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Review Article

Neem (*Azadirachta indica* A. Juss; *Meliaceae*) as the source for plant-based pesticides as an effective and sustainable biocontrol alternative

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Abstract. The neem tree has strengths such as effective and environmentally friendly active compounds, as well as the ability to improve the quality and productivity of plants organically. However, the use of botanical pesticides has several challenges, such as potentially lower effectiveness compared to chemical insecticides, high production costs, and requiring specific knowledge in formulation and application. Botanical pesticides are readily available tools for insect pest management and are eco-friendly. The research results show that a neem formula at a concentration of 20 ml.l-1 water can cause mortality of brown planthopper is 48.75 - 70%, while mortality in the synthetic insecticide (positive control) at a concentration of 2 ml.l-1 water (as recommended) resulted in 45% mortality. It is obvious that there is a need to develop biological control as alternatives for eco-friendly and sustainable for pests' control in insect's pest management strategies. This research study has both qualitative and quantitative approach, data collection strategies were desk review of information and will be based on empirical data and literature. For the desk study, relevant internet web pages were browsed to have an overview of the key concepts of the research issue, problem of pests and diseases control and benefit of neem tree as botanical pesticides. Nevertheless, the use of botanical pesticides can provide long-term benefits to the environment and human health and support more sustainable agriculture. There is a great opportunity for the development of more effective and affordable technology for botanical pesticide production for farmers, but there are also threats such as strong competition from synthetic pesticides. The objective this study aims to determine the potential of neem (Azadirachta indica A.Juss) as a plant producing botanical pesticides as an effective and sustainable biological control alternative.

Keywords: Biological control, environmentally friendly, neem tree, Azadirachtin, Botanical pesticides

1. Introduction

Changes in balance in agricultural ecosystems cause a surge in the population of plant pests. The drastic increase in pests and pathogens causing plant diseases has become a significant hindrance in efforts to increase the quantity and quality of crop yields. In the field of agricultural cultivation, pesticides are an integral part. Farmers, especially those cultivating horticultural crops such as vegetables and fruits, mostly use pesticides excessively due to concerns about the risk of crop failure (Amilia et al., 2016). Since 1986 (Presidential Instruction No. 3 of 1986), the government has launched an Integrated Pest Management (IPM) system as an environmentally friendly effort to control plant pests and improve the quantity and quality of harvests based on ecological and economic aspects (Jamal, 2020 in Gayuh, 2021). IPM is an approach or way of thinking about pest control (plant pest organisms) that combines several compatible methods based on ecological considerations and economic efficiency for the management of environmentally sustainable agroecosystems (Abadi, 2005; Untung, 2006). Environmentally friendly plant pest control is a control step that uses methods that can minimize the potential negative impacts and focus more on the use of bio-products (Prabaningrum et al., 2015).

According to Habazar et al. (2010), the IPM program is more dynamic, not only focusing on ecological aspects but also considering specific farming efforts to minimize the development of plant pests. Therefore, the main principle of plant pest control aims at optimizing biological resources in the agroecosystem (indigenous) with ecological and economic considerations. Botanical pesticides are alternative environmentally friendly pesticides because they are easily biodegradable. These pesticides utilize secondary compounds as active ingredients sourced from plants (Regnault & Roger, 2005). It is reported that many plant species grown in Indonesia, such as cloves, neem, lemongrass, jeringo, tobacco, pyrethrum, turmeric, and castor bean, can be used to control plant pests and diseases. To obtain optimal benefits, the use of botanical pesticides should be aimed at preventing attacks, not for control measures (Wiratno et al., 2013). Among these herbal plants, neem (*Azadirachta indica*; *Meliaceae*) or also widely known as 'Indian lilac' is known as a highly potential biopesticide (Schmutterer, 1990). This specieshas a strong antifeedant property indicated by its effectiveness in suppressing insect feeding, even at concentrations of less than 1 ppm (Isman et al., 1991).

The species is a drought-resistant tree that thrives in various habitats from sub-humid to sub-dry climates with annual rainfall of 400 to 800 mm (Schmutterer, 1990). *Azadirachta indica* is known to consist of more than 200 allelochemicals scattered in varying concentrations in different parts of the plant, providing various pesticidal properties (Koul and Wahab, 2004). The seeds of this tree contain 40% oil with azadirachtin as the main active ingredient, which is primarily responsible for neem's activity as an insecticide (Isman et al., 1991). Furthermore, the seed cake obtained during neem oil processing is an important natural fertilizer used in agriculture in general. In addition, neem leaves have been used for centuries as a repellent for stored grain pests due to their repelling properties (Koul et al., 1990). Plant pests targeted by neem include chewing and sucking pests, nematodes, and fungi. The following are species that can be controlled: *Helopeltis* sp, *Aphis gossypii*, *Agriotis ipsilon*, *Callosobruchus chinensis, Alternaria tenuis, Carpophilus hemipterus, cockroaches, Crysptolestes pusillus, Corcyra cephalonica, Crocidolomia binotalis, Dysdercus cingulatus, Earias insulana, Epilachna varivestis, Fusarium oxyosporium, Helycotylenchus* sp, *Locusta migratoria, Meloidogyne* sp, *Musca domestica, Nephotenttix virescens, Nilapavarta lugens, Ophiomya reticulipennis, Panonychus citri, Planacoccus citri, Pratylenchus sp, Rhizoctonia solani, Sclerotium rolfsii, Sitophilus* sp, *Sogatella furcifera, Spodoptera litura, Tribolium* sp, tungro in rice, *Tylenchus filiformis* (Ditjenbun, 1994 in Ratmawati, 2019). This article aims to determine the potential of neem (*Azadirachta indica* A.Juss) as a plant producing botanical pesticides as an effective and sustainable biological control alternative.

2. Distribution of Neem tree

The origin of the neem tree is not clearly known. Nevertheless, some botanists believe that it is originated from Assam (India) and Burma, while other botanists believe that neem is native to India (Puri, 1999). Currently, neem is cultivated in various tropical countries such as Vietnam, Bangladesh, Pakistan, Sri Lanka, Myanmar, and Indonesia. It is also found in America, Australia, Africa, and Saudi Arabia. The largest population of neem trees is in India, reaching 14-16 million trees (Puri, 1999; Sukrasna and Lentera Team, 2003). In Indonesia, neem trees are found in Lombok, West Java, East Java, Central Java, West Nusa Tenggara, and mostly in Bali, where the species has its most culturally significance (Heyne, 1917; Sujarwo et al., 2016). Lowlands and drylands with elevations of 0-800 meters above sea level are the best habitats for neem tree growth (Puri, 1999; Anonimous, 2009 in S.W. Indiati and Marwoto, 2008).

2.1. Region's name

Scientifically, neem is known as Azadirachta *indica* and belongs to the Mahogany family or *Meliaceae*. The species is a fast-growing tree that can reach heights of 15-20 meters, and even up to 35-40 meters under optimal growth conditions. In Indonesia, neem is known by different names in different regions, such as Imba or Mimba in Java, Mempheuh in Madura, and Intaran in Bali (Sujarwo et al., 2016). In Dutch the tree is known as margosier (Heyne, 1917) and English, it is known as, margosatree, or neem tree.

2.2. Morphology of Neem

The complete morphological of Neem was described by Mabberley et al., 1995) and followed widely in botanical world. Neem (*Azadirachta indica*) is a plant with an upright stem supported by a taproot. Its stem surface is rough, woody, and has thick bark. The height of a neem tree can reach 30 meters with a stem diameter of 2-5 meters and a canopy diameter of 10 meters. The neem tree grows annually and remains green throughout the year. Neem consists of roots, stems, leaves, flowers, fruits, and seeds. The stem is upright, woody, round-shaped, rough-surfaced, and brown in color. The leaves are compound, opposite, elongated, serrated-edged, pointed at the tip, tapering at the base, with pinnate venation, 5-7 cm long, 3-4 cm wide, with leaf stalks 8-20 cm long, and green in color. The fruit is egg-shaped and green. The seed is round, 1 cm in diameter, and white. Neem grows well in hot areas, at elevations of 1-700 meters above sea level, and is resistant to water pressure (Kardinan, 2000).

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Neem is a multifunctional plant, which is why it is also known as a wonderful tree. Almost all parts of the neem tree have specific functions:

- The neem tree stem is classified as first-class wood and can be used for toothpicks.
- Neem leaves are compound leaves arranged opposite each other on the leaf stalk. They are elongated with serrated edges, a pointed tip, and a tapering base. Neem leaves are pinnate. Neem leaves resemble those of the chinaberry tree (Melia azedarach), but they can be easily distinguished. Neem leaves are not symmetrical and are longer, while chinaberry leaves are symmetrical and shorter and wider.
- Neem flowers are white and arranged axially on branches. Neem flowers are bisexual. These flowers have a honey-like aroma, which attracts bees.
- Neem fruit is oval-shaped, like a melinjo fruit, with a maximum size of 2 cm. Ripe fruit is yellow or greenish yellow. Neem fruit is also like mindi fruit, although the two can be easily distinguished. Neem fruit is slightly elongated, while mindi fruit tends to be round.
- Neem seeds are wrapped in fruit flesh, with a fruit-to-seed weight ratio of 50%:50% (Ambarwati, 2011).

2.3 History of Neem as a botanical pesticide

Neem has long been used as a botanical insecticide with efficacy and broad-spectrum application, both in simple use in various developing countries and in formulated forms in developed countries like the United States. In Indonesia, neem has been widely used to control Plant Pest Organisms (PPO) in non-food crops, but recently it has been introduced for PPO control in food crops, especially for organic agricultural products (Mabberley et al., 1995; Kardinan and Dhalimi, 2003). Warden (1888) in Elanchezhyan and Vinothkumar (2015) was the first to study the chemistry of neem oil containing sulfur. Later, margosonic acid and margosopicrin were isolated from neem oil. Chemical research conducted after 1940 resulted in the isolation of the main bitter principle of neem, nimbin, in crystal form. Subsequently, other compounds such as nimbinin from the bark, nimbosterol from the flowers, nimbocinone from the leaves, nimbidin and nimbinin from the oil, and aldobiuronic acid isolated from neem gum were identified. Azadirachtin, isolated in 1968, is the most potent grasshopper antifeedant. Neem has insecticidal, nematicidal, fungicidal, bactericidal (Schmutterer, 1995), and molluscicidal (Mehlhorn et al., 2011a) properties. Azadirachtin has a systemic effect on several cultivated plants, greatly enhancing field effectiveness and resistance (Schmutterer, 2002).

3. Chemical Content of Neem.

Neem is a versatile tree that contains many chemically and biologically active compounds (Brielmann et al.., 2006). Currently, more than 100 triterpenoids have been isolated from neem. Neem constituents can be classified as isoprenoid and other non-isoprenoid compounds. Isoprenoid compounds include diterpenoids and triterpenoids, while non-isoprenoid compounds include phenolic compounds, carbohydrates, proteins, and sulfur compounds. Among the triterpenoids, the bitter taste of neem is caused by the presence of azadirachtin, a group of limonoid compounds. Azadirachtin A was the first member isolated by Butterworth and Morgan (1968 in Puri, 1999; Brielmann et al., 2006) from neem seeds. So far, fourteen azadirachtin analogs have been reported from neem, ranging from Azadirachtin A to K, Vepaol, Isovepaol, and 11-methoxy azadirachtin. Azadirachtin, a tetranortriterpenoid from *A. indica*, is reported as a good insect growth inhibitor derived from plants (Rembold et al., 1982).

Azadirachtin is the main compound in neem oil with insecticidal activity and can be found in the fruit and leaves (Schmutterer, 1988, 1995). Other compounds in neem oil (tetranortriterpenoid group) include desacetylnimbin, desacetylsalannin, nimbin, and salannin). Besides, the compounds that have been most thoroughly investigated for their individual antimicrobial properties thus far are limonoids, which are compounds that typically consist of four, six-membered rings and one five-membered aromatic ring (i.e., a furanolactone core) and make up one-third of the phytochemicals derived from the neem tree (Roy and Saraf, 2006; Gupta et al., 2017 in Wylie and Merrell., 2022).

3.1 Neem Oil

Neem oil contains more than a dozen compounds like azadirachtin, but the main role in its insecticidal activity is played by azadirachtin (Schmutterer, 1988). Other triterpenoids including nimbin, salannin, and their derivatives have a minor role in its effectiveness (Isman, 2006). Interestingly, neem oil is non-toxic to mammals, birds, and fish, and shows lower resistance potential, as it has several effective modes of action on insects (Schmutterer 1988; Brielmann et al., 2006).

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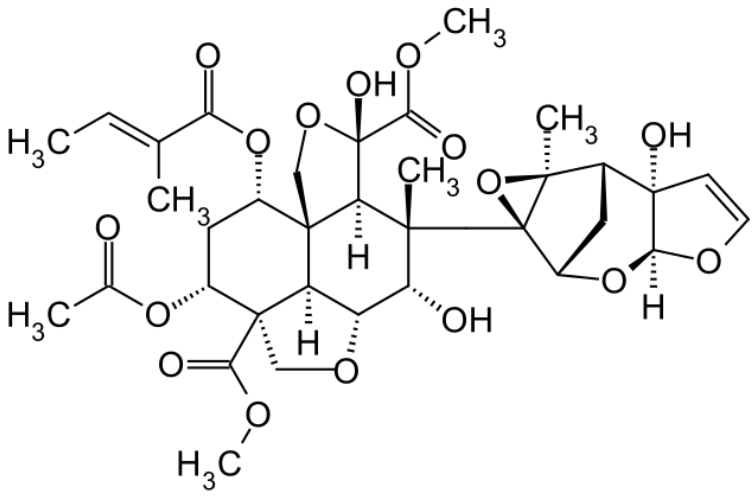


Figure 1. Chemical structures of *Azadirachtin* (Source: Schmutterer, 1988, 1995; Puri, 1999)

Many formulations of neem seed oil show antifeedant, ovicidal, larvicidal, insect growth-regulating, and insect-repelling properties. The larvicidal properties of neem oil against mosquitoes have been studied for a long time (Schmutterer, 1988, 1995). Neem oil is considered a from the fruits and seeds of neem (Noorul Aneesa, 2016). Nevertheless, neem oil can be further processed into various types of extracts, via different solvents, that are then used for subsequent preclinical and clinical studies. Although various solvents can be implemented to extract different active components from plant products, most of the compounds that are thought to be responsible for the biological activities of neem can be found in the extracts that are typically used in laboratories (e.g., water, ethanol, methanol, chloroform, and ether) (Cowan, 1999 in Wylie and Merrell.2022).

In most recent publication, methanol and ethanol extracts are those that are most implemented in antimicrobial testing. The general biological activities of the tested neem oil extracts have been attributed to the presence of many secondary plant metabolites, which include classes of compounds such as isoprenoids (e.g., terpenoids containing limonoid structures) and non-isoprenoids (e.g., tannins) (Saleem et al., 2018 in Wylie and Merrell., 2022).



Figure 2. Neem oil from neem seed

3.2 Neem leaves

Using neem leaves as a botanical pesticide is easier to do. Based on research to determine the effect of neem leaf powder and boiler ash mixed into granular organic fertilizer to increase plant resistance to insect pests. A dose of neem leaves at 1.5 mg/100 g of seeds showed a significant decrease in the number of eggs laid and increased adult insect mortality by up to 62%, indicating its potential as a bioactive anti-feedant during grain storage after harvest (Ahmad et al., 2015).

Recently, the antifeedant and repellent efficacy of neem leaves has been observed in a study where the addition of organic fertilizer with neem leaf powder and boiler ash significantly increased plant resistance to leaf aphid attacks (Brotodjojo and Arbiwati, 2016).

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Figure 3. Neem Leaves

3.3. Neem Bark

The use of neem bark as a bio-insecticide is still limited, as its pesticidal efficacy is lower than other components of the neem tree, including neem seeds and leaves, in controlling insect pests (Schmutterer 1988; Sirohi and Tandon, 2014). However, it is known to have phytotoxic properties when applied to soil to control pests, as demonstrated in a study where neem bark and leaves inhibited the germination and growth of various plants such as alfalfa, carrots, beans, rice, radishes, and sesame along with various weeds, indicating allelopathic properties (Xuan et al., 2004).

Recently, cloth dyed with neem bark extract has also been shown to have more significant anti-moth properties compared to neem leaf extract due to higher levels of azadirachtin, cyanogenic glucosides, and nimbin content (Ahmad et al., 2015).



Figure 4. Neem Bark

4.Activity of Neem tree

4.1. Antifeedant Activity

Neem works as an antifeedant by inhibiting the feeding of insects without directly killing them; insects die due to starvation (Venugopala Rao et al., 2005). Crude neem extract shows the strongest antifeedant activity against pests such as beetles, leaf borers, and sap-sucking insects (Chandel et al., 1995; Santhosh Babu et al., 1996 as cited in Elanchezhyan and Vinothkumar, 2015). Neem products have been reported to significantly increase feeding inhibition against *Brevicoryne brassicae* (Singh and Sharma, 1986); Toxoptera aurantia (Subaharan and Regupathy, 1999); *Helopeltis theivora* (Deka et al., 2000). Neem shows antifeedant activity and growth inhibition against *Helicoverpa armigera* (Murugan et al., 1999). According to Habarurema et. al., 2022. Biological control using the neem based products gave promising perspective, as the results from the dual choice tests, revealed that the extract of the plant had significantly reduced feeding on the third instar larvae of *Spodoptera littoralis* the treated leaf portions at 100 ppm and leaf water extracts at ≥ 500 ppm while the seed water extracts was at ≥ 300 ppm.

4.2. Oviposition Deterrent

Plant products applied in any form, whether as extracts or oils, affect the egg-laying and hatching of eggs, which affects the percentage of pest insect populations. Oviposition deterrent is mainly caused by its pungent aroma and

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ovicidal reaction, which disrupts embryo development in eggs (Venugopala Rao et al., 2005). Neem's repellent action against oviposition by lepidopteran pests has been reported for *Earias vittella* (Sojitra and Patel, 1992). Neem extract shows ovicidal reaction against *Chilo partellus* (Bhatnagar and Sharma, 1995); *Amrasca devastans* (Patel and Patel, 1996); and *H. armigera* (Jeyakumar and Gupta, 1999). Bomford and Isman (1996) reported the inhibitory action of azadirachtin, in pure form and as a component of neem seed extract, against 5th instar larvae of *Spodoptera litura*. Dutta and Saxena (1997) as cited *in* Elanchezhyan and Vinothkumar (2015), reported that Azadirachtin-A is more effective in causing antifeedant activity against *S. litura*. A significant increase in larval mortality, antifeedant, and oviposition deterrent was found in red shoot neem leaf exudate.

4.3. Insect Growth Inhibitor

Based on the dosage or the stage of insects affected by neem, it can cause premature insect death or prolongation of the larval period associated with morphological abnormalities or life cycle disruption in cases of larvae, pupae, and adult insects. Sometimes, at higher concentrations, it can also lead to pest mortality (Venugopala Rao et al., 2005). Azadirachtin is reported as a good insect growth inhibitor from neem plants (Rembold et al., 1982). Azadirachtin can result in ecdysis inhibition in *Rhodnius prolixus* (Rembold and Garcia, 1989). According to Sudarmadji (1994), the chemical compound azadirachtin can inhibit the insect moulting process. The hormone that affects the moulting process in insects is ecdysone hormone. The use of neem seed extract can cause 100% mortality of *Chilo partellus* after 10 days of application (Behera and Satpathy, 1996). Neem oil cake applied to the soil causes a decrease or mortality of white grubs, *Lachnosterna burmeisteri* on betel nut fruit up to 36.9% (Padmanabhan et al., 1997 as cited in Elanchezhyan and Vinothkumar, 2015). Plant parts can be applied to the soil by trenching around the stem to protect against soil pests such as white grubs and termites (Mokabel et al., 2000 as cited in Elanchezhyan and Vinothkumar, 2015).

5. Safety to Natural Enemies

5.1. Effect of Neem on Predators

Non-arthropod predators such as spiders, *Lycosa pseudoannulata* (Shukla et al., 1988), and predatory mites can survive even when Neem Azal is sprayed (Schulz et al., 1979, Subhaharan, 1998 as cited in Elanchezhyan and Vinothkumar, 2015). Neem is also safe for honeybees. Neemax 2.0% is safe for *Crytorhinus lividipennis, brown planthopper* predator, *Nilaparvata lugens*, with a death rate of only 33% (Jhansi Lakshmi et al., 1998); Neemark (0.3%) and Achook (0.3%) are safe for *Syrphus* spp. and *Coccinella septempunctata* on tea pests (Sharma and Kashyap, 2002) without causing death. The safety of various plant materials is also emphasized for *Chrysoperla carnea* (Jayaraj and Regupathy, 1999; Suganthi and Mallik, 2003 as cited in Elanchezhyan and Vinothkumar, 2015), a predator on *Bemisia tabaci* (Jazzer and Hamed, 1999); *Tetragnatha javana* and *C. carnea* (Abdul Kareem et al., 1999 as cited in Elanchezhyan and Vinothkumar, 2015); and *Rhynocoris marginatus* on *A. gossypii* (Sahayaraj and Karthickraja, 2000 as cited in Elanchezhyan and Vinothkumar, 2015). There were no adverse effects observed on larval and pupal development, feeding potential, and developmental potential of *C. carnea*, a lacewing predator commonly used for inoculation release in groundnut, cotton, etc., when feeding on mimba-*treated C. cephalonica* eggs.

***5.2.** Effect of Neem on Parasitoids*

Neem has no harmful effects on the development, fertility, oviposition, offspring, or egg hatching ability of the egg parasitoid, *Trichogramma chilonis*, whether as neem oil or neem formulations like Neemark 0.3% or Achook 0.3% (Balasubramanian and Regupathy, 1994; Jayaraj and Regupathy, 1999 as cited in Elanchezhyan and Vinothkumar, 2015). NSKE (neem seed kernel extract) also enhances the activity of larval parasitoids like *Cotesia flavipes* on *Chilo sacchariphagus indicus* (Reddy and Srikanth, 1996 as cited in Elanchezhyan and Vinothkumar, 2015); *C. plutella* on *Plutella xylostella* (Mani, 1995; Srivastava et al., 1997 as cited in Elanchezhyan and Vinothkumar, 2015); and *Bracon hebetor* (Aghuraman and Singh, 1998). A 2% neem seed extract was also found to be safe without affecting the behavior of *T. indica* on *Planococcus indicus* (Mani and Krishnamurthy, 1996); *Telenomus remus* on *S. litura* (Chari et al., 1996); *Tetrastichus pyrillae* on *Pyrilla* (Deepak and Chowdary, 1998); and *T. japonicum* (Sasikala et al., 1999).

In rice ecosystems, neem formulations like Fortune Aza 0.1% and Neem Azal 0.3% showed a high percentage (79%) of parasitization by *T. japonicum* on yellow stem borer, *Scirpophaga incertulas* (Jhansi Lakshmi et al., 1997). However, neem oil was found to have moderate toxicity to the braconid, *Chelonus blackburnii*, on *P. operculella* (Shelke et al., 1990). Similar observations on the toxic effect of neem products on *R. marginatus* were also conducted by Jansilakshmi et al. (1998) as cited in Elanchezhyan and Vinothkumar (2015). According to Ebeid et.al., 2020 that There was a minimal

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impact of neem on the parasitoids if applied in low concentrations. In addition, neem oil emulsions are less toxic than neem nanoemulsion.

Table 1. List of nanocarriers used to encapsulate neem active components and their potential for agricultural applications.

Neem component	Active ingredient	Carrier	Nanoparticle size	Potential application	Reference
Neem	Azadirachtin	Carboxymethyl chitosan with ricin oleic acid (R-CM-chitosan)	200-500 nm	Botanical pesticide	Feng and Peng. 2012 Da costa et al., 2014
Neem seed kernels	Azadirachtin	Nano emulsion.	1-5 μm	Efficient as a pesticide causing high mortality against a storage pest *Zabrotes subfasciatus*	Carvalho et al., 2021
Neem oil	Azadirachtin	B-cyclodextrin and PCL	PCL: 4 μm B-cyclodextrin 83.2 nm	Exhibits high efficacy against nymphs and eggs of *Bemisia tabaci* infecting soybean. Exhibit 100% larval mortality against *Plutella xylostella.*	Forim et al., 2013
Neem seed kernel: - Neem Extract- Neem oil.	Azadirachtin	PCL	230-245 nm	Exhibit significant insecticidal effect against *Tuta absoluta*	El-Samahy et al., 2014 Choudhury et al., 2016
Neem oil	Azadirachtin	Silica NPs	20 nm	Neem coated silver nanoparticles exhibited strong anti-fungal properties (against *Aspergillus terreus*)	
Neem leaves	Azadirachtin	Silver NPs	100 nm		

Source: Chaudhary et al., 2017

6. Utilization of Neem in Agriculture

The use of neem in agriculture is not new. In India, traditional farming systems use neem extract for pest control and to provide nutrients to plants (Mossini and Kemmelmeier, 2005; Sujarwo et al., 2016 as cited in Campos et al., 2016). According Fite et al., 2020. results revealed that aqueous extracts of *M. ferruginea* and *A. indica* at 5% concentration either individually or in combinations at 2.5% concentration of each were more effective in reducing per plant *H. armigera* larval populations, pod damage with increased the subsequent yields during both cropping seasons as compared to control plot. In Indonesia, neem has been widely used to control Plant Pests (OPT) in non-food crops, but recently it has begun to be introduced for the control of OPT in food crops, especially for organic agricultural products (Kardinan and Dhalimi, 2003). Scientific research has shown that neem is safe for workers, without risk in its application, and can be used throughout the plant's production cycle (Boeke et al., 2004). Based on their complex composition, neem-based products can function as antifeedants, growth inhibitors, sterilants, anti-oviposition agents, and repellents (Gonzalez-Coloma et al., 2013). Another factor that has stimulated the use of neem-based products for pest control in agriculture is ecological and toxicological aspects (low toxicity to non-target organisms), as well as economic aspects (a small amount of product can provide effective pest control; Ogbuewu et al., 2011).

Research on neem as a botanical pesticide such as done by Schmutterer (1988 & 1995) supports its contribution to more sustainable organic farming systems that do not produce chemical residues (plants grown without the use of

synthetic pesticides). This method also helps maintain soil productivity, ensuring longer production times. Organic farming can be a viable alternative production method for farmers, but there are many challenges to overcome. In agricultural practice, herb-based insecticides have weaknesses in degradation when exposed to sunlight, due to their short shelf life. Additionally, the active ingredient of neem causes non-specific toxicity. Therefore, it is very important to consider the ecotoxicological properties of bio-pesticide active ingredients (Alim and Matter, 2015). To overcome this, nanobiotechnology provides great potential, as it involves the production of unique nano formulations that could enhance the physicochemical stability, degradability, and effectiveness of natural products (Perlatti et al., 2013). According to Costa et. al. 2021. they found that some low dose microencapsulated formulations were very efficient in controlling *D. speciosa* larvae, while not impairing the development of maize plants. These results would therefore serve as a standard for future studies using this technology.

The use of neem oil, whether with cotton or wax, is effective in controlling nutmeg stem borers, comparable to synthetic insecticides. Statistical data analysis results show that in the 5th week after application, there was a decrease in nutmeg stem borer infestation in the neem oil + cotton and neem oil + wax treatments, by 47.61% and 56.25% respectively, compared to the use of Deltamethrin + cotton and Deltamethrin + wax, which showed decreases of 60.71% and 55.00% respectively.

The research results of Kardinan et.al., 2019 show that a neem formula at a concentration of 20 ml.l-1 water can cause mortality of brown planthopper is 48.75 - 70%, while mortality in the synthetic insecticide (positive control) at a concentration of 2 ml.l-1 water (as recommended) resulted in 45% mortality. In the negative control (water), no mortality occurred. Subsequent observations in the following hours did not show significant changes, although there was an increase in mortality, especially in the neem botanical insecticide treatment and synthetic insecticide. The effectiveness of the neem botanical insecticide is comparable to synthetic insecticides (Table 3). At the end of the 48-hour observation period after application, the treatments pyrethrum I - 5 ml.l-1 water and pyrethrum II - 5 ml.l-1 water each showed 87.50% mortality, while neem I - 20 ml.l-1 water and neem II - 20 ml.l-1 water showed 70% and 67.50% mortality respectively.

According to Kardinan et. al., 2014 oil from neem seeds can be used to control nutmeg stem borers by soaking cotton in the oil and then plugging the borer holes with wax (Table 2).

Table 2. Intensity of nutmeg stem borer attacked based on protection.

Treatments	Attacked intensity (%) of weeks to				
	1	2	3	4	5
Neem + cotton	71,42 a	47,61 a	47,61 a	47,61 a	47,61 a
Neem + wax	75,00 a	75,00 ab	56,25 a	56,25 a	56,25 a
Deltametrin + cotton	82,14 a	60,71 a	60,71 a	60,71 a	60,71 a
Deltametrin + wax	80,00 a	55,00 a	55,00 a	55,00 a	55,00 a
Water + cotton	100,00 b	90,00 b	85,00 b	85,00 b	85,00 b
Water + wax	95,65 b	86,95 b	86,95 b	86,95 b	86,95 b

Note: Numbers followed by the same letter at the same column were not significantly different at DMRT 5 %.

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Table 3. Effect of botanical insecticides by contact application on the mortality of brown planthopper.

Treatments	Mortality (%) of hours to				
	1 AA	3 AA	6 AA	24 AA	48 AA
Pyrethrum I – 5 ml.l-1 air	85,00 a	85,00 a	85,00 a	85,00 a	87,50 a
Pyrethrum II – 5 ml.l-1 air	87,50 a	87,50 a	87,50 a	87,50 a	87,50 a
Neem I – 20 ml.l-1 air	60,00 b	70,00 b	70,00 b	70,00 b	70,00 b
Neem II – 20 ml.l-1 air	48,75 b	56,25 b	62,50 b	67,50 b	67,50 b
Synthetic insecticide – 2 ml.l-1 air	45,00 b	52,50 b	62,50 b	65,00 b	68,75 b
Water (Control)	0,00 c	0,00 c	0,00 c	0,00 c	0,00 c
CV (%)	18,82	15,73	22,21	19,11	20,25

Note: Numbers followed by the same letter at the same column were not significantly different at DMRT 5 %..AA = After Application

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Table 4. Neem applications and commercial products available worldwide.

Aplication	Product	Manufacturer
Fertilizer	Ozoneem Cake®	Ozone Biotech (India)
	Plant"B" Organics – Neem Cak®	Plant"B" Organics (USA)
	Fortuneem Cake®	Fortune Biotech (USA)
	Bio Neem Oil Folia®	FUSA- Fertilizer of the USA
	Neem Cake®	Unibell Corporation (Russia)
	Ozoneem Coat®	Ozone Biotech (India)
	Parker Neem Coat®	Parker Neem (India)
	Neem Urea Guard®	Neemex (India)
	Fortuneem Coat®	Fortune Biotech (USA)
	Azadirachta-based Products	
Agrochemical	AZA Direct®	Gowan Company (USA)
	Neemix 4.5®	Certis (USA)
	Fortune Aza 3% EC®	Fortune Biotech (USA)
	Azamax®	UPL Ltda. (Brazil)
	Neemazal Technical®	E.I.D. Parry Ltd. (India)
	Ecosense®	Agro Logistic Systems Inc. (USA)
	Safer Brand 3 in 1	Woodstream Corp. (Canada)
	Garden Spray®	
	Azatin XL®	OHP Inc. (USA)
	Azact EC®	EPP Ltda. (Brazil)
	Neem Oil	
	Triact 70 EC®	Certis Company (USA)
	Bioneem®	Woodstream Corp. (USA)
	Shubhdeep Neem Oil®	King Agro Food (India)
	DalNeem®	Dalquim Ltda. (Brazil)
	OzoNeem Oil®	Ozone Biotech (India)
	Neem Drop®	Neem India Products Ltda. (India)

Source: Campous et.al., 2016

7. Commercial products derived from Neem

Neem has gained commercial recognition due to its various beneficial properties, which have been extensively researched over time. Several patents related to neem-based processes and products have been reported in the United States, India, Japan, Australia, and other countries (Table 4). Many products derived from neem are produced by crushing the seeds and other parts of the plant, using various solvents to extract the active ingredients that have pesticide activity. Different methods and techniques used to obtain neem products can result in different concentrations of active compounds, as well as different biological effectiveness (Roychoudhury, 2016 in Campos et al. 2016). Neem oil contains a group of active ingredients with different chemical characteristics. Therefore, it is believed that the development of insect resistance would be very difficult to occur. However, as research has progressed, it has been observed that due to the low residue levels of plant pesticides, multiple applications are needed to control pests, which can increase selection pressure on pest populations, possibly leading to resistance (Ghosh et al., 2012; Tangtrakulwanich and Reddy, 2014; Siegwart et al., 2015).

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Some neem-based pesticide products registered in Indonesia include Nospoil 8 EC (azadirachtin 8 g/l), Natural 9 WSC (azadirachtin 9 g/l), and Nimbo 0.6 AS (azadirachtin 0.6 g/l). However, these products are limited in number and difficult to obtain (Anonymous. 2005 in Subiyakto, 2009).

8. Advantages of Neem as a botanical pesticide

Neem (*Azadirachta indica* A. Juss) as a botanical insecticide has ecotoxicological advantages over synthetic insecticides, as it possesses beneficial ecotoxicological properties (low toxicity to humans, quick degradation, and reduced environmental impact), making it suitable for organic farming. Research has reported that neem oil, *Azadirachta indica* A. Juss (Sapindales: Meliaceae), has insecticidal effects on nearly 550 species of insects (Anuradha and Annadurai, 2008) and inhibits feeding and growth in various taxa of insects including Lepidoptera (moths and butterflies), Coleoptera (beetles), Diptera (flies), Hymenoptera (ants and wasps), Hemiptera (bugs), Orthoptera (grasshoppers and mantises), Dictyoptera, Isoptera (termites), Siphonoptera (fleas), and Thysanoptera (thrips) (Montal and Montal, 2012). Neem is also effective against arthropods, flies, cockroaches, lice, mites, fleas, and ticks (Mehlhorn et al., 2011a). According to Sukrasno and Lentera Team (2003), the main advantage of using natural pesticides is their ability to degrade rapidly. This degradation process is aided by sunlight, air, and moisture. Therefore, pesticides sprayed a few days before harvest do not leave residues, making the resulting products safe for consumption. According to Schmutterer (1990), Howatt (1994) in Ambarwati (2011), neem extract has several effects on insects:

- Disturbing metamorphosis at various stages
- Inhibiting chitin formation, thus hindering the molting process
- Preventing insect feeding (antifeedant)
- Inhibiting the growth of eggs, larvae, pupae, and adult insects
- Repelling larvae and adult insects (repellent)
- Sterilizing adult insects, preventing them from mating.
- Loss of ability to fly.
- Disrupting sexual communication

Reducing the motility of the insect digestive tract Among various herbal plants, neem-based plant insecticides have become the most accepted biopesticides, due to the presence of various limonoids in neem plant extracts and oil, which not only provide sustainable pest control mechanisms but also prevent plant diseases from developing resistance to various synthetic insecticides (Chaudhury et al., 2016).

9. Weakness of Neem as a botanical pesticide

A weakness of neem is its low stability and consistency when applied in the field, mainly due to its high degradation rate or ease of breakdown in the field, and its slow killing rate compared to conventional pesticides (Isman, 2006; de Oliveira et al., 2014; Miresmailli and Isman, 2014 in Campos et al., 2016). The main factor genetically plays a crucial role in determining the chemical composition of neem oil. Neem oil contains a group of active ingredients with different chemical characteristics. Additionally, environmental factors and extraction methods can also cause significant differences in formulation composition. As a result, there is no standard active ingredient composition in these botanical insecticides, limiting their application in pest control in agriculture (Ghosh et al., 2012; Tangtrakulwanich and Reddy, 2014; Siegwart et al., 2015 in Campos et al., 2016). Lack of information and understanding of how to process neem plants into effective and appropriate botanical pesticides, the production cost of botanical pesticides tends to be higher than synthetic pesticides, making it unaffordable for many farmers.

10. Challenges of using botanical pesticides

According to Isman M.B. (2006), there are currently botanical pesticide products circulating in the market that are highly needed in the agricultural industry, including products from Pyrethrum and Neem. Botanical pesticides, including those from plants like neem, have the potential as environmentally friendly alternatives in pest and disease control in plants. Over years of research, there has been much information about neem as a botanical pesticide. This is a cost-effective and environmentally friendly alternative to commercially synthesized chemical pesticides. However, due to its instability to ultraviolet light and its efficiency limitations compared to synthetic pesticides (Barnby et al., 1989), it is crucial to develop new and efficient strategies to replace toxic chemical pesticides. However, despite some challenges

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in the use of botanical pesticides, many studies have shown that the use of botanical pesticides can provide long-term benefits for the environment and human health. Some examples of these benefits are reducing the risk of pesticide poisoning in farmers and consumers, increasing crop productivity, and supporting more sustainable agriculture (Roger et al., 2012).

11. Conclusion

The biodiversity of plants producing botanical pesticides can be a healthier and more sustainable alternative in agriculture. Therefore, the use of botanical pesticides as biological control can be a more environmentally friendly and effective alternative in controlling plant pests in agriculture.

Botanical pesticides have strengths such as effectiveness and environmental friendliness, but there are also weaknesses such as unstable effectiveness and higher production costs compared to synthetic pesticides. There are significant opportunities for the development of more effective and affordable botanical pesticide production technologies for farmers, but there are also threats such as strong competition from synthetic pesticides. Despite the challenges in using botanical pesticides, their use can provide long-term benefits for the environment and human health, as well as support more sustainable agriculture.

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