A Review on Larvicidal Activity of Silver Nanoparticles Derived From Ficus Spp. Against Aedes Aegypti

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ABSTRACT

Insecticidal resistance among mosquitoes has become prevalent due to the continuous use of insecticides to control dengue vectors. This became the catalyst for researchers to come up with an alternative that is mainly organic and biologically synthesized from plants. Silver nanoparticles are widely known as one of the effective alternative larvicides since it has the silver's bactericidal capabilities, the larvicidal activity of the chosen plant, and excellent effectiveness due to its small particle size which measures around 1 nanometer to 100 nanometers, as well as the excellent surface area to volume ratio. Different plant parts such as leaves and fruits from some *Ficus* spp. are widely used and studied in deriving silver nanoparticles to test their larvicidal activities against dengue vectors. Researchers discovered that this is due to the plant extracts from most *Ficus* spp. which contain phytochemical components that are known for having a huge role in ferric reduction and radical scavenging actions. Most researchers used advanced analytical methods to explore the characteristics of the derived silver nanoparticles and used WHO protocol in testing the effectiveness in combating dengue vectors. This review will discuss the possibility that silver nanoparticles derived from an indigenous plants, which are *Ficus* species, can be a feasible alternative to combat dengue outbreaks.

Keywords: *Aedes aegypti*, Dengue virus, *Ficus* species, Insecticidal resistance, Silver nanoparticles

INTRODUCTION

Dengue fever is a mosquito-borne virus that has recently spread to many parts of the world. Mosquitoes commonly transmit Chikungunya, yellow fever, and Zika viruses. The virus is expected to cause 100-400 million illnesses per year. Early diagnosis and adequate medical care can reduce severe dengue mortality to under 1%. Some patients develop severe dengue, affecting various body systems. The virus has four serotypes that can coexist in the same area: bleeding, organ damage, and plasma leakage. Many countries have all four serotypes. (WHO, 2022)

The *Aedes aegypti* mosquito transmits the dengue virus. In addition to the black and white pattern on its legs and other body parts, *Aedes aegypti* adults have white and silver scaly spots on a black background. (European Centre for Disease Prevention and Control, n.d.) They prefer humans because they allow them to rest and seek hosts. *Aedes aegypti* thrives in urban areas with abundant oviposition sites. Human activities such as outdoor water storage must be targeted to control this species. Reducing mosquito populations is more effective than using insecticides and focusing on source reduction.

The *Ficus* genus comprises roughly 850 woody trees, shrubs, vines, epiphytes, and hemiepiphytes. They are endemic to the tropics, with a few species expanding into the semi-warm temperate zone. There are roughly 150 species endemic to the Philippines, a tropical country; among these are *Ficus casiguranensis, Ficus camarinensis, Ficus microcarpa, and Ficus religiosa, Ficus racemosa, Ficus benjamina, Ficus vallischoudae Delile*, *Ficus septica* and, *Ficus benghalensis*. The *Ficus* spp. is extensively used for traditional medicines for different diseases and conditions, such as *Ficus casiguranensis* and *Ficus camarinensis* are known to have antibacterial and larvicidal activity. *Ficus microcarpa*, *Ficus religiosa*, and *Ficus racemosa* are traditionally used for Diabetes, inflammation, and skin diseases. At the same time, *Ficus microcarpa, Ficus benjamina, and Ficus septica* are also good sources of fiber and latex.

Silver nanoparticles are becoming more common in biomedicine. Silver nanoparticles are less than 100 nm in size and contain 20-15,000 silver atoms. (PMC, n.d.) The optical, thermal, and catalytic properties of silver nanoparticles vary in size and shape. Silver nanoparticles are often used to sterilize nanomaterials in food and pharmaceutical goods, such as textiles, food storage bags, refrigerator surfaces, and personal care products. Silver is a popular antibacterial and disinfectant owing to its low toxicity. These silver nanoparticles are antibacterial and antiviral. Bacterial cell walls may be penetrated, affecting membrane structure and perhaps killing cells. Silver ions are released by reactive oxygen species, disrupting DNA replication. (Ramesh et.al, 2018)

An increase in dengue cases showed that numerous people have been affected by the disease, especially those residing in tropical and subtropical areas. As such, to manage and eliminate mosquito-borne diseases, insecticides are being applied. However, the use of insecticides possesses harmful effects both on people and the environment. Also, according to Liu (2015), despite the high effectiveness of insecticides to control vector species, it has become the root cause for the resistance of most mosquitoes leading to an increase in vector capacity. That's why newly improved insecticides are needed to manage the vector without causing harm to the environment and the non-target organisms. Plus, a type of insecticide that is not costly, thus budget-friendly, can attract a lot of consumers to use insecticides to eliminate mosquitoes-borne diseases that are roaming around their area. The use of insecticide by one person will be beneficial to all the people and the environment around them.

Because of synthetic insecticides' toxicity on the environment and humans, as well as the increasing prevalence of insect resistance it has become vital to develop new insecticides. The general objectives of the authors is to identify an alternative larvicide that would help lessen *Aedes aegypti* mosquito viruses that kill thousands of people in a year. The idea of a plant-based insecticide that is safe and effective for everyone, that is not harmful to both the environment and other living things is what the authors want to perceive. A further intention of the authors is to familiarize ourselves with plants that derived silver nanoparticles. It has been demonstrated that by combining AgNPs with insecticidal plant extracts, larvicidal compounds that are effective against mosquitoes can be synthesized. As plants are high in bioactive compounds, are effective against a small number of species, including specific insects, and are biodegradable, they could be a source of alternative mosquito control agents (Morejon et. al, 2018). In this case, the specific objective of the authors is to focus on the larvicidal activity of AgNPs extracted from different *Ficus* spp. as they have the potential to be useful in pest management strategies that are integrated. Specifically this systematic review aims to help the general community and local workers have an idea on what are the possible plant alternatives to synthetic insecticides for killing larvae or adult mosquitoes, and gain knowledge for the future researchers which may also serve as their grounds for future references and background literature.

METHODOLOGY

A. Literature Search

The researchers used different library databases which are PubMed, Google Scholar, EBSCO Information Services, and ScienceDirect to look for reliable and relevant articles and journals for the research. The keywords used were "insecticidal resistance, Dengue virus, *Ficus* spp., silver nanoparticles, larvicidal activity of *Ficus* spp., and *Aedes aegypti"*. The databases were limited to 12 years, starting from the year 2010 to 2022 but not restricted on location. A manual search was performed to narrow down the variety of sources thus making it more efficient to find information about *Ficus* spp., silver nanoparticles, larvicidal activity, and *Aedes aegypti* that the researchers needed.

B. Eligibility Criteria

The researchers use the title and abstract screening to identify the articles of interest which include credible databases such as PubMed, ScienceDirect and NCBI. It was guaranteed that resources were published in English starting from the year 2010 up to present. To that intent, the researchers limit the inclusion to peer-reviewed papers and topic references that include silver nanoparticles, *Ficus* spp., insecticidal resistance, *Ficus* spp. *Aedes aegypti*, silver nanoparticles with larvicidal activity, green-synthesised silver nanoparticles, and silver nanoparticles

As for the exclusion, the researchers particularly excluded articles whose participants are below college students, non-English studies, and sites that are not credible such as wikipedia, social media, and unpublished studies or blogs. Moreover, studies that are outdated and published on or before 2010 and other biological activities of silver nanoparticles, other plants, chemically synthesized silver nanoparticles, other vectors, and are non-peer-reviewed are also excluded.

C. Selection Strategy

The researchers were able to identify and review the inclusions for the selected study together with its eligibility and discrepancies. The authors have scanned the title and abstract of the selected articles with respect to the full-text assessment of the acceptable research articles.

D. Data Extraction

Using a standardized form, the researchers retrieved the following study characteristics from the eligible articles which includes: (i) study characteristics (title, first author's name, journal, year of publication, country of origin, and objective); (ii) methods (research design, sample size, and duration of the study); (iii) subject characteristics (inclusion and exclusion criteria); (iv) results: the key or major findings of the study.

RESULTS

A. Study Selection

The researchers discovered a total of 10 research articles on larvicidal activity of silver nanoparticles obtained from Ficus species against *Aedes aegypti* from 2010 to recent year through screening of title and abstract from 62 articles collected from the initial search on ScienceDirect, NCBI, PubMed, and Google Scholar. The detailed selection procedure is provided by the PRISMA flowchart.

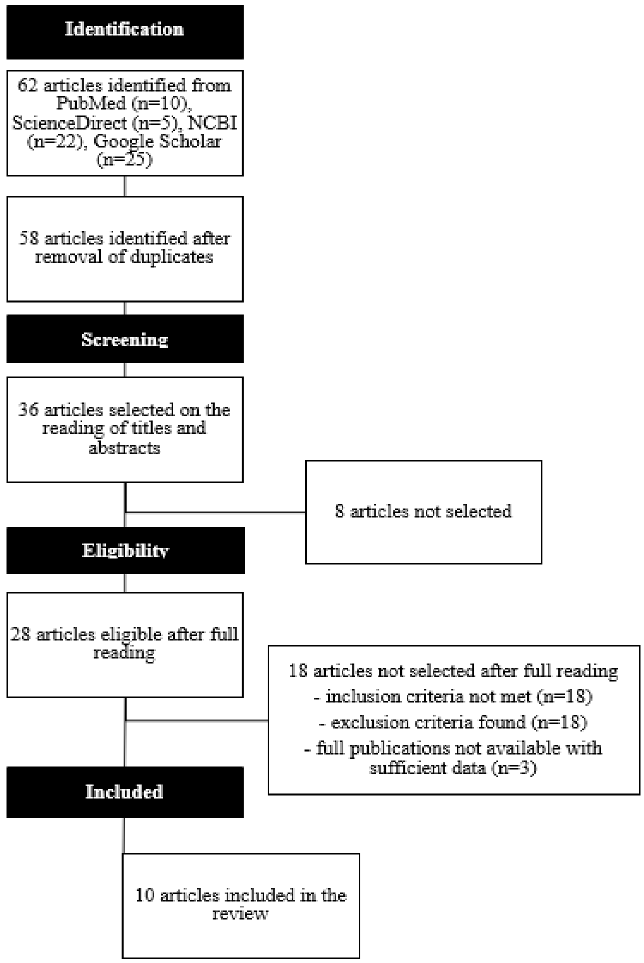

Figure I. PRISMA Flowchart.

B. Characteristics of the Included Studies

All 10 selected articles were experimental studies, and few are cross sectional studies. The articles mainly focus on discussing the larvicidal effects of silver nanoparticles extracted from *Ficus* spp against *Aedes aegypti.* The researchers also included two articles that involve phytochemical reactions and the extract of *Ficus benghalensis*. Most of the study that was analyzed found that the most common vector used was *Aedes aegypti, Culex quinquefasciatus, and Anopheles stephensi.* The articles were mostly published between 2014-2021, and the other two were published around 2010 to 2012. After carefully reading the articles, the researchers observed that most of the specimens were bought or came from Asia, specifically India. The significant findings from the studies were tabulated, summarized, and are briefly discussed in Table I.

No.	References	Study Area	Study Design	*Ficus* Plant/s Used	Vector/s	Findings
1	Bekoe (2015)	Ghana	Experimental	*Ficus exasperata*	-	Only cardiac glycosides and saponins were found in

						Ficus exasperata leaves. The phytochemical identified in the leaves of *Ficus exasperata* indicate that it has the potential to be a source of plant constituents that may supply innovative treatments.
2	Esmaili et. al (2021)	Iran	Experimental	*Ficus glomerata*	*Culex quinquefasciatus, Culex tritaeniorhynchus, Aedes aegypti, Culex pusillus, Anopheles stephensi, Culex pipiens, Ochlerotatus caspius, & Anopheles culicifacies*	Polymeric nanoparticles are better for larvicides, nanoemulsions are better for adulticides, and lipid nanocarriers are better for repellents.
3	Govindarajan (2010)	India	Experimental	*Ficus benghalensis*	*Culex quinquefasciatus, Aedes aegypti, Anopheles stephensi*	Ficus benghalensis extracts are effective in controlling *Culex quinquefasciatus,Anopheles stephensi,* and *Aedes aegypti* mosquito larvae.
4	Heroor et.al (2020)	India	Experimental	*Ficus glomerata*	-	The steroidal compound like Ficus glomerata steroidal compound (FGS) was found to be more immunopotent than all constituents alkaloid, flavonoid and tannins. Therefore, this steroidal compound can be linked to the immunomodulatory property of the plants.
5	Idowu et,al (2021)	Lagos, Nigeria	Experimental	*Ficus exasperata* and *Moringa oleifera*	*Culex quinquefasciatus, Anopheles stephensi,* and *Aedes aegypti.*	On both laboratory and field collected mosquitoes, the efficiency of *Moringa oleifera* nanoparticles was greater at lower concentrations than

						that of *Ficus exasperata*. Factors such as pesticide resistance in the field mosquito population seem to have no influence on the effectiveness of the two extracts, since mortality increased with increasing exposure duration. This demonstrates the nanoparticles' potential for application in an integrated strategy to combating mosquito vectors.
6	Rahman (2018)	India	Experimental	*Ficus religiosa*	-	The biological production of silver nanoparticles using Ficus religiosa leaf extract is an environmentally safe, straightforward, and easy technique to synthesize nanoparticles. This study shows that the Ficus religiosa plant leaf extract may be utilized to successfully synthesize silver nanoparticles.
7	Recuenco et.al. (2020)	Philippines		*Ficus ulmifolia, Ficus pseudopalma, Mangifera altissima, Antidesma bunius, Garcinia binucao, Artocarpus altilis, Citrus hystrix, Canarium ovatum, Rubus rosifolius*	*Escherichia coli, Staphylococcus aureus*	Phytochemical screening showed positive results for phenolics , flavonoids, and tannis. The TPC results for the unripe *M. altissima* was within the range report and the TPC for the ripe *A. bunius* was close to te reported levels of the ripe fruit and lastly the TPC of the pulp and juice of ripe *C. hystrix* may be higher compared to the reported *C. hystrix* juice

8	Soni et. al. (2020)	India	Experimental	*Ficus religiosa*	*Anopheles stephensi*	Probit analysis was used to determine larvicidal mortality after 24 and 48 hours. The well diffusion method was used to assess antibacterial activity. The nanoparticles that were synthesized had an uneven form and varied in size.
9	Suriyakalaa et. al (2022)	India	Experimental	*Ficus religiosa*	Mice Model	Phenolics, alkaloids, flavonoids, steroids, and reducing sugar are all present in both fresh and dry leaf extracts. Only dried leaf extract included saponins, coumarins, tannins, and quinones. Furthermore, as compared to fresh leaf extract, dry leaf extract has a higher level of total phenolics and vitamin C (p0.05), although fresh leaf extract has a higher level of flavonoids and steroids.
10	Velayutham et. al. (2013)	India	Experimental	*Ficus racemosa*	*Culex quinquefasciatus* and *Culex gelidus* fourth instar larvae	The larvicidal activity showed that synthesized AgNPs had the maximum mortality against *Culex quinquefasciatus* and *Culex gelidus* larvae.

Table I. Characteristics of Included Studies.

C. Phytochemicals Present in Ficus Plants

Phytochemicals/secondary metabolites are the bioactive components of plants having a tremendous value in the pharmacological and therapeutic areas. The genus *Ficus* comprises a range of phytochemicals, including phenolics, polyphenols, flavonoids, tannins, anthocyanins, coumarins, volatile components, glycosides, saponins, carotenoids, alkaloids, triterpenoids, and vitamins. Generally, these phytochemical substances have health-enhancing benefits in humans due to their significant antioxidant capability. However, through this paper, another potential use of phytochemicals were discovered and have been discussed.

Chromatography and mass spectrometry are the methods often used to identify plant metabolites. According to Ali et.al (2021), plant-derived secondary metabolites gas chromatography and liquid chromatography-based analysis are commonly employed, while according to Hu et.al (2013), mass spectrometry (MS) is a rapid and sensitive tool for the analysis of metabolites from biological samples.

Upon data collection, the researchers identified five *Ficus* plants that met the requirements which can be used for this review paper. The first one is *Ficus benghalensis* containing important phytochemicals/secondary metabolites, which are saponins, flavonoids, tannins, and alkaloids. These were identified via different methods such as DPPH scavenging assay, Iron chelating assay, Folin-Ciocalteau reagent method, Aluminum chloride method, HPTLC and, HPLC. Another *Ficus* plant is the *Ficus exasperata*, which has cardiac glycosides and saponins as its phytochemicals and were identified by the Rotary evaporator method. The *Ficus glomerata* contains tannins and steroids that TLC and Column chromatography identify. The *Ficus racemosa* with tannins, B-sitosterol, stigmasterol as phytochemicals and were identified with UV-vis spectroscopy, XRD, SEM and, FTIR. And the *Ficus religiosa* with phytochemicals of phenolics, alkaloids, flavonoids, and steroids identified with UPLC-QqQ-MS system and Masslynx MS. Based on the available literature, flavonoid was one of the most commonly reported or projected chemicals responsible for generating silver nanoparticles in the green synthesis method. Table II provides the summary of the phytochemicals identification for each plant and their corresponding methods.

Ficus Species	Phytochemicals/Secondary Metabolites	Method/s	References
Ficus benghalensis	Saponins, Flavonoids, Tannins, Alkaloids	DPPH scavenging assay, Iron chelating assay, Folin-Ciocalteau reagent method, Aluminium chloride method, HPTLC, HPLC	Rao et al. (2014)
Ficus exasperata	Cardiac glycosides, Saponins	Rotary Evaporator	Bekoe (2015)
Ficus glomerata	Tannins, Steroids	TLC, Column chromatography	Heroor (2020)
Ficus racemosa	Tannins, B-sitosterol, Stigmasterol	UV-vis spectroscopy, XRD, SEM, FTIR	Velayutham et al. (2013)
Ficus religiosa	Phenolics, Alkaloids, Flavonoids, Steroids	UPLC- QqQ-MS system, MassLynx MS	Suriyakalaa et al. (2022)

Table II. Phytochemicals Present in Ficus Plants.

D. Syntheses of Silver Nanoparticles using Ficus Plants Extracts

According to Chung et.al (2016), green synthesized nanoparticles have gained increased attention because of consumer interest in environmentally friendly goods. Additionally, the synthesis of nanoparticles using plants has several benefits, including cleaner solvents, a reduction in hazardous chemicals, softer reaction conditions, practicality, and adaptation to medical, surgical, and pharmaceutical applications.

The synthesis of silver nanoparticles has a protocol that is generally followed by scientists and researchers. According to Ahmed et.al (2016), the procedure will start with the plant's leaves being removed and subsequently cleaned with distilled water. Immediately after washing, the leaves are squeezed using a domestic blender to create a juice. Afterward, using filter paper, the fluid is then filtered to produce an extract. The extract was then placed in a container, and silver nitrate was added. When the silver nitrate was added, the solution soon turned yellow, indicating the formation of silver nanoparticles. Figure I depicts the detailed process of the general protocol in synthesizing silver nanoparticles.

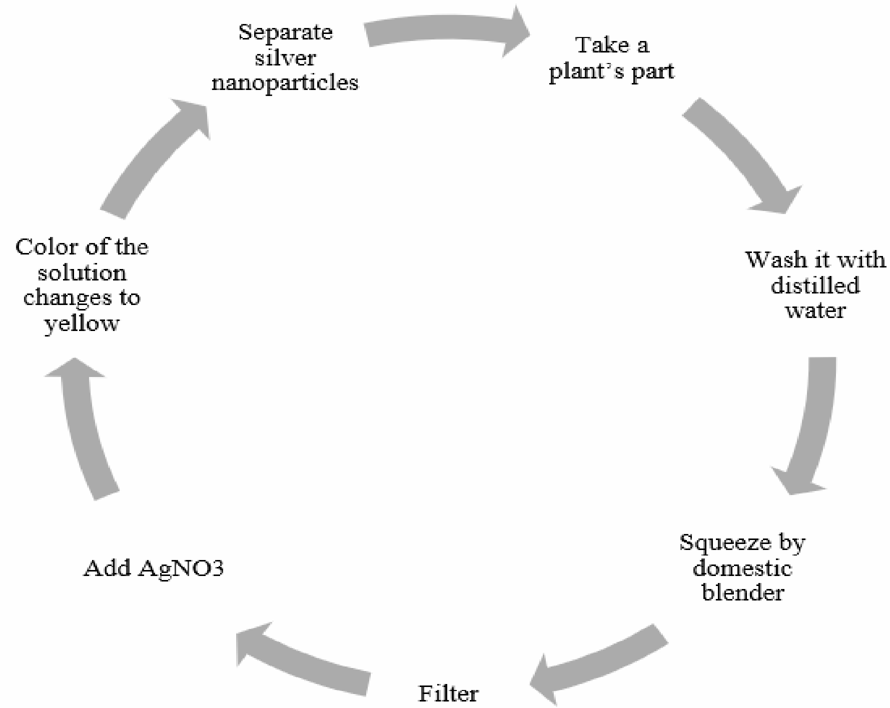

Figure I. General Protocol on Synthesizing Silver Nanoparticles from Plant Extracts. Retrieved from "A review on plants extract mediated synthesis of silver nanoparticles for antimicrobial applications:A green expertise" by Ahmed et.al (2016).

In this review paper, green synthesis of the silver nanoparticles derived from some *Ficus* spp. are also discussed below. Table II shows the characterization of the silver nanoparticles produced from these plant extracts.

Taken from the method done by Govindarajan (2010), the leaf of *F. benghalensis* was carefully cleaned with deionized water prior to the synthesis of silver nanoparticles. The *Ficus benghalensis* leaf underwent washing, drying, and was cut into small pieces, which then combined with deionized water and heated for 5 minutes before removing excess. 103 M aqueous solution of silver nitrate (AgNO3) was also used to reduce silver ions. According to Govindarajan (2010), when the extract of *F. benghalensis* is combined with an aqueous solution of silver ion complex, the color changes from white to yellowish brown, which indicates the creation of silver nanoparticles owing to surface plasmon resonance excitation. The size and shape of the silver nanoparticles, however, are not stated in the said article.

As Idowu et al. (2021) stated in their recent study, *Ficus exasperata* extracts were prepared at Herbarium, Department of Botany, University of Lagos, Lagos, Nigeria. 40g of *F. exasperata* leaves were washed thoroughly in 400mL distilled water for 5 minutes before boiling for 15 minutes, cooled, and filtered with Whatman-1 filter paper, and kept refrigerated until further use. After that, to have a solution of 0.05M silver nitrate solution that will be used to produce a brownish powder of silver nanoparticles, 300mL of distilled water was added to 1.54g of silver nitrate, then stirred with a magnetic stirrer for 5 minutes while adding 20mL of plant extracts, and was observed for a color change. The initial pale yellow color will be changed to dark brown after 72 hours and later on to be subjected to centrifuge at 400rpm for 20 mins. Lastly, the supernatant was discarded, and the residue was oven-dried at 70 °C to have brownish powder silver nanoparticles. Through the use of SEM micrographs, the size of the synthesized particles was found to be around 500 nm. However, the shape of these was not clearly stated.

In a review paper on the use of plants as an essential oil that is based on nanoformulation to serve as a larvicide. Esmaili et al. (2011) stated that nanoemulsion physical stability is high though, during the larvicidal test it greatly decreases which leads to the short-term durability of its larvicidal effect. Based on their study, with the numerous articles being published they discovered that herbal extracts are being used as a reducing agent to synthesize the silver nanoparticles from AgNO3 or AgCl. Silver nanoparticles do not use reducing agents that are toxic plus, can easily interact with functional groups of chemicals. However, in the test conducted the chemically synthesized nanoparticles that have a particle size of 30 nm only showed to have a 20% at 100 ppm larvicidal effect. In the research study, the ethanol extract of the *Ficus glomerata* plant was added in the nanoemulsion of neem oil (NON) for the crystallization emulsion.

Based on the article of Velayutham et.al., (2013), the synthesis of silver, 250 mL distilled water was added to 2.5 g of *F. racemosa* bark powder and boiled for 5 minutes then filtered. The filtrate was incubated at room temperature with an aqueous 1 mM silver nitrate solution. A brown solution was obtained by reducing an 80 mL aqueous solution of 1 mM AgNO with 20 mL bark extract at room temperature for 10 minutes, showing the formation of AgNPs. The produced silver nanoparticles were cylindrical, uniform, rod-shaped, and had an average size of 250.60 nm, which were identified using SEM micrographs.

Referring to the method done by Rahman & Prasanna (2018), a 1 gram of powdered leaves extract of *Ficus religiosa* was added to the 10 ml of methanol or a 1:10 ratio. It was kept in a shaker incubator for 12 hours and was stored at 4°C in the refrigerator. The extract was then added to the AgNO3 solution and a change of color was detected after 24 hours. Due to the surface plasmon resonance vibration, the color changes from pale yellow to dark brown throughout incubation, signifying the synthesis of silver nanoparticles. The silver nanoparticles have the shape of spherical measuring 70.29-84.93 nm.

Ficus Species	**Plant Part Used**	**Size**	**Shape**	**Qualitative Findings**	**References**
Ficus benghalensis	Leaves	-	-	Color changes from white to yellowish brown	Govindarajan (2010)
Ficus exasperata	Leaves	500 nm	-	Color changes from pale yellow color to dark brown	Idowu et.al (2021)
Ficus glomerata	Leaves	30 nm	Spherical	Formation of nanocrystals	Esmaili et al. (2011)
Ficus racemosa	Bark	250.60 nm	Cylindrical, Uniform and Rod	Color changes into a brown solution	Velayutham et.al (2013)
Ficus religiosa	Leaves	70.29-84.93 nm	Spherical	Color changes from pale yellow to dark brown	Soni & Dhiman (2020)

Table III. Characterization of Silver Nanoparticles Derived From *Ficus* Species.

E. Larvicidal Activity of Extracted Silver Nanoparticles Against Aedes aegypti

The WHO's general larvicidal bioassay approach involved batches of 10 to 25 third or fourth instar larvae being put to small disposable test cups holding 200 mL of water each. Starting with the lowest concentration, the required volume of dilution was added to 200mL water in the cups to reach the desired target dosage (concentration ranging from 25 to 200 ppm). Using Probit regression analysis and the statistical software program, the lethal concentrations that killed 50% and 90% of mosquito larvae (LC50 and LC90) were identified (SPSS). The concentration of a substance in the air that, based on laboratory testing, is estimated to kill half of a set of test animals when given as a single exposure.

The methanolic extract of F. benghalensis showed highest larvicidal activity against *Cx. tritaeniorhynchus* and *An. subpictus* which shows 60 to 90% concentration. Meanwhile, for Ficus exasperata, a mortality of 23% -93% were recorded respectively. In *Ficus glomerata*, no larvae died in the observance in negative control while Ficus racemosa was found to have the highest mortality in synthesized Ag NPs against the larvae of *Cx. quinquefasciatus* and *Cx. gelidus* at the concentration of 25 mg/L. Lastly, Ficus religiosa has shown that the fourth instar has 100% mortality after the 24 hour exposure. Table III shows the final results on larvicidal activity of green-synthesized silver nanoparticles from *Ficus* spp. against *Aedes aegypti*.

To summarize the table, all of the journals that the researchers use are under the *Ficus* spp. For the instars which are the larvae, all journals use a 4th instar except for the *Ficus exasperata* while in exposure period are 24 hours except for the *Ficus glomerata.* In lethal concentration 50, the results show different concentrations in each *Ficus* spp ranging from 1 ppm to 80 ppm while in lethal concentration 90, only 3 out of 5 journals use it. The results show that in *Ficus benghalensis*, the lethal concentration 90 is at 169.58 ppm, *Ficus exasperata* is at 8.55 ppm and *Ficus racemosa* is at 64.99 ppm which indicates that there is a huge difference in the lethal concentration 90.

Plant Extract Used	**Instars**	**LC_{50} (ppm)**	**LC90 (ppm)**	**Exposure Period**	**References**
Ficus benghalensis	4th Instar	80.85 ppm	169.58 ppm	24 hr	Govindarajan (2011)
Ficus exasperata	Late 3rd Instar	1.51 ppm	8.55 ppm	24 hr	Idowu et.al (2021)
Ficus glomerata	4th Instar	20 ppm	-	48 hr	Esmaili et.al (2011)
Ficus racemosa	4th Instar	14.55 ppm	64.99 ppm	24 hr	Velayutham et.al (2013)
Ficus religiosa	4th Instar	25 ppm	-	24 hr	Soni & Dhiman (2020)

Table IV. Larvicidal Activity of Extracted Silver Nanoparticles From *Ficus* spp. Against *Aedes aegypti*.

DISCUSSION

The purpose of this study is to review the larvicidal activity of silver nanoparticles extracted from different *Ficus* spp. as they have the potential to be useful in pest management strategies that are integrated. Specifically this systematic review aims to help the general community and local workers have an idea on what are the possible plant alternatives to synthetic insecticides for killing larvae or adult mosquitoes, and gain knowledge for the future researchers which may also serve as their grounds for future references and background literature.

Insecticides sprayed on mosquito larvae habitats or indoors against adult mosquitoes are the most common methods of control. However, although insecticides were historically efficient in managing mosquito-borne diseases, their rising trends may reflect an increase in insecticide resistance or ineffectiveness in controlling disease transmission. Insecticide resistance has emerged in numerous *Aedes aegypti* mosquito populations around the world, and it has hampered control efforts and is a major public health concern. Insecticide resistance mechanisms may include resistance to target-site and penetration. The excessive use of hazardous chemicals to control mosquitoes has also resulted in insecticide resistance. The mentioned mechanisms cause the mosquitoes, like *Aedes aegypti*, to become resistant to insecticides making them less effective in controlling the population. As a result, many studies have been searching for alternative ways such as using an extraction from a plant.

The mechanism of action of silver nanoparticles is defined by Idowu et al. (2021) as a breach of the larval membranes through the binding of the sulfur containing proteins or the phosphorus containing molecules that caused the denaturation of specific proteins. Whereas, Wehab et al. (2021) defined that the silver nanoparticles are able to form an ionic connection with bacterial cell impaired action of the thiol-group enzymes thus, provide an proton motive force that is elevated. Also, it has been stated that the capability of AgNP to activate the antibacterial properties is due to the electrostatic interaction in the bacterial surfaces. In other terms, the bacteria that is exposed in silver nanoparticles showed morphological abnormalities since it has been compromised as compared to bacteria that does not have exposure with the silver nanoparticles showed no alterations both physiologically and morphologically.

In the study of Velayutham, K., et. al. (2013), aqueous crude bark extracts and synthesized AgNPs from *Ficus racemosa* were found to be larvicidal; however, synthesized AgNPs at a concentration of 25 mg/L killed the most *Cx. quinquefasciatus* and *Cx. gelidus* larvae. The same result in the study of Rahuman et.al (2008), the separation and identification of tetracyclic triterpenes derivative from acetone extract of *F. racemosa* were guided by bioassays; gluanol acetate was isolated and identified as a new mosquito larvicidal compound, and it was quite potent against fourth instar larvae of *Aedes aegypti*, *Anopheles stephensis*, and *Cx. quinquefasciatus*. The current green synthesis demonstrates that *F. racemosa*, an environmentally friendly and renewable source, may be used as an effective reducing agent in the production of AgNPs. Rahman & Prasanna (2018) reveal that the leaf extract of the *Ficus religiosa* plant may be used to synthesize silver nanoparticles. The maximum generation of silver nanoparticles was seen at a concentration of 40 ul. The production of silver nanoparticles decreases as the concentration of plant extract decreases. This biological metal reduction would be a benefit to the development of a clean, non-toxic, and environmentally acceptable "green approach" to producing metal nanoparticles, utilizing species ranging from higher plants. Idowu, E. T. et al. (2021) have reported the aqueous extracts of *Moringa oleifera* and *Ficus exasperata* were used to synthesize AgNPs. On both laboratory and field-collected mosquitoes, *Moringa oleifera* nanoparticles were more effective at lower concentrations than *Ficus exasperata*. Insecticide resistance in the field mosquito population appears to have no effect on the efficacy of the two extracts since mortality rose as exposure time increased. This demonstrates the nanoparticles' potential for usage as part of an integrated mosquito vector control strategy. It was believed that phytochemicals are known to have extended efficacy and usually have more than a "contact and kill" effect on insects; they have a variety of effects on mosquitos, including reducing their longevity, exposing them to harsh environments and predation, and making resistance unlikely (Vatandoost & Vaziri; Idowu et al., 2021).

Resources are one of the main limitations of the study. Out of the 62 articles identified, only 12 were included in the study. The resources were limited to credible database and screened studies that are mainly peer-reviewed, with college student respondents, and those that tackled silver nanoparticles, *Ficus spp*, and insecticidal resistance. More specifically, it is pinned down to the silver nanoparticles derived from *Ficus* spp. Additionally, the chosen literature studies also cover larvicidal activity of the silver nanoparticles, green synthesized silver nanoparticles and *Aedes aegypti*. These 12 articles are all experimental and cross-sectional studies. With regards to the materials to be used, only limited studies tackled testing the specimen *Ficus* spp and the test were conducted using spectrophotometry alone.

CONCLUSION AND RECOMMENDATIONS

Silver nanoparticles (AgNPs) are known for having benefits of being cost-effective, energy-efficient, and environmentally-friendly which results in lesser pollution and safer outputs. Silver nanoparticles derived from the extracts of *Ficus* species against *Aedes aegypti* can be a feasible option that outperforms typical solvent extracts in terms of larvicidal activity and can be an effective alternative for controlling mosquitoes. Different natural secondary metabolites were found in some *Ficus* plant extracts which function as agents for reduction and stabilization in the creation of silver nanoparticles. Furthermore, silver nanoparticles produced by these plants are similarly stable because of the presence of natural capping agents such as proteins, resulting in prevention of the particle aggregation. The larvicidal activity of the green-synthesized silver nanoparticles has also been enhanced due to the natural cytotoxicity of the *Ficus* plant extracts.

Unfortunately, the mentioned studies above regarding the larvicidal activity of silver nanoparticles from *Ficus* plant extracts against Aedes aegypti are still insufficient. Therefore, the researchers recommend more studies on this topic to further explore the potential uses of the *Ficus* species as well as to have more alternative strategies to control dengue outbreaks.

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AUTHORS' CONTRIBUTIONS

All of the authors worked together to complete this paper. Asi, A.A.T. led the group and organized the ideas that must be discussed in this paper. She also constructed the abstract and conclusion. Asi, A.A.T., Bagnes, K.J.C., Carbonel, J.C., Cayetano, M.M.M, Chua, O.J.G., Cruz, C.J.S., Mariano, A.T.R., and Yanuaria, D.K.N. contributed to the introduction, results, and discussion. Ganeb, M.D. was the one who analyzed the paper in order to further improve the flow of the review paper. The final version of the paper has been read and approved by all authors.

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