Eco. Env. & Cons. 30 (May Suppl. Issue) : 2024; pp. (S271-S276)
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ISSN 0971–765X

DOI No.: http://doi.org/10.53550/EEC.2024.v30i03s.047

Azadirachta indica Biopesticide: A Sustainable Alternative to Synthetic Chemicals in Pest Control (A Review)

Bidisha Hazarika[1], G.K. Saikia[2], Manuranjan Gogoi[3] and Diganta Kr. Bora[4]

Tea Husbandry & Technology, Assam Agricultural University, Jorhat, Assam, India

(Received 10 June, 2023; Accepted 1 November, 2023)

ABSTRACT

Over time, heavy reliance on synthetic pesticides to combat phytophagous insects has led to their accumulation in the environment, resulting in increased pest resistance and reduced soil biodiversity. Approximately 90% of these pesticides enter various environmental systems through runoff, posing significant health risks to both farmers and consumers. Thus, there's a growing need for eco-friendly alternatives to establish effective pest management while reducing health hazards. One such approach involves harnessing *Azadirachta indica*, commonly known as the neem plant, which contains agro-medicinal components with insecticidal, immunomodulatory, and anti-cancer properties. Azadirachtin, a key ingredient, acts as an insect deterrent, disrupts reproduction, and enhances pest control through innovative nanocarrier-based delivery systems, ensuring stability and sustainability. In this review, we examine the essential components of neem with pesticidal properties, explore their active functional ingredients, and investigate the utilization of nanocarriers for controlled release, thereby enhancing stability and sustainability.

Key words: *Biopesticide, Neem,* Azadiracta indica, *Sustainable, Management, Pesticide*

Introduction

Pesticides, chemical compounds used in agriculture to combat pests (Kumar *et al.*, 2012), pose significant environmental and human health challenges. The continuous use of synthetic pesticides has led to the build-up of pesticide residues in the environment, causing chronic health problems (Bag, 2000). According to a report by the UNEP and WHO, pesticides poison around three million people and cause 200,000 deaths yearly, mostly in developing nations (Yadav *et al.,* 2015). Pesticides, such as insecticides, fungicides, and herbicides, have long-lasting stability, persisting in soil, water, and food chains, elevating health risks (Pimentel *et al.,* 1992). Pesticide exposure can happen through various means, including inhaling tiny pesticide aerosols (smaller than 5 μm), leading to respiratory absorption. Skin contact, consuming contaminated food, or touching pesticide-laden surfaces can also result in poisoning (Yadav *et al.,* 2015). Furthermore, pesticides can cross the placenta, causing fatal defects or death (Woodruff *et al.,* 2008). Although the body typically metabolizes and eliminates toxic pesticides, short-term exposure may lead to accumulation. Pesticide components, including carriers and solvents, can have severe effects (World Health Organisation, 1990), with exposure severity influenced by dose, route, absorption, accumulation, and persistence factors. In some cases, pesticide metabolism can heighten toxicity, as observed with carbosulfan and furathiocarb, producing the more toxic carbofuran

([1]Ph.D. Scholar, [2]Professor, [3]Assistant Professor, [4]Assistant Professor)

(Ntow *et al.,* 2008). Fat-soluble substances can accumulate in fatty tissues, increasing in concentration up the food chain, causing toxic effects such as skin sensitization, allergies, neurotoxicity, cancer, reproductive issues, cataracts, and immune disorders (Owens *et al.,* 2010). Pesticides, including insecticides, herbicides, and fungicides, have been extensively linked to various cancers. Moreover, the extensive use of synthetic pesticides has disrupted ecosystems, fostering pest resistance and harming non-target organisms. This has resulted in acute and chronic poisoning among farmworkers, applicators, and consumers, underscoring the pressing need for alternative approaches. A significant solution lies in the adoption of botanical pesticides, which have proven their effectiveness as replacements for synthetic ones. These plant-based biopesticides, utilizing extracts and oils, not only bolster crop yields but also serve various roles, including insecticides, fumigants, manures, urea coating agents, and soil conditioners. They can be used individually or in combination with other botanicals to enhance their insect-killing effectiveness. The neem tree (*Azadirachta indica*), a hardy evergreen thriving in regions with 400–800 mm annual rainfall, serves as a remarkable botanical biopesticide source. It boasts over 200 allelochemicals in various plant parts, offering diverse pesticidal properties (Koul and Wahab, 2004). Neem seeds, composing 40% oil with azadirachtin as the primary active ingredient, are pivotal for its insecticidal efficacy (Isman *et al.,* 1991). Additionally, the seed cake, a by-product of neem oil processing, serves as a valuable natural fertilizer. Employed for centuries, neem leaves repel stored grain pests (Koul *et al.,* 2004). Neem's multifaceted components establish it as a resilient pest defence, making it an excellent choice for effective pest control.

Furthermore, neem's components possess therapeutic value, including anticancer and antimicrobial properties in neem oil, bark, leaves, and purified biochemicals (Paul *et al.,* 2011; Raut *et al.,* 2014). Neem leaf extracts offers anti-inflammatory effects (Kumar *et al.,* 2015), while neem oil acts as an ant fertility agent (Kaushic, 2004). Particularly noteworthy is NLGP, an active neem ingredient recognized as a potent immunomodulator (Mallick *et al.,* 2013), making neem an ideal agro-medicinal plant. This unique aspect ensures its effectiveness as a biopesticide without causing indiscriminate harm to mammals.

Bio-Pesticidal Activity of Neem

Neem Oil

Cold-pressed from neem seed kernels, neem oil is highly effective against soft-bodied insects and mites, owing much of its bioactivity to disulphide compounds. While neem oil contains numerous *Azadirachtin analogs*, it's primarily *Azadirachta* that lends its potent insecticidal properties, with minimal contributions from other triterpenoids like nimbin and salannin (Isman, 2006). Importantly, neem oil poses no threat to mammals, birds, or fish and exhibits a reduced risk of insect resistance due to its multifaceted impact. Various formulations of neem oil demonstrate antifeedant, ovicidal, larvicidal, insect growth-regulating, and repellent properties against insect pests. Additionally, neem oil has fungicidal effects, inhibiting the growth and development of fungi like *Metarhizium anisopliae* and *Beauveria bassiana* (Hirose *et al.,* 2001). Furthermore, neem oil displays acaricidal activity against *Sarcoptes scabiei* var. cuniculi larvae, which can transmit zoonotic infections, achieving 100% acaricidal activity within 4.5 hours (Du *et al.,* 2009). Neem oil's role as an insect growth regulator has been studied, affecting pest development, particularly in Aphis glycines Matsumura, a soybean pest. Neem formulations induced nymphal mortality and extended the development time of surviving adults, but did not significantly impact fecundity. However, there were observed non-target effects on the larval survival and development time of predators (Kraiss and Cullen, 2008). Neem oil, when compared to synthetic pesticides, displayed substantial efficacy against the mango hopper, suggesting its potential role in reducing reliance on synthetic pesticides (Adnan *et al.,* 2014). Additionally, neem oil delays pest reproduction, causing pupal stage toxicity and morphological deformities (Boulahbel *et al.,* 2015). It's worth noting that neem oil may also affect non-target predators like Podisusnigrispinus, leading to deformities and mortality with increasing concentrations (Zanuncio *et al.,* 2016). Furthermore, The neem seed cake from oil processing serves as both a pesticide and bio-fertilizer, enhancing soil fertility (Lokanadhan *et al.,* 2012).

Neem Leaf

Neem leaves have dual roles in vermicomposting, enhancing earthworm growth and vermicompost production but showing nematicidal effects on annelids (Gajalakshmi and Abbasi, 2004; Akhtar, 2000). They also extend the shelf life of mungbean grain against the pulse beetle (Ahmad *et al.,* 2015) and boost plant resistance to aphids when added to organic fertilizers (Brotodjojo and Arbiwati, 2016).

Neem Bark

Neem bark is less potent in pest control compared to seeds and leaves (Sirohi and Tandon, 2014). It exhibits allelopathic qualities, inhibiting crop and weed growth when added to soil. In dyed fabric, neem bark extract shows stronger anti-lepidopteran properties due to higher azadirachtin, cyanogenic glucosides, and nimbin content (Ahmad *et al.,* 2015). Additionally, neem bark offers therapeutic benefits, including anti-ulcer and anti-secretory properties for managing gastric hypersecretion and gastroduodenal ulcers (Bandyopadhyay *et al.,* 2004).

Active Pesticidal Components of Neem

Neem encompasses various parts, including leaves, seeds, bark, flowers, and oil, each containing a multitude of components contributing to its diverse pesticidal capabilities.

Azadirachtin

Azadirachtin, constituting 0.1-0.3% of neem seeds, is the key insecticidal compound in neem oil, leaves, flowers, and fruits. Isolated by Morgan et al. at Keele University, it's a complex tetranortriterpenoid limonoid with repellent and pesticidal properties. Azadirachtin disrupts insect growth and development while deterring feeding, making it an exceptional botanical pesticide (Morgan, 2009). Research on Azadirachtin's insecticidal activity against *Monochamus alternatus*, a pine sawyer beetle, has unveiled insights into its molecular mechanisms (Lin *et al.,* 2016).

Nimbolide

Nimbolide B and Nimbic acid B, prominent active ingredients in neem, demonstrate herbicidal properties, inhibiting weed growth such as lettuce, crabgrass, alfalfa, jungle rice, and barnyard grass.

Salanin

Salannin, a crucial neem component, acts as an antifeedant and insect growth regulator, delaying molting and reducing larval and pupal weight, leading to mortality. When combined with azadirachtin and nimbin, its effects are more pronounced. Recent research aims to enhance salannin's insecticidal potential through fungal transformation, potentially streamlining insecticidal formulations (Haldar *et al.,* 2014).

Neem Functional Ingredients Extraction Procedures

Water Extraction

A straight forward extraction method involves crushing and grinding neem kernels, followed by extraction with water. Neem seeds are typically soaked overnight, and the resulting crude suspension is filtered and used as an emulsion for spraying. However, due to the limited solubility of active ingredients in water, this process demands a substantial amount of water. In a study assessing the anti-fecundity effect of neem seed kernel aqueous extracts on *Bactrocera dorsalis* and *Bactrocer acucurditaei* development, results showed that pure azadirachtin had a more significant impact on fertility and fecundity compared to aqueous neem seed extract, revealing a cost-effective and eco-friendly alternative to synthetic pesticides (Singh, 2003).

Alcohol Extraction

Alcohol extraction is the most efficient method for obtaining concentrated neem components due to the high solubility of limonoids in alcohol solvents. Neem kernels are grated and soaked in ethanol or methanol, yielding concentrations about 50 times greater than water extraction. For instance, in a study on methanolic neem leaf extracts, a straightforward extraction process produced a concentrated green crude extract (Schumacher *et al.,* 2011). Other research used a 1:5 ratio of hexane and ethanol for neem seed extraction, exploring extraction kinetics and thermodynamics influenced by factors like temperature, solvent type, and particle size (Liauw *et al.,* 2008). The resulting concentrated active ingredients can be further processed into various forms, including dust, granules, emulsifiable concentrates, and wettable powders for advanced applications (Liauw *et al.,* 2008).

Neem Based Nano-Biopesticides

In agriculture, plant-based insecticides like neem face degradation when exposed to sunlight, limiting their shelf life. Some neem extracts can also exhibit non-specific toxicity, affecting aquatic organisms like Oreochromis niloticus (Alim and Matter, 2015).

Nano-biotechnology offers a promising solution by creating stable nano-formulations that enhance the effectiveness of natural products. These nano capsules allow controlled release of active compounds, precise targeting, and reduced non-target effects, while also improving phytochemical stability (Perlatti *et al.,* 2013; Duran and Marcato, 2013). In recent years, controlled release nanotechnology has gained attention for encapsulating neem's active ingredients. Azadirachtin can be loaded into both organic nanoparticles (Feng and Peng, 2012) and inorganic nanoparticles (Choudhury *et al.,* 2016). Neem leaf extracts are used to cap silver nanoparticles, enhancing insecticidal activity. Neem oil on silica-based nanoparticles reduces pests effectively (El-Samahy *et al.,* 2014).Nano emulsions of neem oil combat its high degradability and effectively control storage pests like *Zabrotes subfasciatus* with UV stability (da Costa *et al.,* 2014). Polymeric nanocarriers, such as Poly (γ-caprolactone) (PCL) and β-cyclodextrin, for neem oil exhibit insecticidal activity but are somewhat less effective than commercial neem oil against *Bemisiatabaci* (Carvalho *et al.,* 2012). Neem seed cake in slow-releasing nanostructures promotes rhizobacteria germination and nutrient delivery to plants (Celsia and Mala, 2014; Mala *et al.,* 2016).

These advancements in nanotechnology for agrochemical delivery usher in a new era of biopesticides, offering several advantages, including slow-release properties, improved ingredient stability, reduced usage, limited degradation and leaching losses, ease of handling and transportation, and reduced odour concerns.

Future Prospect

In response to escalating pest resistance in agriculture, there's a shift toward integrated pest management. Neem, a natural, non-synthetic pesticide, offers an eco-friendly and cost-effective alternative to synthetic pesticides. However, challenges like vulnerability to UV light and lower efficiency compared to synthetics highlight the need for innovative pest management. Nanotechnology, with organic and inorganic nanoparticles, presents promising options. These nano formulations can serve various roles in pest control and act as eco-friendly fertilizers. A targeted approach is essential to minimize unintended effects on non-target species and maintain ecological balance (Joany *et al.,* 2015).However, it's crucial to integrate a targeted approach to minimize unintended side effects on non-target organisms and ecologically significant species.

Conclusion

Environmental concerns arising from the prolonged use of synthetic pesticides have spurred interest in plant-based insecticidal agents, which offer selective toxicity to insects with minimal off-target effects. Neem-based insecticides, containing multiple limonoids, are particularly favoured for their eco-friendly pest control benefits. These bio-pesticides not only provide sustainable pest management but also mitigate plant resistance to synthetic insecticides. Enhancing the efficacy of neem's pesticidal components through encapsulation in nanocarriers enables controlled, sustained release of phytochemicals and targeted delivery, ultimately boosting crop productivity and yields.

Acknowledgement

We want to convey our deep appreciation to all those who contributed to this review. Our gratitude goes out to the authors, researchers, scientists, academic institutions, research facilities, and the journal editorial team for their invaluable contributions and support. This collaborative endeavour was made possible by the entire scientific community.

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this review paper.

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