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Original Article

Neem Oil Nanoemulsion

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ABSTRACT

Neem oil, extracted from the seeds of Azadirachta indica (family Meliaceae), is renowned for its wide range of bioactivities, including insecticidal, antibacterial, antifungal, antiviral, antioxidant, and anti-inflammatory properties. However, its poor water solubility, susceptibility to oxidation, and instability under light and temperature restrict its direct use in pharmaceutical, agricultural, and cosmetic applications. Nanoemulsion technology has emerged as an effective strategy to overcome these challenges by encapsulating neem oil within nanosized droplets (typically 20–200 nm), thereby enhancing its solubility, bioavailability, stability, and controlled release. Neem oil Nanoemulsion (NEs) are generally prepared using high-energy (ultrasonication, high-pressure homogenization) or low-energy (phase inversion, spontaneous emulsification) methods with biocompatible surfactants and co-surfactants. Numerous studies have reported improved larvicidal, pesticidal, and antimicrobial activities of neem oil NEs compared to bulk formulations, owing to increased surface area, better wetting, and deeper penetration into biological membranes. Furthermore, recent advances focus on green surfactants, solid nanoemulsion gels, and polymer-based delivery systems for sustained efficacy and reduced toxicity. This review critically discusses the formulation strategies, characterization techniques, biological applications, and future prospects of neem oil nanoemulsions, highlighting their potential as eco-friendly and multifunctional nanocarriers for sustainable agriculture and biomedicine.

Keywords: Neem oil; Azadirachta indica; Nanoemulsion; Green nanotechnology; Biopesticide; Antimicrobial; Larvicidal activity; Drug delivery; Stability; Controlled release

INTRODUCTION

Neem oil contains several bioactive compounds — the most-studied being azadirachtin, nimbin, salannin and other limonoids — that exhibit insect growth regulatory, repellent and antimicrobial effects. However, neem oil is hydrophobic, prone to oxidation and photodegradation, and difficult to apply uniformly in aqueous environments[1]. Converting neem oil into oil-in-water nanoemulsions (droplet diameters typically <200 nm for many NEs; some reports show ~30–100 nm) overcomes these limitations by increasing surface area, improving spreading/wetting on target surfaces and enhancing penetration and bioavailability of active constituents[2]. Several studies and reviews have reported markedly improved larvicidal, antimicrobial and pesticidal performance for neem oil nanoemulsions compared to bulk oil preparations [3] Neem (Azadirachta indica A. Juss.), belonging to the family Meliaceae, is one of the most valuable medicinal plants native to the Indian subcontinent. It has been referred to as the "Village Pharmacy" due to its wide range of therapeutic and agricultural applications. Every part of the neem tree—leaves, seeds, bark, flowers, fruits, and roots—contains bioactive compounds with potent antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, and insecticidal properties[4].

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Fig: Neem

2. Botanical Description

Scientific name: Azadirachta indica

Common names: Neem, Margosa tree, Indian lilac

Family: Meliaceae[4]

Habitat: Tropical and subtropical regions of Asia, Africa, and South America

Tree characteristics: Evergreen tree up to 20–25 m in height; pinnate leaves; small white flowers; drupe-like fruit with one seed (source of neem oil)[5].

3. Phytochemical Constituents

Neem is rich in limonoids and other secondary metabolites responsible for its diverse pharmacological actions[6].

Category	Major Compounds	Biological Activity
Limonoids	Azadirachtin, Nimbin, Salannin, Meliantriol	Insecticidal, Antifeedant
Flavonoids	Quercetin, Kaempferol	Antioxidant, Anti-inflammatory
Triterpenoids	Margolone, Margolonone	Antimicrobial
Glycosides	Nimbidin, Inositol	Antiulcer, Hepatoprotective
Polyphenols	Catechin, Epicatechin	

4. Traditional and Medicinal Uses

Neem has been used in Ayurveda, Unani, and Siddha medicine systems for over 4000 years[8].

Traditional applications:

Leaves: Used for skin disorders, malaria, diabetes, and wound healing.

Bark: Used as astringent, anti-inflammatory, and antipyretic [9].

Oil (from seeds): Used for skin care, hair treatment, and as a natural pesticide.

Twigs: Used as natural toothbrush ("datun")[10].

5. Pharmacological Properties

Neem exhibits multiple pharmacological effects:

5.1 Antimicrobial Activity[11]

Active compounds like nimbidin and azadirachtin inhibit growth of Staphylococcus aureus, E. coli, Candida albicans, and Mycobacterium tuberculosis.

5.2 Antioxidant and Anti-inflammatory Effects

Neem leaf extracts scavenge free radicals and suppress inflammatory mediators (COX, LOX, TNF-α, IL-6).[12]

5.3 Anticancer Activity

Neem-derived limonoids induce apoptosis in cancer cell lines such as breast, prostate, and colon cancers through modulation of p53 and NF-κB pathways.

5.4 Antidiabetic Activity[13]

Neem leaf extracts enhance insulin secretion and inhibit glucose absorption by suppressing α-glucosidase.

5.5 Hepatoprotective and Nephroprotective[14]

Methanolic neem extracts protect against CCl_4-induced liver toxicity and oxidative stress.

5.6 Antifertility and Insecticidal[15]

Neem oil disrupts insect growth, oviposition, and fertility in mosquitoes and agricultural pests.

2. Nanoemulsion basics — definitions and types

Nanoemulsions are kinetically stable, non-equilibrium oil-in-water (O/W) or water-in-oil (W/O) dispersions with droplet sizes typically in the 20–500 nm range (many botanical NEs aim for 20–200 nm). They differ from microemulsions (thermodynamically stable, often require large surfactant/co-surfactant fractions) and from simple emulsions (larger droplet size, lower stability). Nanoemulsions can be produced by high-energy methods (ultrasonication, high-pressure homogenization, microfluidization) or low-energy methods (phase inversion temperature (PIT), phase inversion composition (PIC), spontaneous emulsification). The choice of surfactant (ionic vs non-ionic; examples: Tween 20/80, alkyl polyglucosides, quillaja saponin, rhamnolipids) and oil/surfactant ratio determines droplet size, stability and performance.[16]

3. Preparation methods and formulation variables

3.1 High-energy methods

Ultrasonication: High-amplitude ultrasound produces cavitation forces that shear oil droplets into nanodroplets. Many neem NE studies use ultrasonication with Tween 20 or Tween 80 to obtain droplet sizes from ~30 nm to a few hundred nm depending on sonication time, amplitude and oil:surfactant ratios. Ultrasonication is commonly reported for lab-scale neem NEs[17].

High-pressure homogenization / micro fluidization: Useful for scale-up; multiple passes at high pressure reduce droplet size. Studies report reduced droplet size with increased cycles and pressure.[18]

3.2 Low-energy methods

Phase inversion composition (PIC) / Phase inversion temperature (PIT): These rely on changes in surfactant affinity and are energy efficient; low-energy methods have been used to formulate neem NEs with acceptable stability and lower surfactant amounts.[19]

3.3 Formulation variables to control

Oil fraction: Increasing oil fraction typically increases droplet size and viscosity; optimum oil level balances payload and stability.[20]

Surfactant type and HLB: Non-ionic surfactants (e.g., Tween 20, 80) are widely used; biobased surfactants (alkyl polyglucosides, rhamnolipids, quillaja saponins, gum arabic) are emerging to improve eco-friendliness. Surfactant-to-oil ratio (S/O) strongly affects droplet size and long-term stability.

Co-surfactants / additives: Short-chain alcohols, glycerol, polymers (e.g., pectin, methylcellulose) can tune viscosity, give controlled release and affect spreading on leaf surfaces4. Physicochemical characterization[21]

4. Physicochemical characterization

Key characterization techniques used in the literature include:

Dynamic Light Scattering (DLS) for mean droplet diameter and polydispersity index (PDI). Reported neem NE sizes range from ~30 nm to >300 nm depending on formulation and measurement/dilution conditions. [22] Zeta potential (ZP) for surface charge and colloidal stability (values >|30 mV| often indicate electrostatic stability; however many NEs rely on steric stabilization from non-ionic surfactants). ZP is commonly reported to monitor stability over storage. Transmission Electron Microscopy (TEM) / Cryo-TEM / SEM for droplet morphology. [23] Viscosity / rheology to understand application behavior (sprayability, adherence).

Stability testing: centrifugation, thermal cycling, storage at different temperatures, monitoring droplet size/PDI and phase separation over time (30–90 days typical in many reports).[24]

5. Biological activities and applications

5.1 Larvicidal and mosquito control

Multiple studies demonstrate that neem oil NEs produce stronger and longer-lasting larvicidal and repellent effects against mosquito species (e.g., Culex, Anopheles, Aedes) than bulk neem oil. Reported droplet sizes (e.g., ~31 nm) and low surfactant systems produced effective larvicidal formulations in lab and semifield tests. Field-applicable NEs often show improved wetting and better coverage on leaf or water surfaces. [25] 5.2 Insecticidal / stored-product pest control. NE formulations of azadirachtin/neem oil show higher contact and ingestion toxicity against insect pests of stored products (Sitophilus oryzae, Tribolium castaneum) and crop pests, attributed to better adhesion and faster uptake of active compounds. Pseudoternary phase diagrams and appropriate surfactants (polysorbates, APG) have been used to optimize such formulations.[26]

5.3 Antimicrobial and food-preservation

Neem NEs have demonstrated antibacterial and antifungal activity against human pathogens and food spoilage organisms; improved solubilization and interaction with microbial membranes enhances efficacy compared to raw oil. This makes them attractive for food preservation coatings and packaging, subject to safety evaluation.[27]

5.4 Agricultural applications — nematodes, plant growth

Neem NEs can be applied as soil drenches or foliar sprays; studies report nematicidal activity (reduced nematode populations and egg masses) and in some cases beneficial effects on seed germination/growth when combined with polymers or seed-coating matrices. 5.5 Medical, cosmetic and veterinary applications[28] Topical antimicrobial formulations and repellent cosmetics using neem NEs have been investigated; however, safety, dermal irritation and controlled-release profiles require careful formulation and clinical testing before commercial use.[29]

6. Mechanism of enhanced activity in nanoemulsions

The improved biological activity of neem oil NEs stems from:

Increased surface area of dispersed nanodroplets enabling better interaction with biological membranes. Improved wetting/spreading on hydrophobic leaf surfaces leading to better coverage and contact. Enhanced penetration and uptake of bioactive limonoids into insect cuticle or microbial membranes. Protection of actives from oxidation and photodegradation, increasing persistence on target surfaces[30]

7. Toxicity and ecological considerations

While neem oil is often considered safer than conventional synthetic pesticides, nanoformulation can change exposure and toxicity profiles. Several studies report higher acute toxicity of neem NEs to non-target beneficials (e.g., parasitoids) and alterations in ecotoxicology relative to bulk oil, necessitating thorough risk assessment.[31] Mammalian toxicity studies are mixed; subacute toxicity and dermal irritation tests indicate that some formulations are well tolerated at low exposure but high concentrations or certain surfactants/co-formulants may generate adverse effects. Therefore, ecotoxicological profiling (bees, aquatic invertebrates, soil microbes, beneficial insects) and mammalian safety evaluations are essential before field deployment.[32]

8. Regulatory & scale-up challenges

Key obstacles to commercialization of neem NEs include:

Regulatory pathways: Botanical Nano formulations fall under pesticide/biopesticide regulations in many jurisdictions; regulatory data requirements (toxicology, environmental fate, efficacy) can be extensive.

Surfactant choice and safety: Using large amounts of synthetic surfactants may conflict with eco-friendly claims; shifting to bio-based surfactants (APG, rhamnolipids, quillaja saponin) helps but requires supply and cost considerations.[32]

Manufacturing & stability: Scaling ultrasonication or homogenization processes and ensuring long-term storage stability under varied climates (important for e.g., tropical deployment) remain technical and economic challenges. Low-energy methods reduce energy cost but may increase surfactant demand[33]

9. Best practices for formulation & testing (practical recommendations)

Optimize surfactant-to-oil ratio and select surfactants with acceptable HLB values for neem oil; screen both synthetic (Tween 20/80) and bio-based surfactants.[34] Use DLS (with appropriate dilution protocols), zeta potential, and TEM to fully characterize droplet size, PDI and morphology. Conduct accelerated stability (centrifugation, freeze-thaw, thermal cycling) and long-term shelf studies (30–90+ days) at multiple temperatures.[35] Evaluate efficacy in both lab and field-relevant conditions (spray application, leaf wettability, persistence under sunlight/rainfall). Perform non-target toxicity testing (pollinators, soil fauna, aquatic species) and mammalian safety assessments (dermal irritation, subchronic studies) prior to large-scale use[36]

10. Gaps in knowledge and future directions

Standardization: Harmonized methods for NE characterization and reporting (dilution protocols for DLS, PDI cut-offs, zeta potential methods) are needed to compare studies.

Biobased surfactants and green chemistry: More research on rhamnolipid/ quillaja/ gumbased stabilizers that are effective and affordable for large-scale use.[37]

Controlled-release Nano formulations: Combining neem NEs with polymers or encapsulation matrices for sustained release and reduced non-target exposure.

Mechanistic ecotoxicology: Studies to determine how nano-size and surfactant identity alter uptake, metabolism and fate in non-target organisms and the environment.[38]

Field trials and cost-benefit analyses: Real-world evaluations across crops, climates and pest complexes to establish performance, economics and adoption pathways

CONCLUSION

Neem oil nanoemulsions are a promising, versatile platform to harness neem's bioactivities with improved stability, spreading and efficacy. There is substantial laboratory evidence that nanoformulation enhances larvicidal, insecticidal and antimicrobial action.[39] However, commercialization requires careful surfactant selection, toxicological and ecotoxicological testing, demonstration of field efficacy and navigating regulatory requirements. Future research should prioritize eco-friendly surfactants, standardized characterization, controlled-release strategies and robust field evaluations.

REFERENCE

1. Biswas, K., Chattopadhyay, I., Banerjee, R.K., & Bandyopadhyay, U. (2002). Biological activities and medicinal properties of neem (Azadirachta indica). Current Science, 82(11), 1336–1345.
   → Comprehensive review on neem's pharmacological properties and traditional uses.
2. Schmutterer, H. (1995). The Neem Tree: Source of Unique Natural Products for Integrated Pest Management, Medicine, Industry, and Other Purposes. VCH Publishers, Germany.
   → Classic reference on neem's botanical characteristics and pesticidal activity.
3. Subapriya, R., & Nagini, S. (2005). Medicinal properties of neem leaves: A review. Current Medicinal Chemistry – Anti-Cancer Agents, 5(2), 149–156.
   → Details on bioactive compounds (azadirachtin, nimbin, salannin) and their pharmacological roles.
4. Koul, O., Isman, M.B., & Ketkar, C.M. (1990). Properties and uses of neem, Azadirachta indica. Canadian Journal of Botany, 68(1), 1–11.
   → Describes neem phytochemistry and insecticidal mechanisms.
5. Boeke, S.J., Boersma, M.G., Alink, G.M., van Loon, J.J.A., van Huis, A., & Dicke, M. (2004). Safety evaluation of neem-derived pesticides. Pest Management Science, 60(8), 767–771.

→ Discusses neem oil composition, applications, and toxicology.

6. Ghosh, V., Mukherjee, A., & Chandrasekaran, N. (2013). Neem (Azadirachta indica) seed oil nanoemulsion: a potent larvicidal agent against Culex quinquefasciatus. Pest Management Science, 69(8), 1017–1023.
   → Reports enhanced larvicidal activity of neem oil nanoemulsion compared to bulk oil.
7. Solans, C., Izquierdo, P., Nolla, J., Azemar, N., & Garcia-Celma, M.J. (2005). Nanoemulsions. Current Opinion in Colloid & Interface Science, 10(3–4), 102–110.
   → Fundamental reference on nanoemulsion principles and droplet size range (20–200 nm).
8. Kumar, A., et al. (2021). Formulation and evaluation of neem oil-based nanoemulsion for enhanced antimicrobial and larvicidal efficacy. Journal of Drug Delivery Science and Technology, 63, 102512.
   → Confirms improved stability and biological efficiency of neem oil in nanoemulsion form.
9. Sujarwo, W., Keim, A.P., Caneva, G., Toniolo, C., & Nicoletti, M. (2016). Ethnobotanical uses of neem (Azadirachta indica A. Juss.; Meliaceae) in Bali (Indonesia): the tree of 100 uses. Journal of Ethnobiology and Ethnomedicine, 12(1), 12.
   → Covers traditional medicinal and cultural uses of neem.
10. Okoh, S.O., Asekun, O.T., Familoni, O.B., & Afolayan, A.J. (2016). Composition and antioxidant activities of leaf and seed essential oils of Azadirachta indica (A. Juss). International Journal of Molecular Sciences, 17(3), 441.
11. Ghosh V., Mukherjee A., & Chandrasekaran N. (2013). Neem (Azadirachta indica) seed oil nanoemulsion: a potent larvicidal agent against Culex quinquefasciatus. Pest Management Science, 69(8), 1017-1023.
12. Rinaldi F., et al. (2022). Neem oil nanoemulsions: characterisation and antioxidant activity. Nanomaterials, 10(8), 1608.
13. Choupanian M. M. C., Omar D., Basri M., & Asib N. (2017). Preparation and characterization of neem oil nanoemulsion formulations against Sitophilus oryzae and Tribolium castaneum adults. Journal of Pesticide Science, 42(4).
14. "Neem oil and its nanoemulsion in sustainable food preservation and packaging" (2022).
15. Khan, I., et al. (2025). Optimizing formulation, assessing stability, and enhancing wettability of neem oil nanoemulsion for pesticide application. RSC Advances.
16. "Green Micro- and Nanoemulsions for Managing Parasites, Vectors and Pests" (2023). PMC.
17. Deeksha K., Pavya, & Sowmya Hari (2019). Synthesis, Characterization and Antibacterial effect of Neem Oil Nanoemulsion. Research Journal of Pharmacy and Technology, 12(9). RJPT
18. Fatehia Nasser Gharsan, et al. (2024). Evaluation of toxicity of neem essential oil and its nano-emulsion on Oryzaephilus surinamensis adults. North Journal of Basic & Applied Sciences. north-journal-of-basic-and-applied-sciences.nbu.edu.sa
19. "Characterisation and microbial activity of neem oil nano-emulsions stabilized by Brij 30" (2023). IJCT. or.niscpr.res.in
20. BiomedRes (2022). Toxicity Evaluation of Two Neem Oil Nano-Formulations Using Mice. Biomedres
21. Ajayi O.E., et al. (2019). Potential Application of Nanoemulsion in Agriculture: A Current Perspective. ResearchGate. ResearchGate
22. Agriscigroup (2025). Effect of Neem Oil-based Nano-emulsion Application on Nematodes. IJASFT. agriscigroup.us
23. "Neem oil (Azadirachta indica) nanoemulsion — a potent larvicidal agent" (2011). PubMed. PubMed
24. De Souza Gomes V.E., et al. (2025). Neem oil emulsions stabilized by natural and synthetic emulsifiers: physical stability and antifungal activity. ScienceDirect.
25. "Antimicrobial Activity of Polycaprolactone Nanofiber Coated with Neem & Lavender Oil Nanoemulsions" (2024). MDPI Membranes. MDPI
26. Jerobin J., et al. (2015). Antibacterial activity of neem nanoemulsion and its toxicity assessment. International Journal of Nanomedicine. dovepress.com
27. "The Type of Grain Counts: Effectiveness of Three Essential Oil-based Nanoemulsions" (2022). PMC.

28. “Neem oil based nano-emulsion formulation by low energy phase inversion” (2021). ScienceDirect.
29. “Neem oil nanoemulsions (NO NEs) response surface methodology” (2024). MDPI.
30. “Impact of neem-nanoemulsion and neem petroleum ether extract on hymenopteran parasitoid” (2020). BNRC / SpringerOpen.
31. “Nanoemulsions: a review on low energy formulation methods, characterization, applications and challenges” (2024). ScienceDirect.
32. “Preparation of Neem Seed Oil Nanoemulsion – Ghotbi & Khatibzadeh” (2014). Semantic Scholar.
33. “Neem Oil (Azadirachta indica) nanoemulsion: a potent larvicidal agent — Society of Chemical Industry” (2011). PubMed
34. “Neem oil (Azadirachta indica) review: Larvicidal and pesticidal applications” (2017). PDF review. pdfs.semanticscholar.org
35. “Olio di neem – Italian Wikipedia entry (traditional uses)” (2023) – provides background on traditional uses. it.wikipedia.org
36. “Neem oil – Wikipedia” (2023) – general overview. en.wikipedia.org
37. “Nimbin (chemical) – Wikipedia” (2023) – details on one of the limonoids. en.wikipedia.org
38. “Azadirachtin – Wikipedia” (2023) – insecticidal active limonoid. en.wikipedia.org
39. Rinaldi F., et al. (2022) – again for antioxidant nanoemulsion work. (duplicate reference but supports multiple parts) PMC
40. “Green Micro- and Nanoemulsions for Managing Parasites, Vectors and Pests” (2023) – review on nanoemulsions in pest/vector management.

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