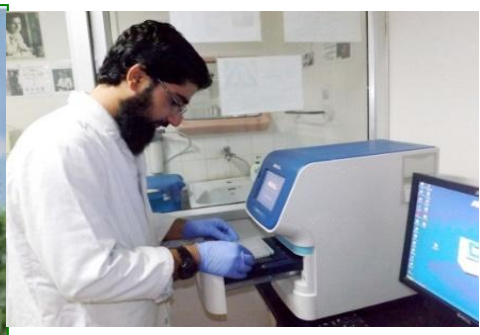
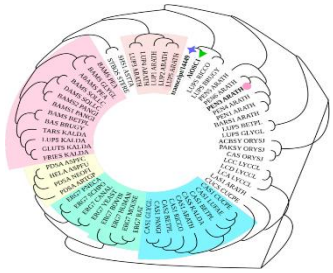
# Neem Research Newsletter

Volume 5, Issue 11, 2025





WNO
World Neem Organisation®
"Neem, the Earth's Saviour" ©

## WORLD NEEM ORGANISATION (WNO)

From

The Editor's Desk……

As we approach the end of the year it is heartening to note that interest in neem research continues unabated. In the agricultural front, use of neem has been highlighted in a review that investigated the synergistic potential of combining microbial biocontrol agents and phytochemical biopesticides as sustainable alternatives to chemical pesticides. In another review that examined the major insect pests affecting rice in Sub-Saharan Africa, successful case studies on neem-based pesticides in Tanzania were reported. NeemAzal®-T/S was shown to activate defense mechanisms in sunflower, offering promise in the management of downy mildew. Neem seed kernel extract and azadirachtin were demonstrated to disrupt the epicuticular wax layer in spiraling whitefly forming a barrier that limits insecticide penetration and contact toxicity. A discrete-time predator-prey model provided evidence that balanced neem application, appropriate timing of interventions, and conservation of natural enemies are key for sustainable guava pest control. Azadirachtin and cold-pressed neem oil were found to show promise against the root knot nematode Meloidogyne incognita. In a 2-year study on wheat crops, although integrated application of liquid nano urea and neem coated urea reduced yield, the agronomic use efficiency was significantly high. A study in Hawaii indicated that azadirachtin soil drenches increased mortality of avocado lace bug nymphs. The polysaccharide material (O-carboxymethyl chitosan, o-cmc) based azadirachtin was shown to enhance the activity of biopesticides against Spodoptera frugiperda.

The potential of neem in mitigating environmental problems and application in the food industry was analysed. Azadirachtin nanoparticles encased in eco-friendly biopolymeric alginate matrix to form reusable AzI@SA beads exhibited significant potential as an eco-friendly, sustainable, and effective nano-adsorbent for wastewater dye remediation. A biocomposite of polyhydroxybutyrate-co-valerate blended with neem oil and threadlets, was found to be antibacterial, non-cytotoxic, and biodegradable with significantly higher tensile strength and an eco-friendly alternative to synthetic plastics. The potential of polyvinyl alcohol (PVA) /neem leaf hybrid films as sustainable and effective active food packaging materials was demonstrated. Incorporation of neem oil into oil-in-water emulsions was shown to exhibit antifungal property besides improving its stability, bioavailability, and enabling controlled release.

In the area of human health, Neem extract demonstrated superior biocompatibility as an endodontic irrigant vital for disinfecting root canals, suggesting its potential as a safer alternative to synthetic agents. It is noteworthy that neem was mentioned as a valuable antifungal source in a review on soft lining materials for dentures. A Sertaconazole Nitrate organogel with neem seed oil was successfully formulated and found to have good physicochemical parameters, drug release behavior, skin compatibility, and improved antifungal activity, which implies its suitability for effective topical drug delivery.An amphiphilic graft copolymer synthesized by grafting polyaniline onto neem gum, was found to be a sustainable, multifunctional biomaterial with strong potential for clinical translation in wound dressing and regenerative applications. A review article documented the role of neem gum and its derivatives in pharmaceutical formulations, wound healing, and regenerative medicine, while addressing stability, scalability, and regulatory considerations. The neem limonoid nimbin was shown to possess cardioprotective properties while nimbolide was found to be promising against sepsis-associated acute lung injury. Azadiradione was demonstrated to be effective against leismaniasis. In a first report from southwest Nigeria, a Serratia endophyte from neem was found to have antimicrobial, antibiofilm, and antioxidant activities. Bioactive components of neem were found to serve as a natural substitute for managing mite infestations.

S. Nagini

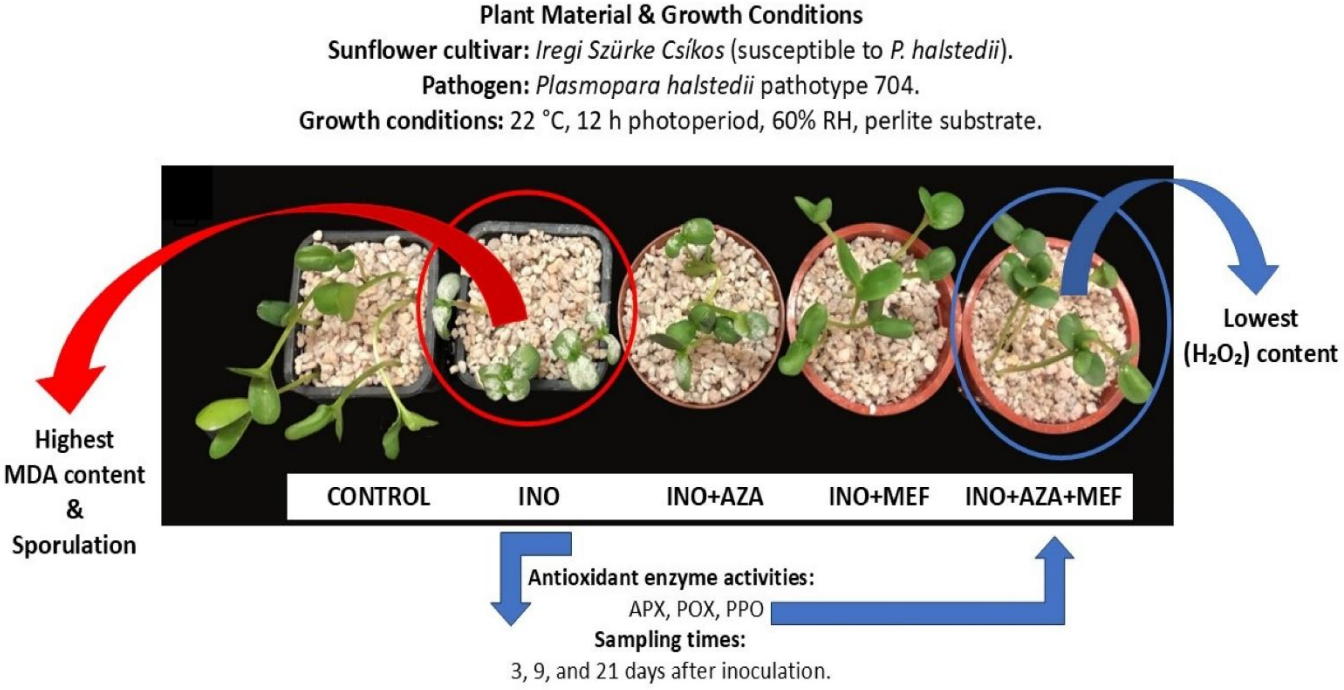
Core Founding Member, WNO
Chief Scientific Coordinator &
Regional Director, South India

# Neem in Agriculture

NeemAzal®-T/S Can Trigger Early Defense Responses in Susceptible Sunflower Seedlings Inoculated with *Plasmopara halstedii*: An Approach Based on the Enzymatic ROS Scavenging System.

Oliveira KR, Körösi K, Barna B, Bán R, Bennett SJ, Gratão PL.Plants (Basel). 2025 Nov 14;14(22):3481. doi: 10.3390/plants14223481.PMID: 41304631

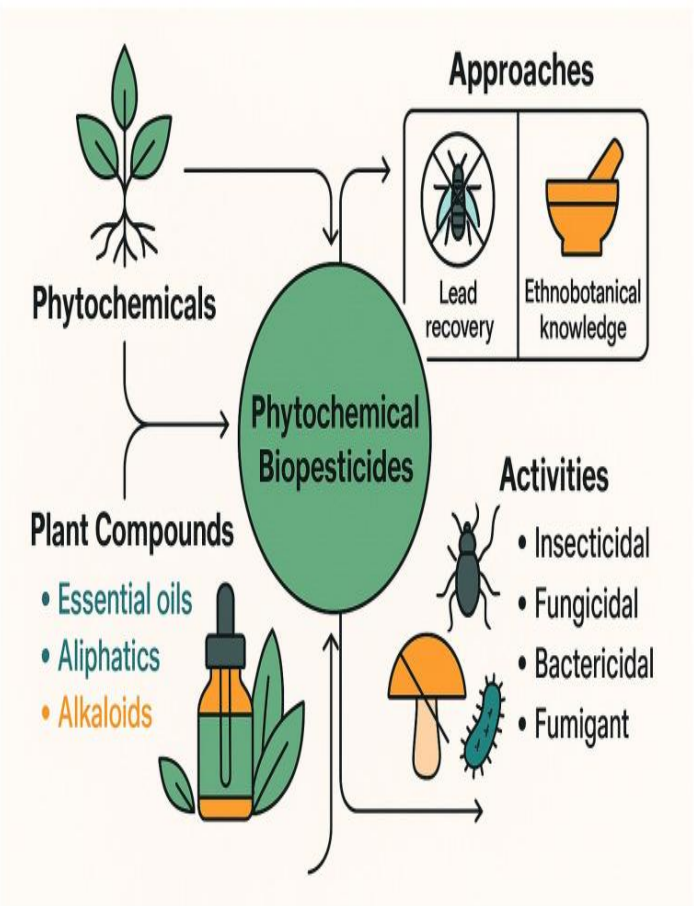
Downy mildew, caused by *Plasmopara halstedii*, is a major threat to sunflower production worldwide, leading to severe yield losses. Since resistance in sunflower hybrids can be easily broken by the pathogen, it is important to find alternative and sustainable control methods against this disease. This study investigated the potential use of NeemAzal®-T/S (a neem-based biopesticide formulation) to induce antioxidant defense responses in sunflower seedlings inoculated with *P. halstedii* (pathotype 704). Its effects, alone, or in combination with a reduced dose of Mefenoxam, were evaluated under controlled conditions. Plant height, sporulation, antioxidant enzyme activities (SOD, CAT, APX, POX, and PPO), lipid peroxidation (MDA), and hydrogen peroxide ($H_2O_2$) contents were measured. Our results indicate that the antioxidant responses of seedlings varied according to the treatment. MDA levels decreased even when NeemAzal®-T/S was applied alone, while $H_2O_2$ production only decreased when both treatments were applied combined. Overall, NeemAzal®-T/S can be a valuable alternative strategy to help control sunflower downy mildew, since it reduced sporulation and MDA content, and increased APX, POX, and PPO activities even at a later stage of infection in susceptible seedlings. These findings indicate that NeemAzal®-T/S can activate defense mechanisms associated with oxidative stress reduction in sunflower, offering a promising strategy to help manage downy mildew in a more sustainable manner.

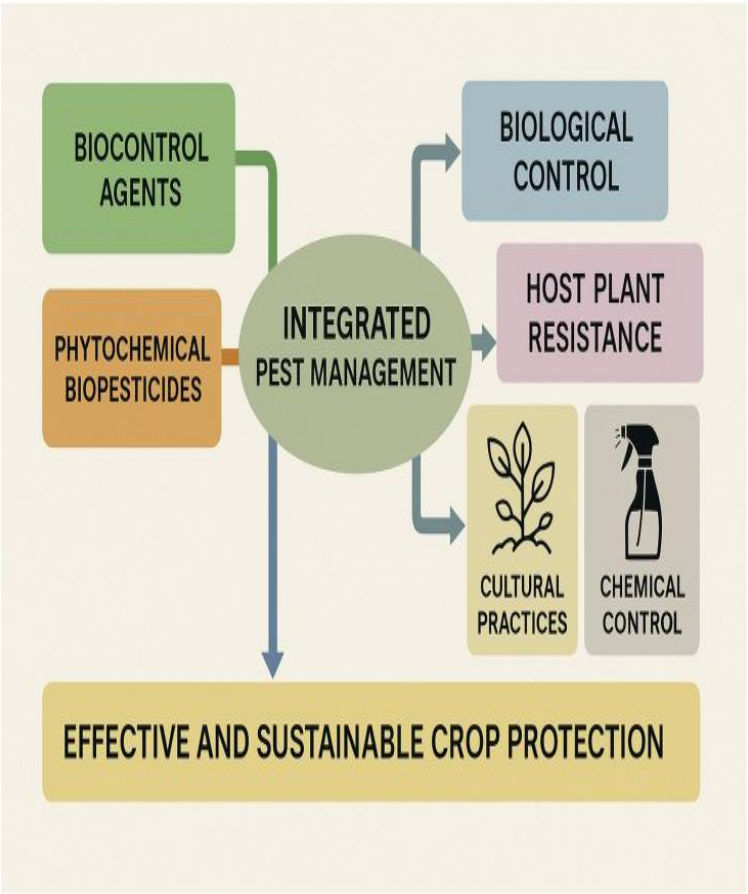


[Bridging Microbial Biocontrol and Phytochemical Biopesticides: Synergistic Approaches for Sustainable Crop Protection.]

Rezaee Danesh Y, Mulet JM, Porcel R.Plants (Basel). 2025 Nov 12;14(22):3453. doi: 10.3390/plants14223453.PMID: 41304604

The increasing prevalence of pests and diseases in agriculture necessitates innovative strategies for crop protection that mitigate environmental impacts. This review paper investigates the synergistic potential of combining microbial biocontrol agents and phytochemical biopesticides as sustainable alternatives to chemical pesticides. Through a comprehensive review of recent literature, we analyze the mechanisms by which beneficial microbes (e.g., *Trichoderma*, *Bacillus*, and *Pseudomonas*) enhance plant resilience and suppress pathogens, and how plant-derived phytochemicals such as essential oils, alkaloids, and flavonoids contribute to pest deterrence and disease resistance. The integration of these bio-based resources forms an actionable framework for sustainable crop protection-enabling reduced chemical dependence, improved soil health, and enhanced biodiversity. Examples of synergistic success, such as the combined use of Bacillus thuringiensis with neem extract and Trichoderma with lemongrass oil, illustrate their field potential. Future research should prioritize the formulation of stable microbial-phytochemical consortia, field validation of synergistic efficacy, and optimization of delivery systems to support commercial-scale adoption. Ultimately, this study promotes a paradigm shift toward eco-efficient pest management, bridging fundamental research and applied innovation for resilient agroecosystems.



[Sustainable Insect Pest Management Options for Rice Production in Sub-Saharan Africa.]

Pegalepo E, Bocco R, Onaga G, Nwilene F, Tamò M, Togola A, Katiyar SK.Insects. 2025 Nov 18;16(11):1175. doi: 10.3390/insects16111175.PMID: 41302920

Rice production in Sub-Saharan Africa (SSA) faces significant challenges due to insect pest infestations, which threaten food security and farmer livelihoods. This review examines the major insect pests affecting rice in SSA and highlights sustainable management strategies, drawing on successful case studies. It explores successful methods, including the use of biological control agents in Nigeria; neem-based pesticides in Tanzania; push-pull technology in Kenya; agroecological practices in Mali; resistant rice varieties in Ghana and Nigeria; integrated farming systems in Liberia, Guinea Conakry, Nigeria, Kenya and Madagascar; and farmer field schools in Zambia. Emerging technologies such as biotechnology and precision agriculture offer further additional opportunities to enhance pest control when effectively integrated within existing IPM frameworks. However, financial constraints, limited awareness, policy-related challenges, and inadequate infrastructure continue to limit widespread adoption. In this context, the review identifies critical research gaps, including the need for region-specific solutions, improved biopesticides, and long-term assessment of sustainable practices. Policy recommendations call for greater government investments, capacity-building programs, supportive regulatory environments, and stronger collaboration among researchers, development partners, and local stakeholders. Addressing these challenges can foster resilient and sustainable rice production systems across SSA.

(a). *Sesamia inferens* Female and male
Source: Viswajyothi et al., 2019

(b). *Dicladispa armigera*
Reproduced with permission from ©IRRI

(c). *Diopsis apicalis*
Source: Bocco et al., 2017

(d). *Nilaparvata lugens*
Reproduced with permission from ©IRRI

(e). *Sesamia calamistis*
Source: Ong'amo et al., 2016

(f). *Spodoptera frugiperda*
Source: Neupane et al., 2023

(g). *Nephotettix virescens*
Reproduced with permission from ©IRRI

(h). *Hydrellia philippina*
Reproduced with permission from ©IRRI

(i). *Aspavia armigera*
Reproduced with permission from ©Georg Goergen/IITA

(j). *Chilo polychrysus*
Source: Mashhoor et al., 2018

(k). *Aphis craccivora*
Source: De La Pava and Sepulveda-Cano, 2015

(l). *Orselia oryzivora*
Williams et al., 2002

(m). *Scirpophaga incertulas*
Source: Mokhtar and Abdullah, 2024

(n). *Maliarpha separatella*
Reproduced with permission from Abou Togola and AfricaRice

Epicuticular Wax Disruption as a Novel Mechanistic Strategy to Enhance Insecticidal Toxicity Against Aleurodicus dispersus on Eggplant and Cassava.

Boopathi T, Anusha N, Prasuna JG, Divya K.J Appl Toxicol. 2025 Nov 25. doi: 10.1002/jat.70001. Online ahead of print.PMID: 41292305

The epicuticular wax layer in Aleurodicus dispersus (spiraling whitefly) serves as a hydrophobic barrier that limits insecticide penetration and contact toxicity. This study evaluated the potential of solvent, enzymatic, and natural agents to disrupt the wax layer and enhance insecticidal efficacy. Laboratory assays screened eight agents-chloroform, hexane, ethyl alcohol, xylene, salt solution, soap solution, lipase, and CTCRI cassava extract-across graded concentrations. Two-way ANOVA revealed significant main effects of solvent type ($F_{7,70}$ = 10.697; $p \leq 0.01$) and concentration ($F_{10,70}$ = 40.936; $p \leq 0.01$) on percent wax removal. Lipase (0.5-2.5 g/L) and soap solution (1.5-10 g/L) exhibited the highest efficacy, confirmed through validation bioassays and Tukey's HSD grouping ($p \leq 0.01$). Pot trials on eggplant (Solanum melongena) and cassava (Manihot esculenta) demonstrated that wax disruption substantially increased toxicological performance. Lipase and soap solution alone reduced whitefly density by 40%-55%, while combinations with botanicals (neem seed kernel extract [NSKE], azadirachtin) achieved 70%-90% mortality. Integration with triazophos or acephate resulted in near-total suppression (95%-100% mortality; ≤ 4 insects/leaf). Three-way ANOVA ($p \leq 0.01$) confirmed significant treatment and interaction effects on both whitefly population and corrected mortality, indicating enhanced penetration and bioavailability of insecticides through wax dissolution. These results introduce epicuticular wax disruption as a mechanistic adjuvant approach in insect toxicology. Lipase and soap solution emerge as potent surface-active agents for improving insecticidal delivery and contact toxicity, offering a new direction in formulation science and integrated pest management.

Machine learning and bifurcation analysis in a discrete predator-prey model with **neem**-induced mortality.

Mehmood T, Rafaqat M, Saleem S, Merga FE.Sci Rep. 2025 Nov 19;15(1):40792. doi: 10.1038/s41598-025-24544-0.PMID: 41258254

This study develops a discrete-time predator-prey model for guava pest management using the piecewise constant argument (PCA) scheme. The model incorporates logistic prey growth, neem-induced mortality, and predator crowding. Analytical and numerical results establish conditions for flip and Neimark-Sacker bifurcations, supported by bifurcation diagrams, Lyapunov exponents. Ecologically, small neem-induced mortality (d) destabilizes prey-predator coexistence, whereas larger d restores stability. The intervention frequency [Formula: see text] further shapes dynamics, with moderate values maintaining stability and large values inducing oscillations. As a proof-of-concept, machine learning (random forest and decision tree classifiers) was explored to efficiently approximate the analytically derived stability regions. Both classifiers successfully replicated the stability map, with Random Forest providing smoother boundaries and higher accuracy, demonstrating the potential of ML as a computational surrogate for more complex models. Parameter importance analysis revealed that prey dynamics are mainly

driven by prey-related parameters (r, a, b), while predator persistence is strongly influenced by conversion efficiency (c) and natural mortality (s). These findings highlight that balanced neem application, appropriate timing of interventions, and conservation of natural enemies are key for sustainable guava pest control.

A novel nematicide application method based on nematode life cycle for managing root-knot nematode, Meloidogyne incognita.

Gitonga D, Hajihassani A.Pest Manag Sci. 2025 Nov 7. doi: 10.1002/ps.70350. Online ahead of print.PMID: 41201020

**Background:** Organic vegetable growers face significant challenges in managing plant-parasitic nematodes, particularly root-knot nematodes (RKN; Meloidogyne spp.), because of restrictions on the use of synthetic chemicals. This study evaluated the efficacy of seven commercially available Organic Materials Review Institute-certified bionematicides against Meloidogyne incognita under greenhouse and field conditions. A cucumber plasticulture field study was also conducted to compare the efficacy of four best-performing bionematicides, including azadirachtin, cold-pressed neem oil, thyme oil and saponins of Quillaja saponaria, identified in the greenhouse study and a chemical nematicde (oxamyl) using two application regimes: calendar-based (following the product label) and nematode life-cycle-based (following the M. incognita life cycle using degree-days assessment).

**Results:** In the greenhouse study with tomato, azadirachtin and thyme oil significantly reduced M. incognita root galling and reproduction factor (final nematode population/initial nematode population) compared with a positive control. In the field trial with cucumber, the nematode life cycle was completed in 23 days during the spring season and 24 days during the fall season, accumulating 380 and 398 degree-days, respectively, above a base temperature of 10 °C. For calendar-based applications, only azadirachtin significantly reduced nematode density, whereas for life-cycle-based applications, all treatments except saponins of Q. saponaria were effective. Oxamyl was more effective when applied according to the nematode life cycle than on a calendar-based regime. Life-cycle-based applications generally outperformed calendar-based applications based on numerical values, even in cases in which the differences were not significant. For the galling index, calendar-based applications of azadirachtin and cold-pressed neem oil reduced the galling index more than life-cycle-based applications at mid-season. At the end of the season, only azadirachtin under the calendar-based application differed significantly from the control, while all other treatments (except saponins of Q. saponaria) had lower root galling indices than the calendar-based applications.

**Conclusion:** These findings indicate that both application regimes can be used to manage M. incognita in organic farming systems. Of particular significance is the novel life-cycle-based approach developed in this study, which may confer enhanced sustainability benefits by optimizing nematicide application timing and reducing treatment frequency, ultimately leading to a decline in soil nematode population densities.

Effect of liquid nano urea and coated urea on gaseous N losses and agronomic efficiency under elevated $CO_2$ and temperature interaction.

Apoorva MS, Bhatia A, Chakrabarti B, Kumar V, Tomer R.Environ Sci Pollut Res Int. 2025 Oct;32(46):26156-26175. doi: 10.1007/s11356-025-36986-0. Epub 2025 Nov 14.PMID: 41239099

Ammonium fertilizers lose significant amounts of nitrogen, primarily through ammonia ($NH_3$) volatilization and nitrous oxide ($N_2O$) emissions, which results in low nitrogen use efficiency. Liquid Nano Urea (LNU) is considered more efficient than traditional soil-applied urea, potentially reducing synthetic N fertilizer use. A two years study growing wheat crop was conducted to evaluate the integrated application of neem coated urea (NCU) and LNU, NCU (100%) and Sulphur coated urea (SCU) under elevated $CO_2$ and temperature interaction in T-FACE rings to assess gaseous nitrogen losses and agronomic use efficiency (AUE). LNU (4%N) was applied as two foliar spray in the first year (50% NCU + LNU), and a single foliar spray in second year (75% NCU + LNU). Exposure to elevated $CO_2$ (seasonal average 580-585-ppm) and elevated temperature (+ 1.68-1.74 °C over ambient), significantly ($p < 0.05$) increased the emissions of nitrous oxide ($N_2O$) and ammonia ($NH_3$) compared to ambient conditions Integrated LNU + NCU exhibited lower $N_2O$ losses, and $NH_3$ was non-detectable post-LNU foliar application. SCU significantly lowered $NH_3$ losses compared to NCU. Soil $NH_4^+$ was the highest with SCU under ambient, but reduced under elevated temperature (ET) and elevated $CO_2$ and elevated temperature interaction (ECT). Wheat yield increased under elevated $CO_2$ (EC) and declined under ET in all N treatments. The decrease in grain N concentration under EC was the lowest with SCU. Microbial biomass carbon and nitrogen increased significantly under ECT. The agronomic use efficiency (AUE) reduced in all fertilized treatments under ECT as compared to the ambient. Wheat yields reduced with LNU + NCU application; however, this approach resulted in higher AUE due to the lower amount of N applied and reduced $NH_3$ and $N_2O$ losses. The amount and timing of the foliar LNU application may need further optimisation for countering the lower wheat yields.

Azadirachtin soil drenches show increased mortality of avocado lace bug nymphs (Hemiptera: Tingidae), in Hawai'i with evidence of multiweek residual activity.

Bosch MJ, Acebes-Doria AL.J Econ Entomol. 2025 Nov 15:toaf302. doi: 10.1093/jee/toaf302. Online ahead of print.PMID: 41240355

Avocado lace bug, Pseudacysta perseae (Heidemann) (Hemiptera: Tingidae), is a sap-feeding insect that feeds on avocado leaves. Injury from P. perseae is indicated by areas of leaf chlorosis/necrosis. Large areas of injury can lead to premature leaf drop, and severe infestations can lead to large proportions of leaves dropping, adversely affecting fruit development and quality. Since its establishment in Hawai'i, P. perseae has become a ubiquitous pest across the islands and is correlated with yield decline. Due to the challenging topography of Hawai'i, lack of biocontrol agents, and mixed fruit tree orchards, effective management strategies are limited to pesticide use. Even so, routine foliar sprays

of pesticides are not economically or logistically feasible for controlling P. perseae in Hawai'i. While synthetic systemic pesticides can be used as soil drenches, many show toxicity to nontarget animals and have limited application frequencies. However, research shows azadirachtin, an active component in the organic pesticide neem oil, has some systemic properties. This study investigated soil drenches of varying concentrations of azadirachtin in avocado seedlings on P. perseae nymphal mortality over eight weeks. Results showed mortality had an 85% to 98% probability of occurrence in the first week following drenching for nymphs feeding on azadirachtin-treated trees compared to 14% for untreated trees. Mortality for treated trees decreased through time but remained significantly higher than untreated trees 3 to 6 weeks following drenching. The findings from this study will aid in developing a more practical and economically reasonable management strategy for P. perseae in Hawai'i.

O-Carboxymethyl chitosan-based **azadirachtin** enhances anti-degradation properties of **azadirachtin** and antifeedant activity against Spodoptera frugiperda.

Wu H, Lin YG, Du PR, Hou RQ, Zeeshan M, Xu HH, Zhang ZX.Pest Manag Sci. 2025 Nov 14. doi: 10.1002/ps.70373. Online ahead of print.PMID: 41235696

**Background:** The environmental safety of biopesticides presents a viable alternative to mitigate the risks associated with chemical pesticides. However, the swift ecological degradation of these biopesticides often compromises their efficacy in pest control. In this study, the performance analysis of polysaccharide material (O-carboxymethyl chitosan, o-cmc) based azadirachtin (Aza) was used to enhance the activity of biopesticides.

**Results:** The constructed O-carboxymethyl chitosan-based azadirachtin (Aza@o-cmc) with a mean diameter of 326.33 ± 27.14 nm had better dilution stability (zeta potential = -31.6 ± 5.04). It was indicated that Aza@o-cmc exhibits superior foliar adherence and resistance to leaching compared to Aza. Additionally, Aza@o-cmc has significantly improved indoor resistance to various conditions, including rainwater solubilization, ultraviolet (UV) light, pH fluctuations, and microbial degradation. The antifeedant activity indicated that Aza@o-cmc significantly repressed the SeTre-2 and SeCHBE genes expression of chitin metabolism pathway. Importantly, field trials have revealed that Aza@o-cmc has a substantially prolonged half-life on foliage compared to Aza.

**Conclusion:** Our findings reveal that Aza@o-cmc holds considerable promise for pest management within the framework of sustainable agricultural practice, and features the technological potential of O-carboxymethyl chitosan-based biopesticides for performance enhancement.

# Neem for Sustainable Environment

Alginate encapsulated fluorescent carbon-core regenerative Azadirachta indica flower-derived nanoparticles for efficient cationic dyes removal.

Dwivedi TS, Borah SJ, Gupta A, Singh PP, Kumar V.Environ Sci Pollut Res Int. 2025 Oct;32(47):26970-26989. doi: 10.1007/s11356-025-37119-3. PMID: 41272261

Azadirachta indica, a medicinal plant widely grown across the globe, is renowned for its multifaceted bioactivity and environmental compatibility. Its potential as a green adsorbent offers advantages such as biogenic composition, low cost, and sustainability in wastewater treatment. In this study, Azadirachta indica-derived nanoparticles (AzI NPs) were synthesized and evaluated for the adsorption of cationic dyes (malachite green (MG), methylene blue (MB), and crystal violet (CV)). PXRD, SEM, and BET revealed irregular porous morphology of NPs with an average crystallite size of 9 nm, while zeta potential confirmed a negatively charged surface. The carbon-rich core contributed to a strong blue emission at 270 nm excitation, which may be linked to surface defects and conjugated domains. Dye adsorption efficiencies were optimized across various parameters, including dye concentration, pH, adsorbent dosage, contact time, water quality, and temperature. AzI NPs achieved adsorption efficiencies of 95% (MG), 86% (MB), and 85% (CV) within just 3 minutes of contact time. Kinetic studies followed pseudo-second-order (PSO) model, indicating chemisorption, while Elovich model suggests surface heterogeneity and IPD model indicates that pore diffusion may contribute. Furthermore, isotherm analysis aligned with the Langmuir and Temkin models, suggesting monolayer adsorption on a homogeneous surface with moderate adsorbate-adsorbent interactions. Thermodynamic parameters confirmed a spontaneous process and endothermic behavior. At room temperature, ΔG and ΔH were determined to be −3.695kJ/mol$-3.695$kJ/mol and 39.17kJ/mol$39.17$kJ/mol , respectively. To improve applicability, AzI NPs were encased in eco-friendly biopolymeric alginate matrix to form reusable AzI@SA beads, minimizing NP leaching, secondary pollution, and enabling multiple adsorption cycles. AzI@SA beads demonstrated reusability across eight consecutive cycles with minimal loss in performance. Therefore, AzI@SA has significant potential as an eco-friendly, sustainable, and effective nano-adsorbent for wastewater dye remediation.

Development of a bio-based composite from in situ extracted **neem** oil, threadlets, and Bacillus sp. PhNs9 synthesized PHBV utilizing sugarcane molasses.

Bajirao Patil P, Sarkar D, Poddar K, Gorde PM, Singh SK, Sarkar A.Prep Biochem Biotechnol. 2025 Nov 14:1-16. doi: 10.1080/10826068.2025.2585925. PMID: 41238515

Environmental concerns over synthetic plastics highlight the need for sustainable alternatives, among which bacterial polyhydroxyalkanoates (PHAs) have emerged as promising. However, their commercialization is limited, owing to their higher production cost and lower applicability. Hence, this study employs ANN-GA-based optimization of a novel *in-situ* fed-batch process using a self-isolated *Bacillus* sp. PhNs9 utilizing untreated sugarcane molasses as a cost-effective substrate. The bioreactor scale production at

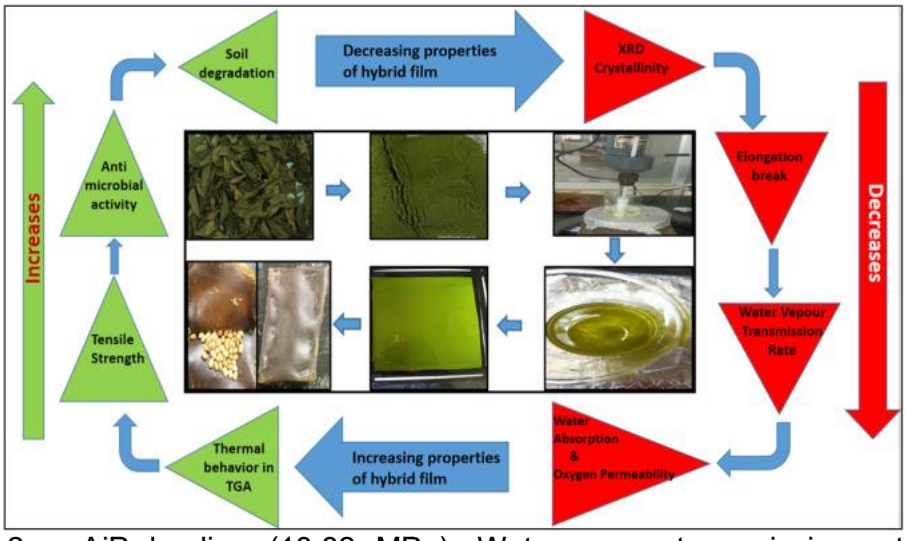
optimized conditions resulted in a PHA production of 3.47 ± 0.11 g/L, whose GC-MS and DSC analysis revealed it to be Polyhydroxybutyrate-co-valerate (PHBV). This PHBV was successfully blended with *in-situ* extracted neem oil and threadlets to form a biocomposite, which was found to be antibacterial, non-cytotoxic, and biodegradable with significantly higher tensile strength. The HR-MS analysis of the extracted neem oil revealed the presence of bioactive compounds like nimbin, azadirachtin, and Salannin, providing medicinal properties. The techno-economic analysis of the whole process resulted in the cost of PHBV production and extraction as ₹1.03/g, extraction of neem oil as ₹5.75/mL, which further resulted in the biocomposite preparation cost to be ₹0.30 $cm^{-2}$. This accentuates the commercial feasibility of the developed biocomposite as an eco-friendly alternative to synthetic plastics.

## Neem in Food Processing

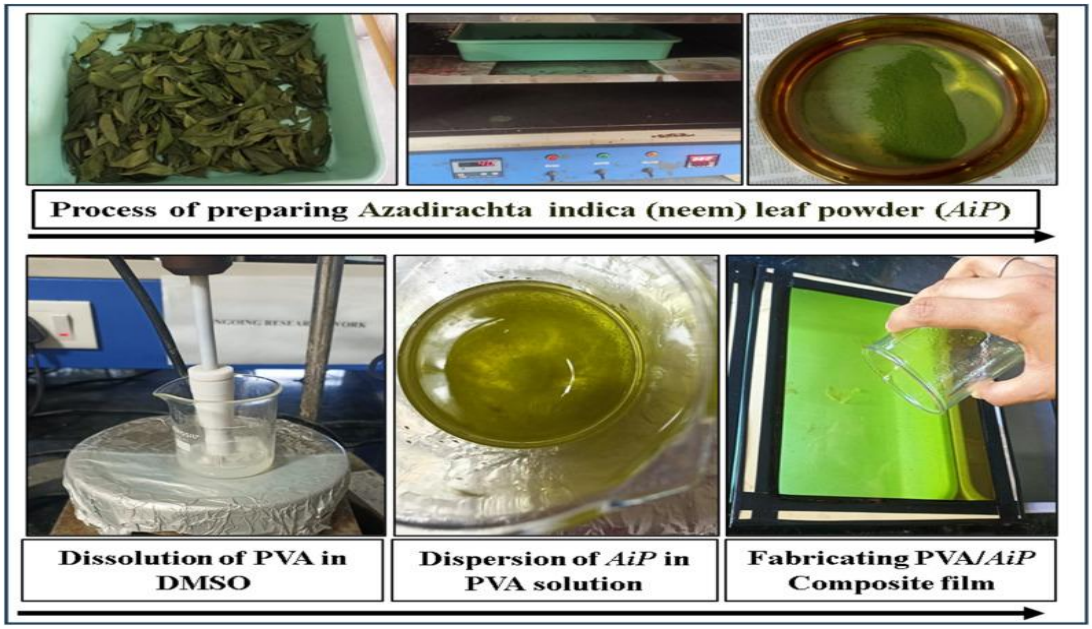
Enhancement of antimicrobial and structural properties of PVA packaging films using **neem** leaf powder: an example for extending the shelf life of cowpeas.

Solaikannan T, Paramasivan S, Nagarajan R, Ayrilmis N.RSC Adv. 2025 Nov 3;15(49):42176-42191. doi: 10.1039/d5ra05486a. Oct 28.PMID: 41190137

This study focused on the fabrication and characterization of polyvinyl alcohol (PVA)/*Azadirachta indica* (neem leaf) hybrid films for use in active food packaging. PVA/AiP hybrid films were prepared using a solution casting technique with varying concentrations of AiP (0.1, 0.5, 1.0, 1.5, and 2.0 g) as a bio-filler. The films were comprehensively characterized using FTIR, XRD, SEM, optical microscopy, TGA/DSC, water absorption, oxygen permeability, mechanical strength, water vapor transmission rate, soil degradability, and antimicrobial activity tests. TGA/DSC showed improved thermal stability of the hybrid films (up to 330 °C) with increasing AiP content. Water absorption increased with AiP incorporation, peaking at 0.5 g, (130% at 60 min) while oxygen permeability was highest for the 0.5 g AiP film (~8.0 mg $L^{-1}$ at 72 hours). At 2 g AiP loading, the film showed noticeable brittleness, making it unsuitable for conventional film applications. Hence, it was not compared with the lower concentration films, but its barrier properties were evaluated separately. Tensile strength significantly improved at 2 g AiP loading (18.82 MPa). Water vapor transmission rate progressively reduced with increasing AiP content. Soil degradability was enhanced at 0.1 g AiP (74.5%) but decreased at higher loadings (55.4%). Antimicrobial activity against *E. coli* increased with AiP concentration. Compared to pure PVA films (tensile strength 12-15



MPa, WVTR 6.0-7.2 g mm $m^{-2}$ $day^{-1}$ $kPa^{-1}$) and commercial PET films (tensile strength 55-75 MPa, WVTR 2.0-3.0 g mm $m^{-2}$ $day^{-1}$ $kPa^{-1}$), the PVA/AiP hybrid films exhibited superior barrier performance and antimicrobial activity while being biodegradable. The findings demonstrated the potential of PVA/AiP hybrid films as sustainable and effective active food packaging materials. This supports the achievement of sustainable development goal (SDG) 12, which focuses on responsible consumption and production. Unlike pure PVA or conventional plastics, PVA/AiP hybrid films combined superior performance with biodegradability and antimicrobial activity.




**Neem** oil emulsions stabilized by natural and synthetic emulsifiers: a study on physical stability and antifungal activity.

Gomes VES, Lüdtke FL, Chevalier RC, da Silva LAGA, Rodrigues MS, de Oliveira Rocha L, Cunha RLD, Ribeiro APB, Marangoni Júnior L. Food Res Int. 2025 Dec;221(Pt 4):117530. doi: 10.1016/j.foodres.2025.117530. Epub 2025 Sep 18.PMID: 41185286

Neem oil (NO) is a plant-derived bioactive compound with known antimicrobial properties. Incorporating NO into oil-in-water (O/W) emulsions can improve its stability, bioavailability, and allow controlled release. This study developed and characterized O/W emulsions using NO as the dispersed phase and active agent. Emulsions were formulated with natural emulsifiers (soy lecithin - SL, pea protein - PP), a synthetic emulsifier (Tween 80 - T80), and their combinations. Over 21 days, formulations were analyzed for chemical interactions, droplet size ($D_{4,3}$), polydispersity (Span), zeta potential (ZP), microstructure, color, kinetic stability, and antifungal activity (AFA) against Alternaria alternata and Penicillium expansum. All emulsions showed stable chemical interactions and ZP values above |38 mV|. $D_{4,3}$ ranged from 0.59 to 2.01 μm, influenced by emulsifier type. Thermally treated PP in alkaline conditions produced stable, slightly polydisperse emulsions for 14 days, while SL led to larger droplets and instability. PP:T80 and T80:SL combinations showed synergistic effects and good stability, unlike PP:SL, which resulted in unstable emulsions. The PP-only emulsion had the highest AFA, inhibiting P. expansum (85.06 %) and A. alternata (79.97 %). These findings highlight the critical role of emulsifier selection in enhancing the stability, controlled release, and antifungal efficacy of NO in emulsified systems.

Cytotoxic Effects of Synthetic and Herbal Endodontic Irrigants on Human Red Blood Cells: An In Vitro Study.

Mangat P, Chandel B, Biswas M, Trivedy S, Gupta A, Shree N, Gupta S.Cureus. 2025 Sep 29;17(9):e93522. doi: 10.7759/cureus.93522. eCollection 2025 Sep.PMID: 41179071

**Introduction:** Endodontic irrigants are vital for disinfecting root canals; however, their potential to harm healthy cells drives the search for safer options. Herbal extracts may offer natural antimicrobial benefits with reduced toxicity compared with synthetic agents. This study aimed to evaluate the cytotoxicity of synthetic irrigants (5.25% sodium hypochlorite (NaOCl) and 2% chlorhexidine (CHX)) versus herbal options (neem and garlic extracts) on human red blood cells (RBCs) in vitro. The objectives of this study were to assess RBC viability across different concentrations to identify the least cytotoxic irrigant and evaluate neem and garlic extracts as biocompatible alternatives for endodontic therapy.

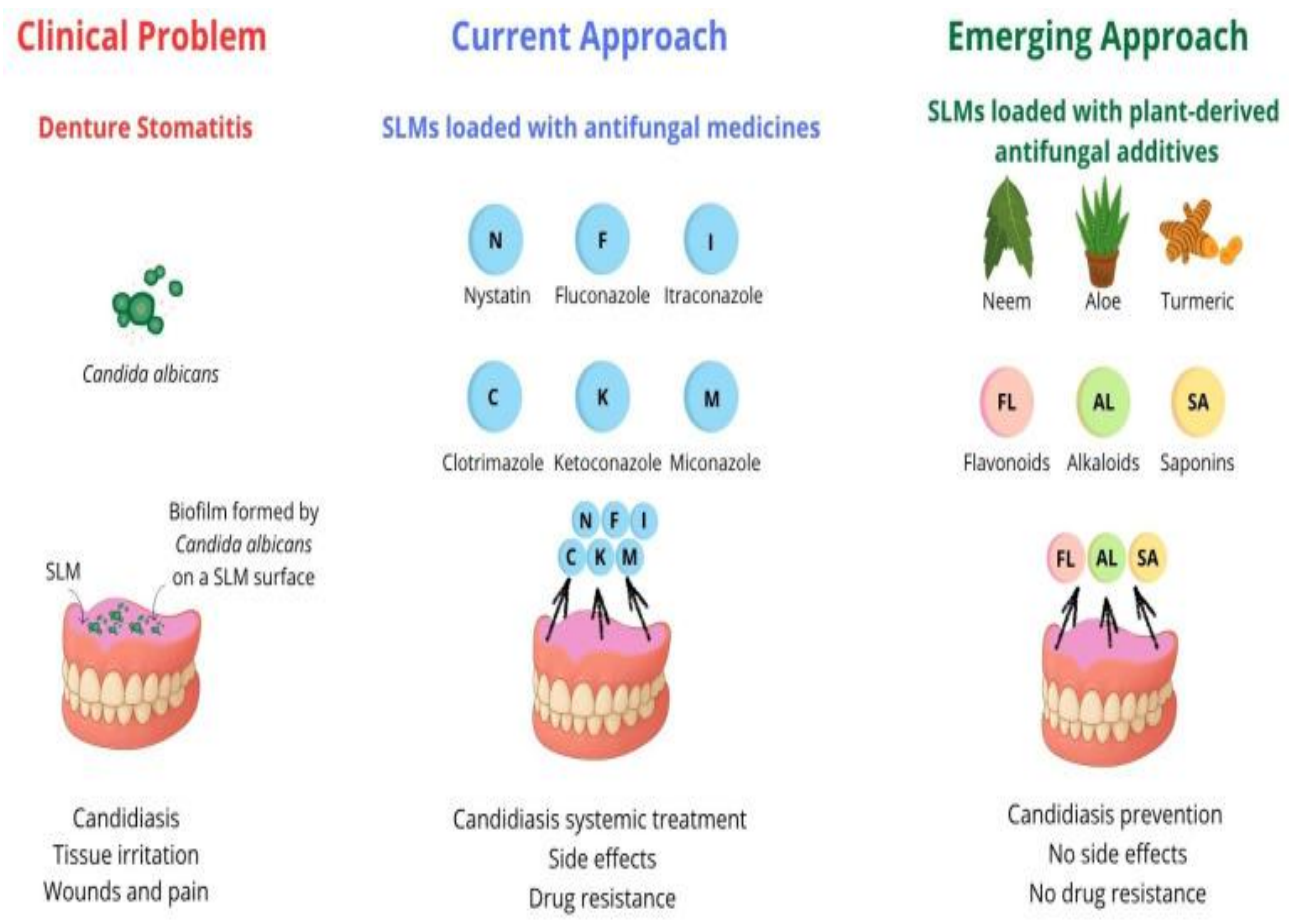
**Materials and methods:** This in vitro study was conducted at the Department of Conservative Dentistry and Endodontics, Kalka Dental College, Meerut, India. The study involved collecting 5 mL of venous blood from a healthy volunteer, followed by centrifugation at 1000 rpm for 10 minutes to isolate packed human RBCs. RBCs were washed with 0.9% saline and diluted to create a suspension, with 100 µL aliquoted into 164 test tubes per trial. Four experimental groups (5.25% NaOCl, 2% CHX, neem extract, and garlic extract) each had 40 tubes subdivided by irrigant volume (10-50 µL), and a saline control group had four tubes. Neem extract was prepared by boiling fresh leaves to a 25% concentration, whereas garlic extract was subjected to ethanol treatment and homogenization to 25%. After adding irrigants and incubating for three minutes, RBC viability was measured using an automated hematology analyzer. The experiment was repeated eight times to ensure reliability. Data were statistically analyzed. The tests used were the intraclass correlation (ICC) test and the Kruskal-Wallis test with Bonferroni post-hoc tests, with significance at $p < 0.05$.

**Results:** All groups showed significant ICC ($p < 0.05$), with NaOCl at 0.99 and neem at 0.58. Intergroup analysis revealed the lowest RBC viability for NaOCl (median = 3.26%), while neem (4.91%) and control (5.53%) showed the highest viability. Post-hoc tests confirmed the inferior performance of NaOCl ($p < 0.01$ vs. all). Concentration-dependent declines were significant across the groups ($p < 0.001$), with NaOCl showing the steepest drop. Within the concentrations, neem consistently outperformed the others.

**Conclusion:** Neem extract demonstrated superior biocompatibility as an endodontic irrigant, suggesting its potential as a safer alternative to synthetic agents, such as NaOCl.

Plant-Derived Modifiers for Antimicrobial Soft Denture Liners: A Review.
Kula P, Chladek G, Barszczewska-Rybarek I.Int J Mol Sci. 2025 Nov 8;26(22):10848. doi: 10.3390/ijms262210848.PMID: 41303338

This review examines strategies to enhance the antifungal properties of commercial soft lining materials (SLMs) through modification with plant-derived oils, extracts, and powders. These natural bioactive compounds act via multiple mechanisms, including disruption of fungal cell membranes, inhibition of biofilm formation, and interference with *Candida albicans* metabolism, the pathogen causing denture-associated candidiasis. Their incorporation into SLM provides localized antifungal activity at the denture-mucosa interface. The review highlights *Aloe vera* (aloe), *Azadirachta indica* (neem), *Ocimum basilicum (basil)*, *Melaleuca alternifolia* (tea tree), *Cocos nucifera* (coconut), *Allium sativum* (garlic), *Thymus vulgaris* (thyme), and chitosan as notable sources of phytotherapeutics that consistently inhibit *C. albicans* growth. In addition to antimicrobial effects, studies assessed both intrinsic (hardness, tensile strength, tear strength) and interfacial (bond strength) mechanical properties, as well as surface roughness. Most formulations maintained acceptable mechanical performance and improved surface smoothness. Key limitations include rapid leaching of active compounds, variability in testing methods, and insufficient in vivo and cytotoxicity data. Future research should prioritize the high-quality purification of natural extracts, the isolation of well-defined bioactive compounds, and the design of systems enabling selective and sustained release of these agents, ensuring reproducibility, enhanced stability, and clinical reliability of next-generation bioactive SLMs.



Development and Evaluation of Antifungal Activity of Carbopol and **Neem** Seed Oil-Based Organogels.

Jain P, Chandrakar S, Gupta PP, Gidwani B.Antiinflamm Antiallergy Agents Med Chem. 2025 Nov 5. doi: 10.2174/0118715230381640250905045919. Online ahead of print.PMID: 41208067

**Introduction:** The present study focused on the formulation of a Sertaconazole Nitrate (SN) organogel with neem seed oil through microwave irradiation, optimizing the formulation by Box-Behnken Design (BBD) and Response Surface Methodology (RSM). The research explored the effect of Neem Seed Oil (NSO), Carbopol-934 (CP), and Polyethylene glycol-400 (PEG) on viscosity (VS), spreadability (SP), and drug content (DC).

**Methods:** A 15-run BBD was utilized to investigate the impact of the independent variables. The organogels obtained were analyzed for viscosity, spreadability, and drug content. The optimized formulation was also characterized for homogeneity, pH, swelling index, extrudability, drugexcipient compatibility, moisture content, and gel-sol transition temperature (GSTT). In-vitro and ex vivo release studies and antifungal activity against Candida albicans and Trichophyton rubrum were also carried out.

**Results:** The measured viscosity (0.40±11 Pa.s), spreadability (14.98 ± 74 gm.cm/sec), and drug content (97.11 ± 27 %) of the optimized formulation were very close to the calculated values. The optimized organogel had a skin-compatible pH (6-7), high in-vitro (98.55±0.32%) and exvivo (88.95 ± 1.55 %) drug release, and a wider zone of inhibition (22 mm) against Candida albicans and Trichophyton rubrum than a commercial product.

**Discussion:** The microwave-irradiation-synthesized BBD-optimized SN organogel with neem oil showed excellent drug release (>98%), skin-friendly pH, and improved antifungal activity (22 mm inhibition) compared to commercial preparations in line with green pharmaceutical trends. The scalability of microwave procedures, stability over extended periods, and sparse excipient screening require investigation to extend laboratory success to clinical application.

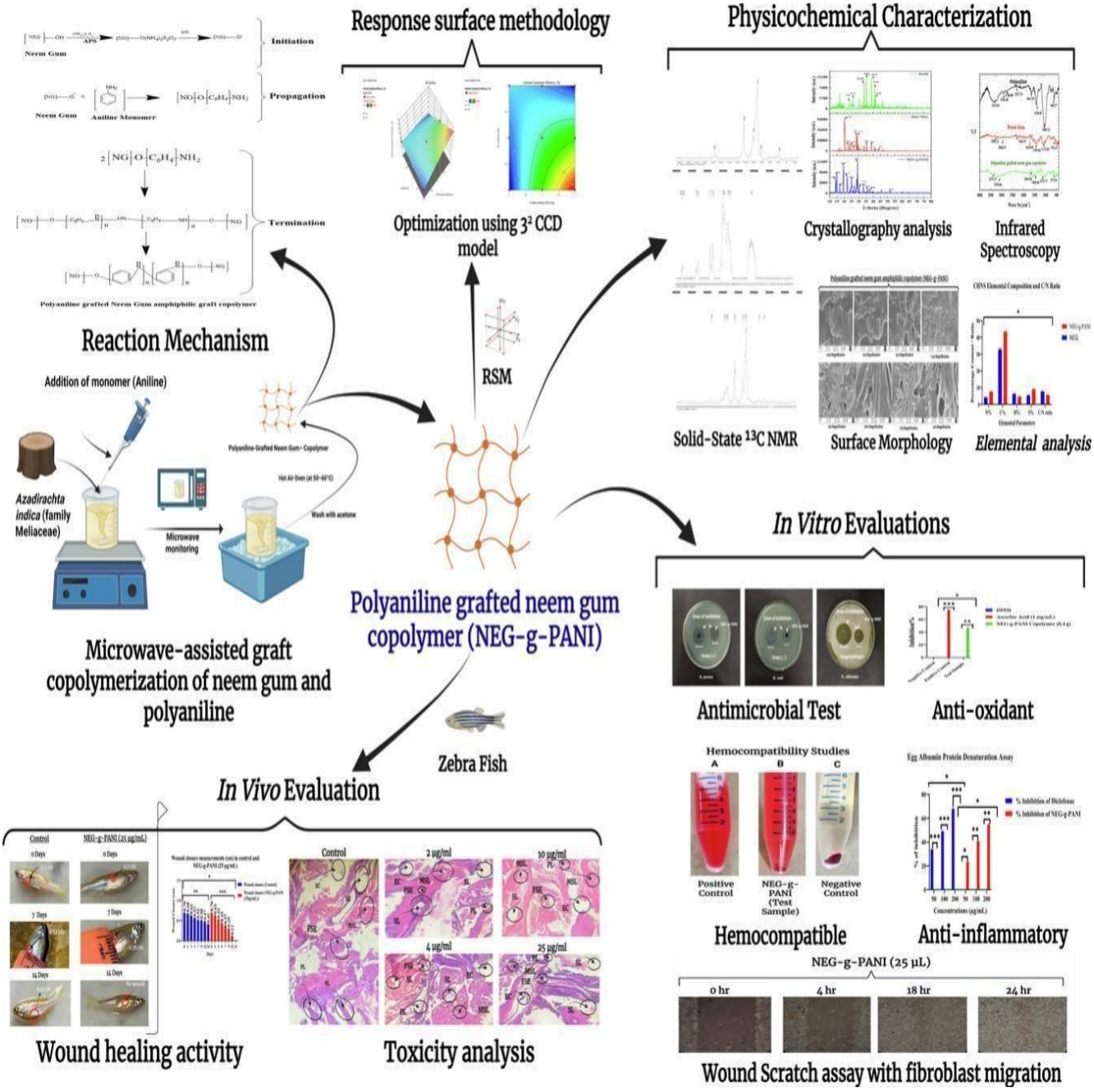
**Conclusion:** The research was able to successfully develop and optimize a Sertaconazole Nitrate organogel through a microwave-assisted process with a natural oil. The optimized formulation was found to have good physicochemical parameters, drug release behavior, skin compatibility, and improved antifungal activity, which implies its suitability for effective topical drug delivery.

A multifunctional polyaniline-grafted **neem** gum copolymer (NEG-g-PANI) for wound healing: Synthesis, comprehensive in vitro and in vivo biocompatibility evaluation.

Ghosh S, Bal T, Majumder S.Int J Biol Macromol. 2025 Dec;333(Pt 2):148752. doi: 10.1016/j.ijbiomac.2025.148752. Epub 2025 Nov 11.PMID: 41232886

Traditional wound healing therapies often face limitations such as inadequate localized drug delivery, poor responsiveness to the wound environment, and systemic side effects. To address these challenges, an amphiphilic graft copolymer was synthesized by grafting polyaniline (PANI) onto neem gum (NEG), a natural, biocompatible polysaccharide, using

a green, microwave-assisted free radical polymerization method. A $3^2$ factorial Central Composite Design (CCD) model was employed to optimize the formulation, with FM3 identified as the optimal grade based on grafting efficiency and physicochemical performance. The optimized NEG-g-PANI exhibited high molecular weight, enhanced viscosity, and improved structural features confirmed by FTIR, $^{13}C$ solid state NMR, XRD, and CHNS analyses. It exhibited pH-responsive swelling, sustained release characteristics, and effective solubilization of hydrophobic drugs, indicating its suitability as a multifunctional drug carrier. Biological assessments demonstrated excellent antimicrobial, antioxidant, and anti-inflammatory properties, along with hemocompatibility, cytocompatibility, and in vivo wound-healing efficacy in zebrafish. Overall, this study highlights NEG-g-PANI as a sustainable, multifunctional biomaterial with strong potential for clinical translation in wound dressing and regenerative applications.



Physicochemical Properties, Drug Delivery, and Tissue Engineering Applications of **Neem** Gum and Its Derivatives: A Comprehensive Review.
Prakash A, Malviya R, Sridhar SB, Wadhwa T, Shareef J.
Mini Rev Med Chem. 2025 Nov 4. doi: 10.2174/0113895575403808251008045503. PMID: 41193455

Neem gum, a biocompatible and biodegradable polysaccharide, has broad applications in drug delivery and tissue engineering. Its hydrophilic and bioadhesive properties make it ideal for controlled drug release and scaffold fabrication. This review examines the role of neem and its derivatives in pharmaceutical formulations, wound healing, and regenerative medicine, while addressing stability, scalability, and regulatory considerations. Future directions include the integration of nanotechnology and chemical modifications for enhanced biomedical applications. Neem gum has been developed into various forms, including hydrogels, nanoparticles, films, and coatings, for targeted drug delivery and tissue regeneration. Its antimicrobial, antioxidant, and anti-inflammatory properties enhance wound healing and infection control, but challenges like batch variability and mechanical limitations remain. Neem gum is a promising natural biomaterial for pharmaceutical and biomedical applications. Further research on stability, large-scale processing, and clinical validation is essential for commercialisation and clinical use.

Modulatory Effect of Nimbin on Isoproterenol Induced Mitochondrial and Lysosomal Enzymes Activities and Apoptosis Signaling in Rats.
Wang Y, Chen J, Jiang H, Li X.Physiol Res. 2025 Dec 2;74(5):743-753.PMID: 41329533

Nimbin, a bioactive triterpenoid compound isolated from the neem tree (Azadirachta indica), is known for its anti-inflammatory, antioxidant, antimicrobial, and hepatoprotective properties. The study aimed to explore the impact of nimbin on cardiac markers, mitochondrial and lysosomal enzyme activities, as well as apoptotic signaling in rats induced with isoproterenol. The subcutaneous injection of isoproterenol (ISO) at a dosage of 85 mg/kg body weight over the last two consecutive days led to notable increased in the activities/levels of the cardiac markers, lysosomal glycohydrolases and cathepsins. Conversely, reductions in the functioning of mitochondrial tricarboxylic acid cycle enzymes and respiratory chain enzymes in ISO-induced rats. In ISO-induced rats, there was an augmentation in the expressions of Bax, caspase-3, caspase-9, and cytochrome c, along with a diminished level of Bcl-2. Administration of nimbin resulted in decreased activities/levels cardiac markers, lysosomal glycohydrolases, cathepsins and increased functioning of mitochondrial tricarboxylic acid cycle enzymes and respiratory chain enzymes. Additionally, decreased expressions of Bax, executioner caspases and cytochrome c, along with heightened expression of Bcl-2, were noted in rats treated with nimbin. This indicates that nimbin possesses cardioprotective properties and mitigates mitochondrial and lysosomal dysfunction in rats induced with ISO.

**Nimbolide** inhibits NLRP3 inflammasome activation via blocking NEK7-NLRP3 interaction and alleviates sepsis-induced lung injury.

Wang X, Li J, Yu B, Gong H, Li Z, Bai Y.Int Immunopharmacol. 2025 Nov 29;168(Pt 2):115954. doi: 10.1016/j.intimp.2025.115954. Online ahead of print.PMID: 41319565

**Background:** Sepsis-associated acute lung injury (ALI) remains a critical clinical challenge with limited therapeutic options. The NLRP3 inflammasome drives pathological inflammation in ALI, yet clinical translation of existing inhibitors is hindered by toxicity. Natural products offer safer alternatives, but their mechanisms in targeting NLRP3 assembly are poorly defined.

**Methods:** We screened a natural compound library for NLRP3 inhibitors using LPS/nigericin-stimulated murine peritoneal macrophages, measuring IL-1β release by ELISA. Mechanistic studies included immunoprecipitation (NEK7-NLRP3/ASC-NLRP3 interactions), ASC oligomerization/speck formation assays, DARTS, CETSA, and molecular docking. In vivo efficacy was evaluated in LPS-induced ALI and endotoxemia mouse models (histopathology, cytokine analysis, immunoblotting).

**Results:** Nimbolide was identified as a potent NLRP3 inhibitor. It dose-dependently suppressed IL-1β secretion and caspase-1/GSDMD cleavage in murine/human (THP-1) macrophages, without affecting AIM2/NLRC4 inflammasomes or TNF-α production. Mechanistically, Nimbolide disrupted NEK7-NLRP3 binding and ASC oligomerization, thereby blocking NLRP3 inflammasome assembly. Further investigations revealed that Nimbolide enhanced the thermal stability of NLRP3 as demonstrated by the cell thermal shift assay (CETSA), conferred protease resistance as evidenced by the drug affinity responsive target stability (DARTS) assay, and exhibited high-affinity binding to NLRP3 with a binding energy of -7.62 kcal/mol through molecular docking studies. These results collectively suggest that Nimbolide can directly bind to NLRP3. In vivo, Nimbolide reduced pulmonary IL-1β levels, suppressed GSDMD cleavage, and attenuated lung injury pathology.

**Conclusion:** Nimbolide is a new natural inhibitor that selectively targets the NLRP3 interface and block NLRP3 inflammasome activation, offering a promising therapeutic strategy for NLRP3-driven inflammatory disorders like sepsis-associated ALI.

Exploring the phytomedicine properties of **azadiradione** against leishmaniasis: in silico and in vitro insights.

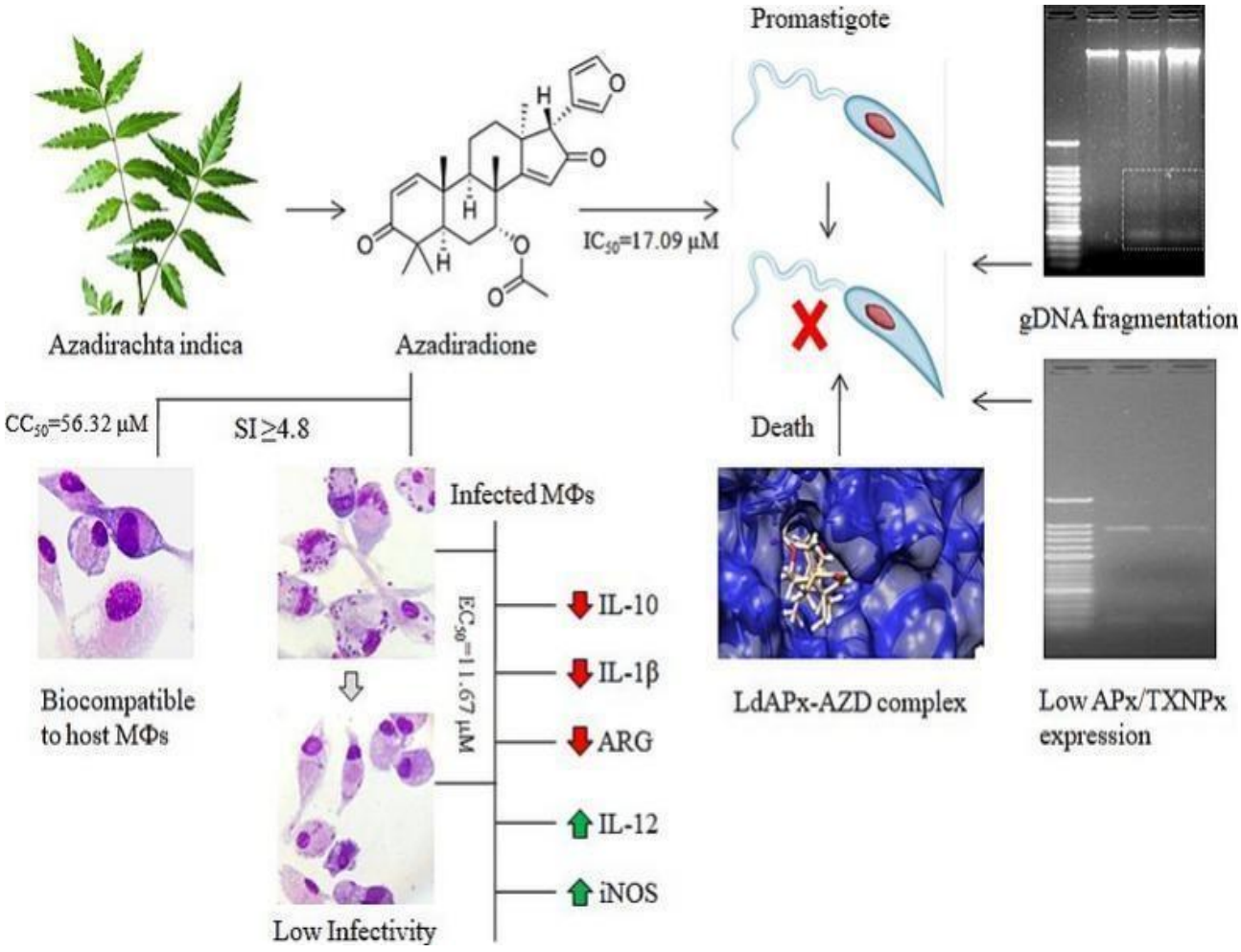
Vijayakumar S, Kumari S, Ranjan R, Kumar A, Kumar V, Vedika S, Pandey K, Singh PN, Alti D.Int Immunopharmacol. 2025 Oct 10;163:115283. doi: 10.1016/j.intimp.2025.115283. Epub 2025 Jul 28.PMID: 40730118

**Background:** Leishmaniasis continues to pose a significant global health challenge, exacerbated by the increasing resistance to current therapeutic agents such as miltefosine and amphotericin B. This growing resistance highlights the urgent need for alternative treatment strategies. In this context, phytomedicine has emerged as a promising avenue for novel antileishmanial therapies. In our previous study, the crude extract derived from neem (Azadirachta indica) leaves exhibited notable antileishmanial activity. Subsequent analysis using LC-MS/MS enabled the identification of bioactive constituents within the

active fraction, including azadiradione (AZD), a drug with potential therapeutic effects unexplored against leishmaniasis.

**Results:** AZD exhibited dose-dependent growth inhibition along with structural disruption and DNA fragmentation in promastigotes with an $IC_{50}$ of 17.09 µM. In silico docking and simulation with AZD identified Leishmania peroxidases (e.g., ascorbate peroxidase and tryparedoxin peroxidase) as probable molecular targets, with subsequent downregulation of their expression confirmed in vitro. The $CC_{50}$ on human macrophages (MΦs) and $EC_{50}$ on intracellular amastigotes were determined as 56.32 µM and 11.67 µM for AZD, respectively. The dose-dependent reduction in MΦs' infectivity demonstrates the drug potential of AZD against the pathogenic stage of Leishmania. However, the selectivity index (SI) of AZD was calculated as 4.83, indicating a moderate Leishmania-specific drug potential of AZD. The decrease in IL-10, IL-1β, and arginase expression and the increase in IL-12 and iNOS expression reinforce the immunoregulatory potential of AZD in favour of the host. Further investigations are required to optimize the dosage and improve the selectivity of AZD before proposing it for the treatment of Leishmania infection.

**Conclusion:** This study demonstrated the novel findings related to the drug potential of AZD with defined Leishmania targets and host protective cytokine response. Studies on animal models may deliver further insights into its therapeutic potential.

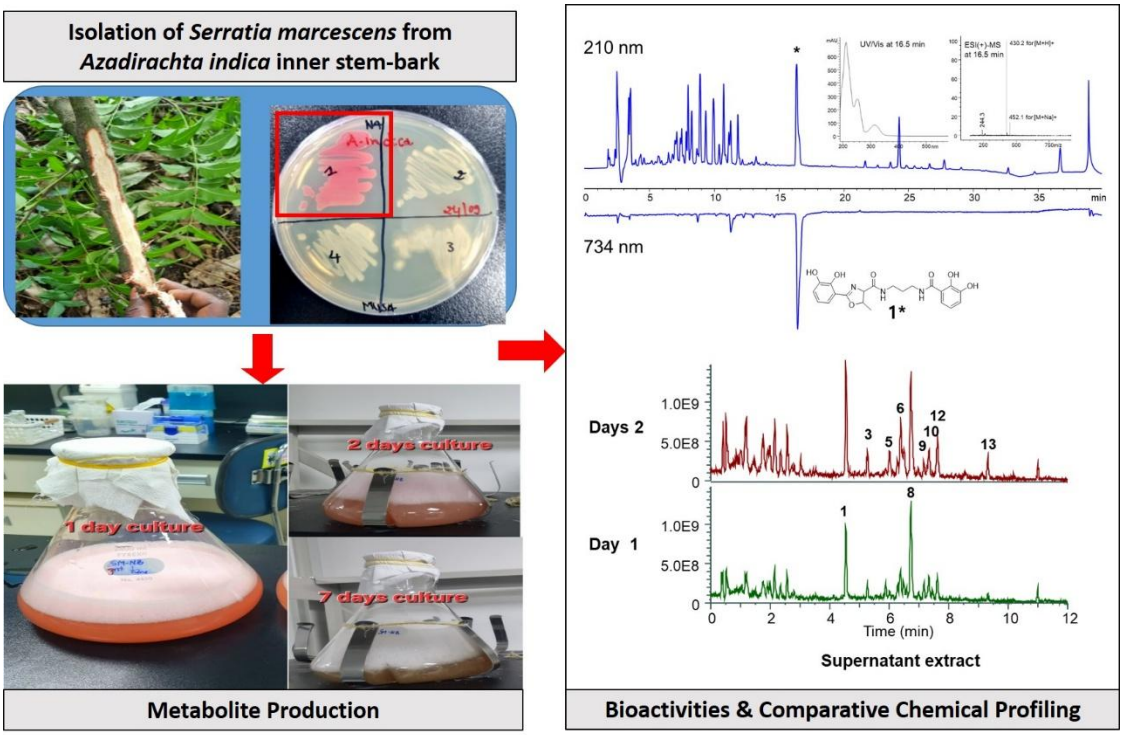


[Chemical Profiling and Antibacterial, Anti-Biofilm, and Antioxidant Activities of Endophytic Serratia marcescens AI-N-1 from **Azadirachta indica**.]

Moussa HH, Sonibare MA, Park JS.

J Microbiol Biotechnol. 2025 Nov 26;35:e2508044. doi: 10.4014/jmb.2508.08044.PMID: 41309395

The rising need for new antibiotics and antioxidants highlights endophytic bacteria as promising sources of bioactive compounds. Medicinal plants such as *Azadirachta indica* harbour diverse endophytes, yet their potential in southwest Nigeria remains largely underexplored. This study investigated the antimicrobial, biofilm inhibitory, and antioxidant activities of bioactive compounds produced by the bacterial endophyte *Serratia marcescens* AI-N-1, isolated from *A. indica*. Crude extracts of *S. marcescens* showed strong antimicrobial activity against *Bacillus subtilis* (79.79% inhibition) and *Salmonella typhi* (77.04% inhibition) at 5 mg/ml. In addition, most extracts also displayed potent biofilm inhibition (>80%) against both pathogens, comparable to the positive control baicalein ($P < 0.05$). Antioxidant assays revealed high radical scavenging activity, with the supernatant extract obtained after 2 days of culture exhibiting the strongest effect (DPPH: 86.61% at 0.1 mg/ml; ABTS: 99.64% at 0.1 mg/ml). Online HPLC-ABTS$^{+}$ analysis identified serranticin as a major contributor to these antioxidant effects. HR-MS/MS profiling further revealed prodigiosin, serratamolides, and serranticin, along with putative novel lipopeptides and other metabolites, as key bioactive compounds. To our knowledge, this is the first report of a Serratia endophyte from *A. indica* in southwest Nigeria with combined antimicrobial, antibiofilm, and antioxidant activities, as well as the discovery of putative new lipopeptides. These findings highlight endophytic bacteria from Nigerian medicinal plants as promising sources of novel antimicrobial and antioxidant agents for pharmaceutical development.



Unlocking the Antioxidant, Enzyme Inhibitory and Acaricidal Potential of **Azadirachta indica** Phytoconstituents Using In Vitro and In Silico Approaches.

Fatima T, Abbas M, Zafar K, Zafar MG, Haider W, Zafar MH, Riaz M, Iqbal M, Mtewa AG.Food Sci Nutr. 2025 Nov 29;13(12):e71204. doi: 10.1002/fsn3.71204. eCollection 2025 Dec.PMID: 41323825

The study evaluated the acaricidal potential of bioactive components of *Azadirachta indica* against scabies mortality using both in vitro and in silico approaches. *Sarcoptes scabiei* were stimulated with *A. indica* at four concentrations (25-100 mg/mL) at different intervals. The study assessed the cytotoxic, neuroactive, and detoxification-modulating potential of *A. indica*, emphasizing their antibacterial, antioxidant, and enzyme-inhibitory potential. LCMS was used for the characterization of phytoconstituents. In silico analysis encompassed target prediction, toxicity assessment, biological activity prediction, protein structure modeling, and gene expression analysis. Molecular docking assesses the binding affinities of bioactive components, and the ExPASy database predicts the physiochemical properties of glutathione transferase. In vitro analysis suggests that *A. indica* has a dose-dependent effect on *S. scabiei* at different time intervals. It highlights the extract's multifaceted bioactivity with strong antioxidant activity ($IC_{50}$ = 3.15 mg/mL) and potent antibacterial effects at higher concentrations. It exhibited mild to moderate hemolytic and significant AChE activity. Furthermore, it also showed GST inhibition, suggesting possible disruption of toxins. The binding affinity of 7-desacetyl-7-benzoylazadiradione showed significant inhibitory interaction with glutathione transferase (-12.324 kcal/mol). This phytoconstituent exhibited a high hyper-geometric *p* value; the total interactions between transcription factors, kinases, and intermediate proteins are observed. *A. indica* serves as a natural substitute for managing mite infestations and offering insights into mechanisms by which its phytochemicals show inhibitory effects.