhibitory effect of *D. stramoniun* extracts**	**References associating the bacteria genus to *Anopheles* mosquito.**
Elizabethkingia	Unknown	Wong *et al*., 2020, Baldini *et al*., 2014, Gomes *et al*., 2017, Cirimotich *et al*., 2011, Bahia *et al*., 2014, Daiamini *et al*., 2020, Wu *et al*., 2006.
Aeromonas	Unknown	Soltani *et* al., 2017.
Pseudomonas	Inhibited	Hu *et al*., 2014, Arruda *et al*., 2021, Wu *et al*., 2006, Cirimotich *et al*., 2011, Soltani *et al*., 2017, Bahia *et al*., 2014, Feng *et al*., 2021, Soni *et al*., 2012, Takhi and Quinten, 2011, Dada *et al*., 2018 and 2019
Enterobacter	Inhibited	Wu *et al*., 2006, Gendrin *et al*., 2013, Diamini *et al*., 2020, Sharma *et al*., 2021.
Actinobacter	Unknown	Wu *et al*., 2006, Gendrin *et al*., 2013, Diamini *et al*., 2020, Sharma *et* al., 2021.
Asaia	Unknown	Wu *et al*., 2006, Gendrin *et al*., 2013, Pelloquin *et al*., 2021, Feng *et al*., 2021.
Ewingella	Unkown	Gendrin *et al*., 2013.
Bacillus	Inhibited	Wong *et al*. 2020, Baldini *et al*., 2014, Gomes *et al*., 2017, Sharma *et al*., 2021.
Pantoea	Unknown	Wong *et al*. 2020, Baldini *et al*., 2014, Gomes *et al*., 2017, Bahia *et al*., 2014, Cirimotich *et al*., 2011, Diamini *et al*., 2020.
Bifidobacterium	Unknown	Feng *et al*., 2021
Ruminococcaceae	Unknown	Feng *et al*., 2021
Streptococcus	Unknown	Wang *et al*., 2021, Ochomo *et al*., 2023
Rubrobacter	Unknown	Wang *et al*., 2021, Ochomo *et al*., 2023
Sphingobacteriae	Unknown	Wang *et al*., 2021, Ochomo *et al*., 2023
Lysinibacillus	Unknown	Wang *et al*., 2021, Ochomo *et al*., 2023, Bando *et* al., 2023.
Salmonella	Unknown	Dada *et al*., 2018 and 2019.
Comamonas	Unknown	Bahia *et al*., 2014, Cirimotich *et al*., 2011.
Acinetobacter	Unknown	Dada *et al*., 2018 and 2019.

Discussion

Datura stramonium as a Bio-pesticide for Mosquitoes: Global Perspective

Datura stramonium is a perennial shrub that grows to about 1 to 1.5 meters tall it has a thornyfruit, foul-smelling leaves, and highly scented flowers (CGAIR, 2012; Bussman *et al*., 2020). This weed grows in India, the Himalayas, North America, Mexico, Bangladesh, North Africa, Uganda, and also in Kenya. It has been used as medicine by the Chinese, traditional African, Ayurvedic medicine, indigenous Americans, and medieval Europeans. Several phytochemicals of medical and insecticidal interest have been described from this weed. Steroids, phenols, flavonoids, alkaloids, terpenoids, tannins, saponins, organic compounds, and minerals have been described from *D. stamonium* extracts of its different parts obtained using different solvents (Al-Snafi *et al*., 2017; Rehman *et al*., 2022, Dermergi *et al*., 2023, Srivastava *et al*., 2022; Bazaoui *et al*., 2012). Agglutin, an insecticidal and chitin-binding lectin has also been isolated from its seeds. Atropine an alkaloid from *D. stramonium* is documented to have multiple modes of action on insects (Al-Snafi *et al*., 2017; Al-Ajmi *et al*., 2021). This weed, therefore, is currently gaining research interest for its potential both as a medicinal plant and as a biocide. Different studies have tested its potential as an insecticide, paraciticide, acaricide, and bactericide (Jemberie *et al*., 2016; Al-Snafi *et al*., 2017, Ayodele *et al*., 2024; Srivatsava *et al*., 2022, 2023).

A study by Swathi, 2012, tested 16.07 ppm of ethanolic leaf extracts against *An. stephensi* larvae and documented larvicidal potential. They also reported 71.66 minutes of complete protection time in a repellency test of 1% concentration of extracts. This species of mosquitoes are resistant to most conventional pesticides (Ochomo *et al*., 2023), even though the study did not mention the resistance status of the mosquitoes they used. The results obtained from this study raise concerns about the inhibitory effect of *D. stramonium* extracts on microbial-mediated resistance in mosquitoes. When tested on mosquito larvae the extracts had between 50% to 100% mortality.

In another recent study, a protein RPS 19, *Chaetospharidiun globosum*, isolated from crude extracts of *D. stramonium* leaves exhibited insecticidal potential with a lethal concentration (LC) 50 of 0.027mg/ml and LC 90 of 0.06 mg/ml after 24 hours post-exposure (Ochomo *et al*., 2015). Aqueous extracts of *D. stramonium* were effective on larvae of two species of mosquitoes with mortality of between 50% to 100% 24 hours post-treatment (Al-Snafi, 2017; Goyal *et al*., 2020). A study in Sudan by Ali and others revealed that methanolic leaf extracts of *D. Stramonium*, one week post-exposure, had toxicity on larvae of *Culex quiquefasciantas*, *Anopheles*, and *Aedes* mosquitoes (Mukherjee, 2013). This study reports that *C. quiquefasciantas* had LC 50 at 844.43 mg/l of the extracts, *Aedes* had an LC50 at 636.62 mg/l and *Anopheles* had LC 50 at 401.7 mg/l with mortality of 96.3% and 3.7% developing to pupae but none surviving by the seventh day. 100% concentration of aqueous root extracts showed 100% mortality of *Anopheles* and *Culex* mosquito larvae 24 hours post-treatment (Mohamed *et al*., 2022).

Mosquito Developmental Stages Commonly Used for D. stramonium Extracts Bio-assays

While most mosquito related illnesses are spread by adult female mosquitoes, this study reveal that a lot of toxicity experiments with *D. stramonium* extracts have been done on larvae 77%. Nearly all the articles included larvae as part of the experiment or used larvae only (Srivastava *et al*., 2023; Ullah *et al*., 2018, Borah *et al*., 2012; Swathi, 2012; Kirar *et al*., 2022; Olofintoye *et al*., 2011; Mohamed *et al*., 2022, Owoeye *et al*., 2016; Olajide *et al*., 2018). Most of these studies were on mosquito larvae whose resistance status is not mentioned. Adults which are very important in disease transmission were included in experiments rationed at 14% and reported in three studies. The experiments did not mention the resistant status of the *Anopheles* mosquito adults used (Srivastava *et al*., 2023; Owoeye *et al*., 2016; Olajide *et al*., 2018). Regionally In Africa for example where morbidity and mortality due to mosquito related illnesses is high, the mosquito studies with *Anopheles* species and *D. stramonium* extracts were majorly done in Nigeria and only one study in Sudan. There is need for more research with *D. stramonium* extracts and resistant adult strains of *Anopheline* mosquitoes which are vectors of malaria.

Solvents Frequently Used in Extractions of Different Parts of D. stramonium.

Experiments in four studies selected in this research were done with *D. stramonium* extracts used ethanol (39%) (Mohamed *et al., 2022;* Swathi, *2012;* Olajide *et al., 2018;* Asrar *et al., 2023);* followed by petroleum ether experiments(26%) in five different studies (Rajasekaran *et al*., 2012; Borah *et al*., 2019; Ahmed *et al*., 2019; Srivastava *et al*., 2023; Olajide *et al*., 2018; Owoeye *et* al., 2016); water (13%) (Rajasekaran *et al*., 2012; Olofintoye *et al*., 2011) and hexane (8%) (Owoeye *et al*. 2018) to extract phytochemicals and bio-active compounds of *D. stramonium*. Very few studies used methanol, and acetone, and none used ethyl acetate. All these experiments reported mosquitocidal potential of the extracts. The experiments done with *Anopheles* species majorly used ethanol. There is need to extract bio-active compounds of *D. stramonium* extracts using different solvents with different levels of polarity and with a focus on bio-active compounds of interest. Most of the articles used leaf extracts of *D. stramonium*. 18 experiments (66%) out of the 27 in Table 1, were done with leaf extracts and reported in eleven articles (Srivastava *et al*., 2023; Ullah *et al*., 2018, Borah *et al*., 2012; Swath, 2012; Kirar *et al*., 2022; Olofintoye *et al*., 2011; Mohamed *et al*., 2022, Owoeye *et al*., 2016; Olajide *et al*., 2018; Asrar *et al*., 2023, Rajasekaran *et al*., 2021). The data on parts of plants used is too skewed to leaves and there is need to research more on the other parts of the plant as well. Fruit, stem and seed were reported in one article each while flower was used four experiments but in two studies. There is little information about the least used parts of the plant.

Anopheles mosquito micro-biome and their growth response to D. stramonium extracts.

Anopheles mosquitoes harbor a diversity of bacteria in their tissues (Akorli *et al*., 2016, Djihinto *et al*., 2022). From wild-collected *An. darlingi*, 14 species of mosquito microbiota have been described from different genera such as *Staphylococcus*, *Burkholderia*, *Cedocea*, *Enterobacter*, *Klebsiella*, *Pantoea*, *Serratia* and *Acinetobacter* (Arruda *et al*., 2021). In this study, the most common bacteria species were *Serratia liquefaciens* and *Serratia marcenscens*. In another study, silica or RNA later solution was used to preserve *An. arabiensis* and *An. funestus* and an examination of their mid-gut microbiota revealed *Bacteriodetes* and *Protobacteria*, with the *Protobacteria* being dominant in the mid-gut of *An. funestus* (E Silva *et al*., 2021; Wang *et al*., 2021). In their findings, the common genera in *An. arabiensis* females and males were *Serratia* and *Elizabethkingia* but *Elizabethkingia*, *Serratia*, and *Aeromonas* were dominant in males. At the species level, *E. anopheles*, *S. oryzae*, and *A. hydrophila* were seen to be common in both the male and female *An. arabiensis*. The study also examined field-together *An. Arabiensis* and *S. epidermis* and *S. hominis* were isolated from males eight weeks post-preservation. *E. cloacae* was isolated from female arabiensis. *S. marcenscens* and *Creseobacterium meninqosepticum* have been associated with *An. stephensi* reared in the laboratory (Rani *et al*., 2009). *E. cloacea* and *S. marcenscens* have been reported to being isolated from *An. gambiae s.l* (Ezemuoka *et al*., 2020).

The microbiota of *Anopheles* mosquito differs from region to region with some species of bacteria that are similar regardless of region (Ezemuoka *et al*., 2020; Krajacich *et al*., 1018). *An. gambiae s.l* collected from the field in Zambia had a diversity of mid-gut microbiota including *Comamonas sp*., *Acinetobacter sp*., *P. putida*, *Pantoea sp*., *P. rhodesiae*, *S. marcenscens*, and *Elizabethkingia anophelis* (Cirimotich *et al*., 2011; Bahia *et al*., 2014). In China, several studies reported a diversity of different microbiota on different species of *Anopheles* mosquitoes. From *An. lesteri* were mostly *Bifidobacterium*, *Escherichia-shigella*, *Faecalibacterium*, and *Blautia* (Feng *et al*., 2021). In the same study, *Pseudomonas* and *Ruminococcaceae* were isolated from *An. dirus* while *Asaia* was isolated from *An. sinensis* (Feng *et al*., 2021), *An. stephensi* (Favia *et al*., 2007), and all stages of *An. gambiae* (Damiani *et al*., 2010). *An. darlingi* eggs, larvae, and pupa had *Actinobacteria* such as *Arthobacter sp*., *Brevibacterium sp*., *Leucobacter sp*., and *Microbacterium sp*. Abundant genera were *Enterobacter*, *Acinetobacter*, *Serratia*, *Pantoea*, *Klebsiella*, *Bacillus*, *Elizabethkingia*, and *Stenotrophomonas*. *Wolbachia* species have been isolated from field-collected *An. maculatus* and *An. sinensis* species in Burkina Faso (Baldini *et al*., 2014), Mali (Gomes *et al*., 2017), Malaysia (Wong *et al*., 2020) a huge number reported in Gabon (Ayala *et al*., 2019), and Senegal from *An. funestus* as reported by Niang *et al*., (2018).

Several bacteria of medical importance are associated with resistant malaria vectors. Table five gives a summary of the gram-positive bacteria genus reported from *Anopheline* mosquitoes. Some of these bacteria are of the same genus as others which affects vector competence and physiology inhibiting *Plasmodium* development in the vector (Dada *et al*., 2019; Omoke *et al*., 2021; Shane *et al*., 2018; Shane *et al*., 2021; Damergi *et al*., 2023; Grant *et al*., 2016). A number of these bacteria are gram-negative bacteria (resistant to antibiotics) and have been associated with *Anopheles* mosquitoes (Gendrin, *et al*., 2013). In the family *Enterobacteriaceae*, the gram-negative bacteria are genera *Serratia*, *Ewingella*, *Enterobacter*, and *Klebsiella*. *Actenobacteriae* family are genera *Actenobacter* and *Asaia*. *Flavobacteriacea* are genera *Elizabethkingia* and *Chryseobacterium*. Mid-gut of *Anopheles*, *Serratia*, *Asaia*, *Acinetobacter*, *Aeromonas*, and *Pantoea* bacteria have been isolated. In the salivary glands and reproductive tissue, isolation of *Asaia*, *Serratia*, *Acinetobacter*, *Pseudomonas*, and *Klebsiella* which are associated with insecticide detoxification have been reported (Wu *et al*., 2006).

Extracts of *D. stramonium* had both duration and dose-dependent effects on gram-positive bacteria except for *Escherichia* and *Pseudomonas* species. (Takhi and Ouinten, 2011; Soni *et al*., 2012). Pyrethroid-detoxifying taxa of bacteria have been identified as *Sphingobacterium*, *Lysinobacillus*, and *Streptococcus*. A radio-tolerant taxa *Rubrobacter* have been also isolated from resistant *An. gambiae* species resistant to five-fold diagnostic doses of permethrine (Ochomo *et al*., 2023; Wang *et al*., 2021). This study reports significant differences in the species composition of the bacterial community of *An. gambiae* with krd-east alleles (L1014S) to those of susceptible ones. They reported 21 bacteria specific to *An. gambiae* with kdr-east alleles and 16 others specific to susceptible ones with *Myxococcus* species most abundant in susceptible samples and not found in the resistant groups (Ochomo *et al*., 2023). In a different study, *Anopheles coluzzii* resistant to deltamethrin had several gram-negative bacteria genera such as *Onchrobactrum, Stenostrophonomas,* and *Lysinibacillum* unlike their susceptible counterparts which had less bacteria diversity and with S*erratia* and *Asaia* as the dominant genera (Pelloquin *et al*., 2021). *Lysinibacillus sphaericus* was able to detoxify 83%of cyfluthrin and have used insecticide as a source of nitrogen or carbon (Bando, *et al*., 2013). From the gut of fourth instar larvae of multiple-resistant *An. arabiensis*, *Klebsiella*, *Staphylococcus*, *Enterobacter*, and *Aeromonas* were isolated (Barnard, *et al*., 2019). *An. albimanus* resistant to organophosphate fenitrothion were dominated by insecticide-degrading bacteria of the genus, *Klebsiella*, *Acinetobacter*, *Escherichia*, and *Salmonella* (Dada *et al*., 2019). *A. albimanus* larvae and adults, exposed to pyrethroid insecticides indicated alterations in their cuticular and internal microbiota (Dada *et al*., 2019, Dada, *et al*., 2018). The study exposed *An. albimanus* adults to alphacypermethrine and permethrin and found *P. fragi* and *P. agglomerans* abundant in the treated samples as compared to the non-treated samples that had large numbers of *Acinetobacter* and *Serratia* (Dada *et al*., 2018). The midgut of *An. stephensi* resistant to temephos had *Pseudomonas*, *Aeromonas*, *Exiguobactrium*, and *microbactrium* (Soltani, *et al*., 2017). These studies have documented evidence of bacteria-mediated resistance which possibly is initiated when the vectors pick insecticides through feeding, inhalation, or contact with their cuticle. The insecticide-degrading bacteria make the vectors non-responsive to insecticides adversely affecting their control. the speculations by researchers is that the type of resistance reported in this study is metabolic (Barnard, *et al*., 2019, Dada *et al*., 2019). Susceptible mosquitoes exhibited substantial microbial diversity (Dada *et al*., 2019, Barnard, *et al*., 2019, Ochomo *et al*., 2023) than resistant ones. Changes in susceptibility to insecticides, therefore, can be improved by increasing bacteria diversity on the vectors (Djihinto, *et al*., 2022).

Datura Stramonium has been researched in the laboratory for medicinal considerations for its antibacterial activity. In Pakistan, chloroform extracts from fruits impeded the growth of *P. aeruginosa* and leaf extracts inhibited the growth of *K. pneumoniae* (Bhakta *et al*., 2013). Banso and others documented the inhibitory effect of *D. stramonium* on gram-positive bacteria. Ethanolic, leaf extracts at 25% W/V obstructed the growth of *P. aeruginosa*, *Klebsiella pneumoniae,* and *E. coli*. (Hu *et al*., 2014). In other studies (Al-Snafi, 2017; Saab, *et al*., 2020; Gupta *et al*., 2009; Gupta *et al*., 2021), 2.5, 1.25, and 0.75 mg/l concentrations of *D. stramonium* extracts inhibited the growth of *S. haemolytus*, *S. aureus, Shyngella dysentriae, Bacillus cereus*, *P. aeruginosa*, *K. pneumonia,* and *Escherichia coli*. *Enterobacter* and *Micrococcus lutius* have also been inhibited (Al-Snafi, 2017; Rehman, *et al*., 2022). Even though *D. stramonium* has dose-dependent antibacterial properties on human disease-causing bacteria, further research needs to be done to establish the correct human dosage to avoid human poisoning as the plant is highly poisonous. Information on its effects on resistant mosquito tissue bacteria is not well understood to confirm its effectiveness on bacteria-mediated resistance in malaria vectors.

Of the many compounds in *D. stramonium*, atropine has been described to have a multiple mode of action on insects. It impedes the release of the ecdysone enzyme responsible for molting. This causes deformed and sterile adults. It has an anti-oviposition effect on insects (Juss *et al*., 2015; Srivastava *et al*., 2023; Waleed *et al*., 2021; Eukubay *et al*., 2021). It also acts as a feeding deterrent with an anti-muscarinic agent that hinders insects' ability to swallow by blocking the muscarine-like effects of acetylcholine and other esters (Djibril *et al*., 2015; Iqbal, 2019).

CONCLUSION AND RECOMMENDATIONS

From the web search results above, research gaps have been identified that need to be filled that can aid in understanding the role of *D. stramonium* extracts on the diversity of the malaria vector bacterial community. The *D. stramonium* extracts mode of action on the bacteria community associated with in *Anopheles* mosquito resistance is not clear. It is as well not clear whether phytochemicals in *Datura* extracts known to be an antidote to pesticide poisoning have the same effect on resistant mosquitoes making them susceptible to chemical pesticides post-treatment. There is a need to understand the effect of *D. stramonium* extracts on blood-fed, *Plasmodium*-infected mosquitoes to understand their longevity, oviposition behaviour, reproductive cycle, and physical properties of the treated mosquito offspring. The mode of action of the various individual compounds of *D. stramonium* on resistant mosquitoes is not well understood. A lot of research needs to be done on *D. stramonium* as a potential medicine and biocide for mosquito vector control.

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