Neem Research Newsletter

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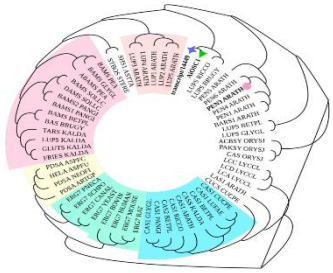

WORLD NEEM ORGANISATION (WNO)

From

The Editor's Desk……

In this issue of the newsletter we record research findings in agriculture, fisheries, synthetic chemistry, sustainable environment, human and animal health. Nanoformulation of neem oil was shown to exert insecticidal effect against red palm weevil larvae. Azadirachtin was demonstrated to be lethal to *Sitophilus zeamais* that attacks corn with toxicity at the larval, pupal, and adult stages. Green synthesis of neem extract and neem oil-based Azadirachtin nanopesticides was accomplished using cellulose acetate (CA) as a carrier polymer, focusing on their efficacy against fall amyworm (FAW). The nanopesticide formulations were found to provide a promising, eco-friendly alternative for sustainable FAW control and management with enhanced efficacy and safety. The leaf traits exhibited by neem was found to confer competitive advantage and invasiveness compared to native species of northeastern Brazil raising environmental concerns regarding natural ecosystems. Experimental evidence indicated the potential of azadirachtin in controlling a wide range of ectoparasites in ornamental fishes.

Stereoselective total synthesis of nimbolide was achieved in a 11-step sequence from α-methyl-(*R*)-carvone. Treatment of *Oreochromis niloticus* fillets with neem oil nanoemulsions was demonstrated to improve color, flavor, juiciness, aroma, and overall quality highlighting the potential of neem as a suitable green preservative for fish and possibly other meat-based products. A review article compiled the diverse applications of neem gum in sustainable technologies and emerging fields like self-healing materials and smart polymers. The potential of neem oil biodiesel blends enhanced with alumina nanoparticles was found to achieve a sustainable balance between improved engine performance and reduced emissions.

Molecular modelling approaches suggest that margolonone and isomargolonone from neem have the potential to inhibit dengue virus protease. A chitosan-based nanomembrane incorporating nanovesicles from Aloe barbadensis, Azadirachta indica, and Zingiber officinale was shown to accelerate diabetic wound healing. Neem fruit extract exhibited significant antibacterial, antifungal, anti-inflammatory, muscle-relaxant and sleep-enhancing effects. Neem leaf paste was reported to be a cost-effective and natural alternative for managing dandruff. Copper-doped manganese oxide nanozymes from aqueous extracts of neem demonstrated antibacterial and anticancer activities. The neem limonoid nimbolide was found to exert anticancer effects against carcinogen induced stomach cancer in rats. In veterinary practice, neem oil emulsion was reported to be effective for controlling tick infestations and reducing tick-borne diseases in cattle. Further, ethanolic neem extract exhibited antiviral activity against small ruminant lentiviruses.

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Preparation, characterization and insecticidal activity of nanoformulation of some essential oils against red palm weevil (RPW), *Rhynchophorus ferrugineus*.

Adel MM, Gendi YMO, Abd El-Latif AO.Nat Prod Res. 2025 Apr 22:1-19. doi: 10.1080/14786419.2025.2495163. Online ahead of print.PMID: 40261283

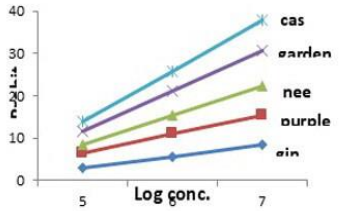
The insecticidal activity of the bulk oils and its nanoformulation was determined against the 11 days old larvae of *Rhynchophorus ferrugineus* using the dipping method techniques. All the tested oils showed insecticidal activity against RPW larvae. The highest toxicity was obtained in the case of garden cress oils with LC_{50} value of (1.27%) followed by ginger oil (1.28%), Neem oil (1.40%), and purple nutsedge oil (1.58%). However, the lowest toxicity was obtained in the case of castor oil (1.75%). A lower larval mortality percentage was observed in the nanoformulation compared to the bulk oils even when high concentrations of nanoformulation were used. Feeding bioassay with no choice test techniques was evaluated too the results indicate significantly reduced nutritional indices (RGR, ECI, FDI, and GII) of the treated *R. ferrugineus* concluded that tested oils and its nanoformulations may be useful for reducing the population of *R. ferrugineus*.

Preparation, Characterization and Insecticidal activity of Nano formulation of some essential oils against Red Palm weevil (RPW), *Rhynchophorus ferrugineus*

Red Palm weevil (RPW), *Rhynchophorus ferrugineus*

Common name	Scientific name	Family
Ginger oil	Zingiber Officinale	Zingiberaceae
purple nutsedge	Cyperus rotundus	Cyperaceae
Neem	Azadirachta indica	Meliaceae
Garden Cress	Lepidium sativum	Brassicaceae
Castor	Ricinus communis	Euphorbiaceae

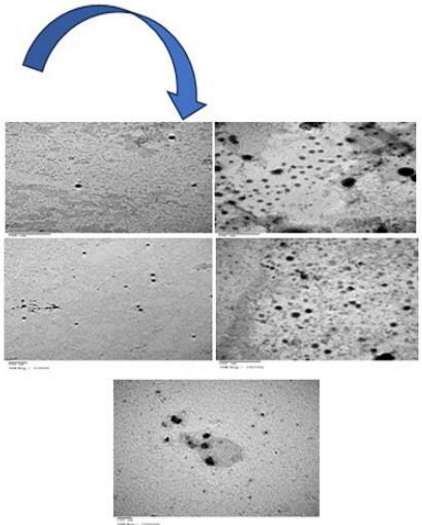
essential oils



Log concentration vs probit mortality regression lines of 11-days old palm weevil larvae treated with plant bulk oils

Nano Oils	Concentration	No. of dead larvae							Total
		D1	D2	D3	D4	D5	D6	D7	
Control		0	0	0	0	0	0	0	0
Ginger	5%	2	0	0	0	1	0	0	3
	10%	3	0	0	0	1	0	0	4
	20%	0	0	2	2	0	0	0	4
Purple nutsedge	5%	0	0	0	0	0	0	0	0
	10%	0	0	0	0	0	0	0	0
	20%	0	0	0	0	0	0	0	0
Neem	5%	0	0	0	0	0	0	0	0
	10%	0	0	0	0	0	0	0	0
	20%	2	0	0	0	0	1	0	3
Garden cress	5%	0	0	0	0	0	0	0	0
	10%	0	0	0	0	0	0	0	0
	20%	0	2	0	0	0	1	0	3
Castor	5%	0	0	0	0	0	0	0	0
	10%	0	0	0	0	0	0	0	0
	20%	6	0	0	0	0	1	0	7

Effect of nano oil on the number of dead larvae of 11 days old larvae of red palm weevil

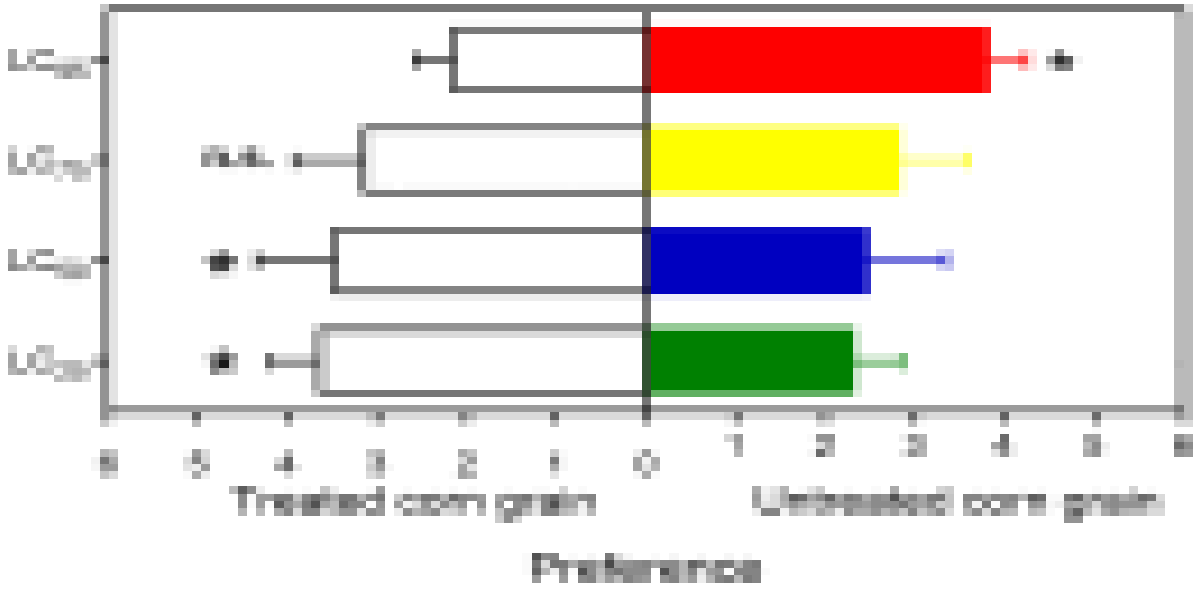


TEM morphology of the tested nano-emulsions prepared from each essential oil

Azadirachtin-Mediated Responses in the Maize Weevil, Sitophilus zeamais (Coleoptera: Curculionidae).

Quintero H, Quintero Cortes J, Plata-Rueda A, Martínez LC.Insects. 2025 Mar 12;16(3):294. doi: 10.3390/insects16030294.PMID: 40266806

Corn is one of the world's most economically important cereal crops and can be attacked by *Sitophilus zeamais*. The control of *S. zeamais* is mostly based on synthetic insecticides; however, populations of this insect have developed resistance to various chemical compounds. New rational insecticides that prevent the development of resistant populations need to be continuously evaluated. This research aimed to assess the effects mediated by azadirachtin on *S. zeamais* populations in terms of mortality, survival, food preference, and repellency. Azadirachtin is toxic to *S. zeamais* at the larval (LC_{50} = 3.36 ppm), pupal (LC_{50} = 23.0 ppm), and adult (LC_{50} = 37.7 ppm) stages. At all stages of insect development, the survival rate was 99.9% in insects not treated with azadirachtin, decreasing to 29.9%, 44.9%, and 68.5% in larvae, pupae, and adults treated with the LC_{50} of the bioinsecticide, respectively. The preference for untreated corn grains was higher with the LC_{25} and LC_{50} of azadirachtin, while the LC_{95} (209 ppm) repelled adults. Azadirachtin causes lethality in *S. zeamais*, compromising its survival and reducing the feeding preference on grains protected with repellent activity at high concentrations. Therefore, the use of this bioinsecticide may offer an alternative to control *S. zeamais* in the field and post-harvest.



Green synthesis of **neem** extract and **neem** oil-based azadirachtin nanopesticides for fall Armyworm control and management.

Oyege I, Switz A, Oquendo L, Prasad A, Bhaskar MSB.Ecotoxicol Environ Saf. 2025 Apr 10;295:118168. doi: 10.1016/j.ecoenv.2025.118168. Online ahead of print.PMID: 40215685

The global spread of Fall Armyworm (FAW, Spodoptera frugiperda) has posed significant challenges to crop productivity and food security, with current pest management relying heavily on synthetic pesticides. This study explores the green synthesis of neem extract

and neem oil-based Azadirachtin nanopesticides using cellulose acetate (CA) as a carrier polymer, focusing on their efficacy against FAW. The objective was to assess whether CA-NEP (neem extract nanopesticides) and CA-NOL (neem oil nanopesticide) formulations were effective at FAW control with minimal ecological impact. The nanopesticides were synthesized by electrospinning at concentrations of 5 %, 10 %, 20 %, 33 %, and 50 % (w/w) and characterized using Scanning Electron Microscopy and Fourier Transform Infrared spectroscopy. Azadirachtin content was quantified using Liquid Chromatography-Mass Spectroscopy. CA-NEP and CA-NOL followed first-order, and Korsmeyer-Peppas release kinetics, respectively. Feeding bioassays showed high FAW mortality rates, with 20 %-50 % CA-NEP achieving greater than 40 % mortality in less than 3 days and 50 % CA-NEP reaching 100 % mortality by day five. The mortality rates of FAW due to feeding on CA-NOL-treated corn leaves reached 40 % after 4 and 6 days, respectively, for 50 % and 33 % CA-NOL. Placing nanopesticide fibers next to corn seeds during planting significantly reduced FAW leaf damage. The lethal dose 50 (LD50) analyses showed that 13 % CA-NEP is the optimal concentration for FAW control. Environmental safety assessments on earthworms showed no acute or chronic toxicity, indicating that the nanopesticides suit ecologically sensitive areas. Therefore, these nanopesticide formulations provide a promising, eco-friendly alternative for sustainable FAW control and management with enhanced efficacy and safety.

Leaf trait divergence between **Azadirachta indica** (exotic) and native species of the northern Brazilian coast.

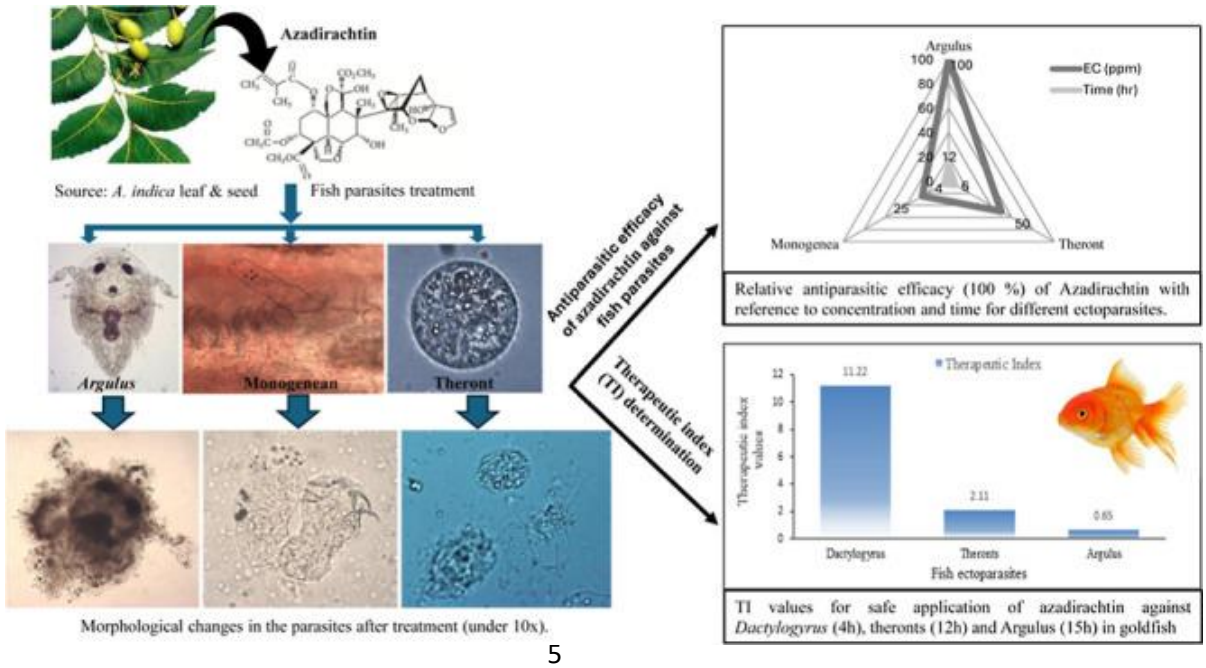
Souza ML, Andrade FG, Fonteles MRV, Costa FWR, Saporetti Junior AW, Silva IHCVD, Maia RC.An Acad Bras Cienc. 2025 Apr 11;97(2):e20240960. doi: 10.1590/0001-3765202520240960. eCollection 2025.PMID: 40243807

The introduction of exotic plants can pose ecological threats as they may become invasive. We investigated leaf traits potentially linked to competitive advantage and invasiveness in Azadirachta indica, a widely used exotic tree in northeastern Brazil's urban forestry, compared to native species Ouratea fieldingiana and Myrcia multiflora. We tested the limiting similarity hypothesis, evaluating how leaf characteristics influence the ecological responses of these species and A. indica's potential invasiveness. A. indica exhibited larger leaf area, specific leaf area (SLA), and leaf area ratio (LAR) compared to native species, but lower specific petiole length (SPL) and specific internode length (SIL). Additionally, A. indica displayed greater phenotypic variation in these traits. The larger leaf area, SLA, and LAR suggest a strategy in A. indica favoring rapid carbon gain through increased growth. The higher phenotypic variation observed may facilitate adaptation to new habitats, potentially enhancing its competitive ability and invasiveness. These findings highlight distinct functional strategies between exotic and native species, raising concerns regarding the potential invasiveness of A. indica in northeastern Brazil's natural ecosystems.

[Biopesticidal Efficacy and Safety of Azadirachtin: Broad-Spectrum Effects on Ectoparasites Infesting Goldfish, *Carassius auratus* (Linn. 1758).]

Sharma A, Kumar S, Raman RP, Kumar K, Kumari P, Brahmchari RK, Pawar NA, Dalvi RS, Jadhao SB.ACS Omega. 2025 Mar 25;10(13):13269-13277. doi: 10.1021/acsomega.4c10920. eCollection 2025 Apr 8.PMID: 40224446

Ectoparasites are a serious concern for the ornamental fish industry, causing severe pathological and behavioral changes that diminish the aesthetic value of fish and adversely affect trade. Recently, phytotherapy, application of plant extracts or their active biomolecules, has gained attention for the control and treatment of various diseases of humans and animals, including fish. The present study evaluated the broad-spectrum antiparasitic activity of azadirachtin, a neem-based bioactive molecule, under *in vitro* condition against adult protozoan (*Ichthyophthirius multifiliis*) and adult metazoans ectoparasites, including *Dactylogyrus* sp. and *Argulus* sp., as well as juvenile stages and eggs of the latter, for its prevalence in infesting goldfish (*Carassius auratus*). Azadirachtin was tested at concentrations of 9.52-47.61 mg L^{-1} against *I. multifiliis* theronts; 1-30 mg L^{-1} for *Dactylogyrus* sp.; and 25-125 mg L^{-1} for *Argulus* sp. The median effective concentration (EC_{50}), antiparasitic efficacy (AE), relative antiparasitic efficacy, and therapeutic index (TI) were estimated for azadirachtin. EC_{50} of azadirachtin against different parasites was estimated to be in the range of 6.08 to 61.29 mg L^{-1}. Relative antiparasitic efficacies were found to be 25 mg L^{-1} for 4 h, 50 mg L^{-1} for 6 h, and 100 mg L^{-1} for 12 h against *Dactylogyrus* sp., *I. multifiliis* theronts, and *Argulus* sp., respectively. *Argulus* egg hatching was inhibited above 100 mg L^{-1}, with eggs at 125-175 mg L^{-1} becoming unclear by day 14. The 15 h median lethal concentration (LC_{50}) of azadirachtin (EC = 21.5%) against *C. auratus* was 20.48 mg L^{-1}. The TI indicates a safe dose in *C. auratus* against *Dactylogyrus* sp. (11.22 for 4 h) and *I. multifiliis* theronts (2.11 for 12 h) while showing a critical value for *Argulus* (0.65 for 15 h). The present findings provide evidence for the broad-spectrum antiparasitic activity of azadirachtin against protozoan and metazoan ectoparasites, suggesting its potential as an agent for controlling a wide range of ectoparasites in ornamental fishes.

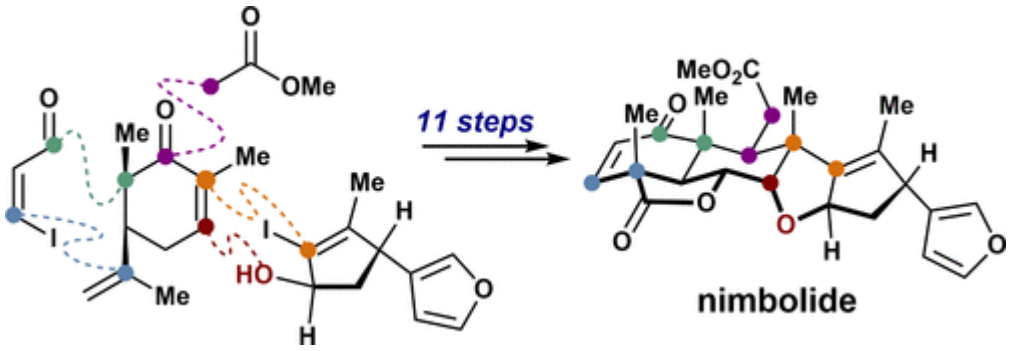


Neem Phytochemicals

Stereoselective Total Synthesis of **Nimbolide**.

Ryffel DB, Ryffel PC, Martinelli M, Pillai VR, Sarlah D.J Am Chem Soc. 2025 Apr 21. doi: 10.1021/jacs.5c04899. Online ahead of print.PMID: 40258594

A stereoselective total synthesis of nimbolide has been achieved in a convergent, 11-step sequence from α-methyl-(*R*)-carvone. The strategy relied on a stereoselective palladium-catalyzed borylative Heck cyclization where the A-ring of the nimbolide core was constructed while simultaneously performing oxidation at C(28). Selective manipulations delivered a fully decorated decalin moiety on large scale. Then, a stereoretentive etherification reaction brought together two fragments and forged the critical C-O bond with high selectivity. Finally, a regioselective radical cyclization and late-stage lactonization completed the total synthesis of nimbolide.



Neem in Food Industry

Neem Oil (Azadirachta indica L.) Response Surface Methodology (RSM)-Optimized Nanoemulsions for Sensory Quality Preservation of Oreochromis niloticus Fillets.
Kazam J, Iqbal KJ, Shafi A, Majeed U, Lackner M.Biology (Basel). 2025 Apr 10;14(4):400. doi: 10.3390/biology14040400.PMID: 40282265

Neem oil nanoemulsions (NO NEs) have gained attention as natural antibacterial agents due to toxicity concerns surrounding synthetic preservatives. This study aimed to prepare a response surface methodology (RSM)-optimized NO NE < 200 nm to achieve a stable dip solution to maintain the sensory quality of *Oreochromis niloticus* fillets. The NO NE achieved a stable formulation with a particle size of 160.2 ± 0.04 nm on average. The polydispersity index (PDI) was 0.1 ± 0.05, and the zeta potential was found to be 18.2 ± 0.09 mV. Gas chromatography confirmed the presence of nimbiol, nimbandiol, 6-deacetyl nimbinene, and azadirachtin in NO after ultrasonic homogenization for 10 min (alternating

between 30 s rest and 30 s work time). The NE had a spherical shape with a smooth surface, as was evident from transmission electron microscopy (TEM). Furthermore, NO:PM (neem oil-potassium metabisulphite) had an MIC (minimum inhibitory concentration) value of 150 ppm, compared to 210 ppm for the NO NE alone, against *Staphylococcus aureus*. Time-kill dynamics revealed the more effective control of *S. aureus* until 72 h with NO:PM. Moreover, DNA and protein leakage also increased from 0.145 ± 0.001 to 0.769 ± 0.002 OD (optical density) and from 0.142 ± 0.002 to 0.740 ± 0.001 OD, respectively, with the co-formulation of NO:PM. Conclusively, NO:PM inhibited *S. aureus* at a lower dose compared to the NO NE alone. Time-kill dynamics revealed complete inhibition of *S. aureus* in vitro for a period of 72 h. On the other hand, a proximate analysis of *O. niloticus* fillets showed no alteration in pH, no protein loss, and juiciness/moisture retention during 30 days of storage (4 °C). Sensory panelists reported that *O. niloticus* fillets treated with NE NO had improved color, flavor, juiciness, aroma, and overall quality. These results show that NE NO is a suitable green preservative for fish and possibly other meat-based products.

Neem for Sustainable Environment & Green Synthesis

Neem gum and its derivatives as potential polymeric scaffold for diverse applications: a review.

Ghosh S, Bal T.Int J Biol Macromol. 2025 Apr 9:143012. doi: 10.1016/j.ijbiomac.2025.143012. Online ahead of print.PMID: 40216102

Naturally occurring polymers, particularly polysaccharides, are gaining significant attention for their eco-friendly, non-toxic nature and abundant availability. Neem Gum (NEG), a natural exudate from the neem tree (Azadirachta indica), is secreted as a defense mechanism to protect against microbial invasion and physical damage. Unlike common polysaccharides, NEG exhibits a distinct composition rich in bioactive constituents, including heteropolysaccharides and secondary metabolites, contributing to its diverse functional and therapeutic potential. These unique characteristics make NEG a promising biopolymer for applications in pharmaceuticals, food, cosmetics, and environmental industries, where it serves as a binding, emulsifying, gelling, and stabilizing agent. Recent advancements have focused on developing NEG composites and derivatives with enhanced properties and broader applications. Structural modifications like grafting and

carboxymethylation have improved its utility in drug delivery, wound healing, and biodegradable materials. Modified NEG derivatives exhibit superior antimicrobial, anti-inflammatory, and antioxidant effects, expanding their biomedical potential in tissue engineering and controlled drug release. NEG-based hydrogels and films show promise in eco-friendly packaging and self-healing biomaterials. This review compiles NEG's diverse applications, highlighting its role in sustainable technologies and emerging fields like self-healing materials and smart polymers. It addresses challenges in scaling production, regulatory compliance, and technical constraints.

Prediction of performance and emission features of diesel engine using alumina nanoparticles with **neem** oil biodiesel based on advanced ML algorithms.

Aswathanrayan MS, Santhosh N, Venkataramana SH, Kumar KS, Kamangar S, Arabi AIA, Algburi S, Al-Sareji OJ, Bhowmik A.Sci Rep. 2025 Apr 12;15(1):12683. doi: 10.1038/s41598-025-97092-2.PMID: 40221480

The growing need for sustainable energy sources and stricter environmental regulations necessitate the development of alternative fuels with lower emissions and improved performance. This study addresses these challenges by optimizing the performance and emission characteristics of a single-cylinder diesel engine powered by neem oil biodiesel blends enhanced with alumina nanoparticlesusing the powerful desirability-based optimization. Neem oil, a non-edible feedstock, was selected to avoid competition with food resources, while alumina nanoparticles were utilized for their catalytic properties to enhance combustion efficiency. The process involved experimental evaluation of biodiesel blends (B10, B20, and B30) combined with alumina nanoparticles at concentrations of 100 ppm, 150 ppm, and 200 ppm using a design of experiments approach. With the engine running at maximum load of 100% and an aluminum oxide concentration of 100 parts per million, the optimal fuel mix comprises of 89.85% diesel and 30% biodiesel. The lowest brake-specific fuel consumption of 0.45 kg per kilowatt-hour that the optimization produced points to effective fuel use. With a little variance of 3.33%, the brake thermal efficiency was maximized at 38.18%, quite near to the validation result of 37.89%. The alumina nanoparticles enhanced combustion through improved fuel atomization and oxidation due to their high surface area and catalytic effects. To further validate the effectiveness of RSM, the results are compared with the performance of several advance machine learning algorithms, including linear regression, decision tree, and random forest. The random forest model demonstrated the highest predictive accuracy for performance (test R^2 = 0.9620, Test MAPE = 3.6795%), making it the most reliable statistical approach for predicting BSFC compared to linear regression and decision Tree models. The random forest model also outperformed other approaches in predicting emissions, achieving the highest accuracy with a test R^2 of 0.9826 and the lowest test MAPE of 9.3067%.This integrated experimental and predictive approach provided a robust framework for optimizing biodiesel formulations, identifying the ideal combination of biodiesel blend ratio and nanoparticle concentration. The findings highlight the potential of neem oil biodiesel blends enhanced with alumina nanoparticles to achieve a sustainable balance between improved engine performance and reduced emissions in CI engines.

Inhibition potential of margolonone and isomargolonone against the dengue virus protease using molecular modeling approaches.

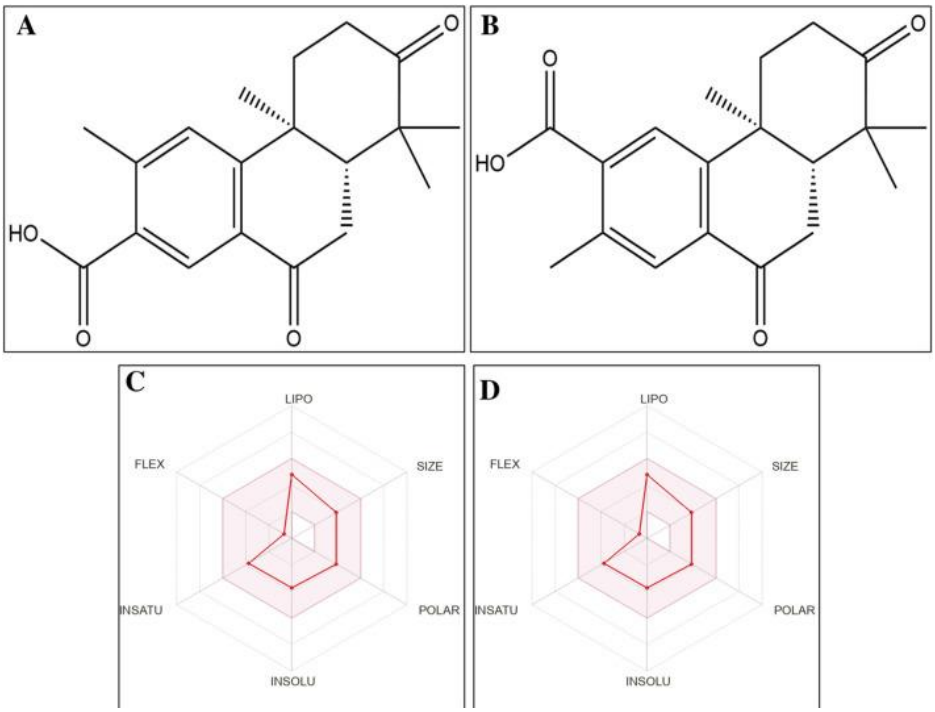
Choudhir G, Iram F, Israil, Shahid M, Shamsi A, Hassan MI, Islam A.Front Bioinform. 2025 Mar 26;5:1517115. doi: 10.3389/fbinf.2025.1517115. eCollection 2025.PMID: 40206633

Background: Dengue is a mosquito-borne viral disease with no cure. Inhibiting key enzymes vital in replication could manage the dengue virus infection. This study investigated the potential of margolonone and isomargolonone from *Azadirachta indica* to inhibit dengue virus replication.

Methods: The 3D structure of margolonone and isomargolonone were obtained from the PubChem database. The drug-likeness properties of these molecules were performed using a Swiss-ADME server. The molecular docking and molecular dynamics simulation assessed binding affinity and interactions.

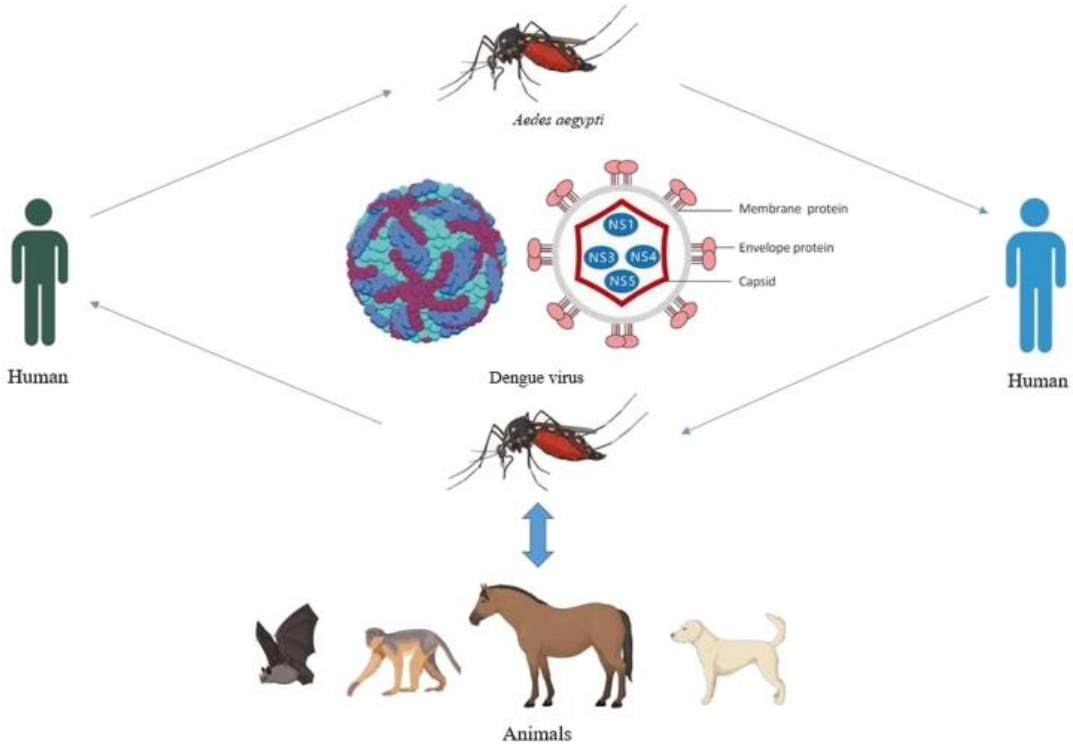
Results: The drug-likeness of parameters showed that Margolonone and isoMargolonone showed zero violation of Lipinski rules. Docking simulations showed that both compounds bind to the active site of a critical enzyme (NS3 protease) essential for viral replication. Molecular dynamics simulations suggested that isomargolonone may bind more stably to NS3 than margolonone. Additionally, MMPBSA analysis showed that Margolonone does not show favorable binding energy.

Conclusion: These findings warrant further investigation of isomargolonone as a potential anti-dengue drug. Further *in-vitro* and *in-vivo* evaluations need to be done before accepting it as drug molecules.



[Recent advances in the control of dengue fever using herbal and synthetic drugs.](#)
Hasani SJ, Sgroi G, Esmaeilnejad B, Nofouzi K, Mahmoudi SS, Shams N, Samiei A, Khademi P.Heliyon. 2025 Jan 18;11(3):e41939. doi: 10.1016/j.heliyon.2025.e41939. eCollection 2025 Feb 15.PMID: 40196797

Dengue virus represents a global public health threat, being prevalent in tropical and subtropical regions, with an increasing geographical distribution and rising incidence worldwide. This mosquito-borne viral agent causes a wide range of clinical manifestations, from mild febrile illness to severe cases and potentially fatal outcomes due to hemorrhage and shock syndrome. The etiological agent, dengue virus (DENV), has four distinct serotypes, each capable of inducing severe clinical outcomes. The current therapeutic landscape remains limited, with management strategies mainly focused on supportive cares. However, recent advances in pharmaceutical research have yielded promising developments in anti-dengue drugs. Extensive investigations have been conducted on various synthetic compounds, including JNJ-1802, 1,4-pyran naphthoquinones, and arylnaphthalene lignan derivatives. Additionally, natural compounds derived from medicinal plants such as *Hippophae rhamnoides*, *Azadirachta indica*, and *Cymbopogon citratus* have demonstrated potential antiviral properties in both *in vitro* and *in vivo* studies, based on inhibition of DENV replication. However, none of these compounds are to date approved by the U.S. Food and Drug Administration (FDA). Although many vaccines have been recognized as candidates in various stages of clinical trials, only a limited number of these have demonstrated a protective efficacy against the infection. This aspect underscores the need for both highly effective immunization strategies and therapeutic interventions, whether derived from botanical sources or through synthetic manufacturing, that exhibit low adverse effects. This review examines innovative approaches to DENV prevention and treatment, encompassing both phytochemical and synthetic therapeutic strategies.



Accelerated diabetic wound healing using a chitosan-based nanomembrane incorporating nanovesicles from Aloe barbadensis, **Azadirachta indica**, and Zingiber officinale.
Miya MB, Ashutosh A, Maulishree M, Dey D, Pathak V, Khare E, Kalani K, Chaturvedi P, Singh V, Chaturvedi P, Kalani A.Int J Biol Macromol. 2025 Apr 14:143169. doi: 10.1016/j.ijbiomac.2025.143169. Online ahead of print.PMID: 40239792

Diabetic wounds pose a substantial clinical challenge due to delayed healing, persistent inflammation, and susceptibility to infections. This study investigates the therapeutic efficacy of a chitosan-polyvinyl alcohol nanomembrane (OXY-NM^{Aloe}) plant-derived extracellular vesicles enriched with extracellular vesicles derived from Aloe barbadensis, Azadirachta indica, and Zingiber officinale. Chitosan, a natural biological macromolecule, forms the nanomembrane's matrix, contributing to its flexibility, porosity, and structural integrity, essential for maintaining optimal wound hydration and supporting tissue regeneration. In in vivo studies on streptozotocin-induced diabetic rats, OXY-NM^{Aloe} significantly accelerated wound closure by approximately 23 % compared to just 7 % in the control-treated group, even after one day. This effect was achieved by modulating pro-inflammatory cytokines, activating collagen synthesis, and restoring mitochondrial function. The membrane also inhibited matrix metalloproteinase overexpression, reducing excessive extracellular matrix degradation by ~40 % and promoting tissue regeneration. Furthermore, OXY-NM^{Aloe} demonstrated potent antimicrobial activity against Staphylococcus aureus and Pseudomonas aeruginosa, decreasing microbial colonization and fostering a favorable healing environment. By integrating the structural properties of chitosan with the bioactivity of plant-derived extracellular vesicles, the nanomembrane offers a multifunctional therapeutic platform for accelerating tissue repair and addressing key challenges in diabetic wound management.

Pharmacological insights into **Azadirachta indica** fruit: GC-MS Profiling and evaluation of key bioactivities on experimental animals.
Razzak M, Riaz A, Rajput MA, Wahid S, Alqahtani A, Saeed Khan S, Nawaz M, Ahmed A.Pak J Pharm Sci. 2025 Jan-Feb;38(1):139-150.PMID: 40188472

Azadirachta indica, fruit with significant therapeutic potential, was evaluated using a multidimensional approach to systematically evaluate its pharmacological spectrum covering antimicrobial, antifungal, anti-inflammatory, analgesic, muscle-relaxant and sleep-inducing effects using in vitro and in vivo models. The study found that fruit extract, when administered at different doses, showed significant antibacterial effects against Gram-positive and Gram-negative bacteria along with a highly significant antifungal effect against Aspergillus niger that might be due to identified azol compounds. Azadirachta indica extract showed significant anti-inflammatory effects at doses of 200 and 400mg/Kg, reducing paw oedema volume and exhibiting analgesic and muscle relaxant activity. Unique findings included significant muscle relaxation and enhanced locomotor activity observed specifically at 400mg/Kg on the 7th and 14th days. Azadirachta indica showed significantly increased sleep duration and reduced sleep onset time in Na-thiopental-induced sleep tests at doses of 200 and 400mg/Kg. Through GC-MS analysis, bioactive compounds, including 2,3-propanetriol, 7-methoxy-1,3,4,5-tetrahydrobenzo[b]azepin-2-

one, piperazine and 4-amino-4,5-dihydro-1H-1,2,4-triazol-5-one, were identified, which likely contribute to the observed pharmacological activities. This study first reports Azadirachta indica's muscle-relaxant and sleep-enhancing effects, expanding its known therapeutic potential.

Effect of **Neem** Leaf Paste Application on Dandruff.

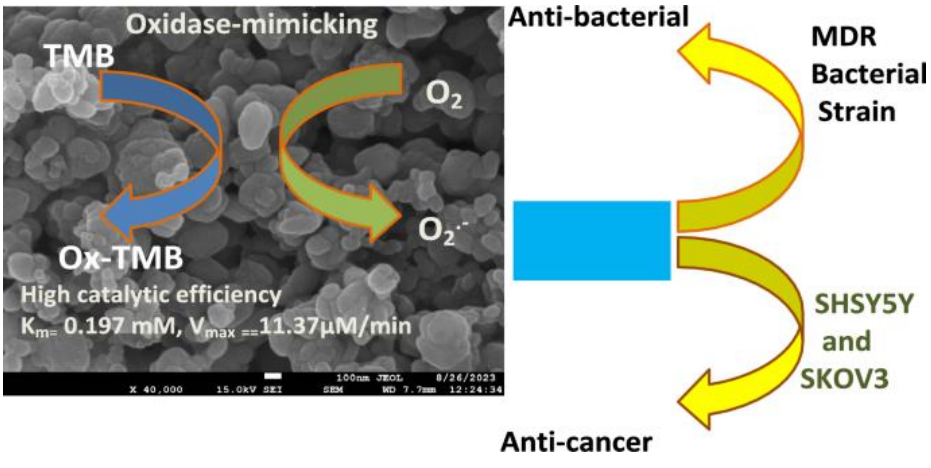
Dani PB, Ghorpade VK.Cureus. 2025 Mar 16;17(3):e80685. doi: 10.7759/cureus.80685. eCollection 2025 Mar.PMID: 40242687

Background: Dandruff is a widespread scalp issue that affects many people worldwide, often causing itching and discomfort. It is linked to the presence of certain microorganisms on the scalp, especially *Malassezia* yeast, which interacts with skin cells to trigger dandruff. This condition can lead patients to experience health concerns and social or emotional distress. Common treatments include antifungal shampoos. Neem leaves have been selected for their natural ability to fight germs, reduce inflammation, and support immune health. They contain beneficial compounds that help treat infections, aid healing, and have long been used in traditional medicine as a natural remedy. This study aims to evaluate the effectiveness of neem leaf paste in treating scalp dandruff among female students. **Materials and methods:** A quasi-experimental pre-test post-test control group study was conducted on female students aged 18-24 with minimal, moderate, and severe dandruff levels. The modified Van Abbe's scale was used to assess the dandruff level. A total of 100 female students were selected using non-probability purposive sampling with no history of allergy to neem leaf formulations. The primary objective was to reduce the dandruff score. The dandruff levels were assessed before and after the application of neem leaf paste at baseline, Week 1, and Week 2. Statistical analysis was performed using frequency and percentage for demographic variables, and a t-test was used to compare dandruff levels between the control and experimental groups. A p-value of 0.05 was considered statistically significant. **Results:** The study included 50 female students in the experimental group and 50 in the control group. Before applying neem leaf paste, 66% (n=33) in the experimental group and 60% (n=30) in the control group had a moderate level of dandruff, while 10% (n=5) and 14% (n=7) in the respective groups had severe dandruff. After the intervention, 44% (n=22) in the experimental group had no dandruff, compared to just 4% (n=2) in the control group. Additionally, 42% (n=21) in the experimental group had a minimal level of dandruff, whereas 28% (14 participants) in the control group had the same. Only 14% (n=7) in the experimental group still had moderate dandruff, compared to 60% (n=30) in the control group. The control group also had 8% (n=4) with severe dandruff, while none remained at this level in the experimental group. After one week, the mean dandruff score significantly dropped to 0.7 in the experimental group, compared to 1.72 in the control group (p-value = 0.00001), indicating a statistically significant reduction in dandruff severity due to neem leaf paste application. **Conclusion:** The application of neem leaf paste was effective in managing dandruff among the participants. Neem leaf paste, known for its antimicrobial and anti-inflammatory properties, offers a cost-effective and natural alternative for managing dandruff. Its effectiveness in reducing dandruff levels among study participants highlights its potential as a safe and accessible treatment option.

[Phyto-assisted eco-benevolent synthesis of oxidase-mimic Cu-Mn_3O_4 as an antibacterial and antiproliferative agent.]

Shome A, Ali S, Roy D, Dey S, Sinha S, Barman P, Kumar A, Chakroborty R, Haydar MS, Roy S, Ghosh S, Roy MN.Bioprocess Biosyst Eng. 2025 Apr 3. doi: 10.1007/s00449-025-03149-x. Online ahead of print.PMID: 40180623

In recent years, the marked augment of antibiotic resistance hampered the development of antibacterial agent. Nanozymes by their in situ ROS production capability oxidize cellular substances of bacterial cell and eliminate MDR bacteria. Therefore, synthesis of effective nanozymes from green precursors is rarely reported, so the prime objective of this study was to synthesize Cu-Mn_3O_4 nanozymes from aqueous extracts of medicinal plant Azadirachta indica via co-precipitation approach and to endorse their biomedical applications. The synthesized materials were characterized by X-ray diffraction (XRD), Fourier Transform Infrared spectrometer (FTIR), Scanning Electron Images (SEM), and Field-Emission Scanning Electron Microscopy (FESEM) images. X-ray Diffraction (XRD) patterns revealed the formation of hausmannite Mn_3O_4 crystal system. Fourier Transform Infrared spectrometer (FTIR) spectra revealed functional groups on the surface nanoparticles for their stabilization. Energy-Dispersive X-ray spectroscopy (EDAX) profile confirmed the existence of desired elements in the synthesized nanozymes. B1 mimics oxidase enzyme most effectively with K_m = 0.175 mM and V_{max} = 10.34 µM/min. The low K_m and high V_{max} indicates the strong binding affinity and high catalytic activity. From the agar diffusion antibacterial assay, it can be concluded that B3 is the most potent antibacterial agent specifically against Gram-positive bacteria Bacillus subtilis with inhibition zone of 27 mm at 250 µg/mL. Their cytotoxic activities on neuroblastoma (SHSY5) cell line were investigated for the first time. The data revealed that synthesized nanooctahedrons possess a significant cytotoxicity against cancer cell lines SHSY5Y (IC_{50} = 137.47 ± 14.11 µg/mL) and SKOV3 (IC_{50} = 72.72 ± 9.33 µg/mL). Overall, with increasing Cu amount, the percentage growth inhibition of Mn_3O_4 crystal system enhanced. The improved antibacterial activity and cytotoxicity is due to synergy between metal and phytochemicals. Radical scavenging activity of synthesized nanozymes is comparatively lower than their green source and the comparatively lower IC_{50} values of B1, 234.12 ± 15.13 and 220.12 ± 10.37 respectively, which indicates that it is more active in scavenging DPPH and ABTS radical. B2 (IC_{50} = 310.56 ± 5.92 µg/mL) and B3 (IC_{50} = 43.56 ± 3.03 µg/mL) scavenge superoxide radicals and FRAP more effectively. It is noticed that synthesized nanozymes have greater antibacterial and anticancer activity but low scavenging ability compared to green extract. Thus, Cu-Mn_3O_4 NPs from Azadirachta indica leaf extract could be utilized as a replacement of potential antibiotic drug candidate against MDR bacteria and in cancer avenues.



Chemoprotective effect of **nimbolide** against N-methyl-N-nitrosourea induced gastric cancer via alteration of apoptosis and NF-kappaB signaling pathway.

Gu Y, Liu B, Xia X, Luo C, Ren Y.Acta Cir Bras. 2025 Mar 31;40:e402125. doi: 10.1590/acb402125. eCollection 2025.PMID: 40172365

Purpose: Gastric cancer (GC) ranks as the third most common cause of cancer related mortality and as the fifth most frequently diagnosed cancer globally. Less than 30% of people with GC survive for more than five years. **Methods:** Nimbolide has been shown to have anticancer, anti-inflammatory, antiparasitic, and antioxidant properties. The current investigation showed the anticancer effect of nimbolide against N-methyl-N-nitrosourea (MNU) induced GC in rats. Rats were given MNU (100 mg/kg) orally to induce GC and received the oral administration of nimbolide (10, 20 and 40 mg/kg). The different biochemical parameters were estimated. **Results:** Nimbolide significantly ($p < 0.001$) altered the level of lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), cytochrome P450, cytochrome B5 and histone deacetylase (HDAC) activity. Nimbolide treatment significantly ($p < 0.001$) altered the level of antioxidant parameters like superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT), malondialdehyde (MDA); cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-2, IL-6; inflammatory parameters viz., cyclooxygenase-2 (COX-2), prostaglandin E2 (PGE2), vascular endothelial growth factor (VEGF), nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) in the serum and stomach tissue. Nimbolide considerably altered ($p < 0.001$) the level of apoptosis parameters (Bcl-2, Bax and caspase-3), and the mRNA expression of VCAM-1, ICAM-1, TNF-α, IL-1β, IL-6, MCP-1, TLR4 and NF-κB. **Conclusion:** Nimbolide treatment considerably altered the GC against MNU induced GC via alteration of apoptosis and NF-κB signaling pathway.

Neem in Veterinary Science & Medicine

Piroplasm infestations in cattle: exploring tick control using Chrysanthemum extract and **neem** oil emulsion.

Abd-Elrahman SM, Kamel FA, Abdel-Hakeem SS, Khedr AA, Mohamed SM, Abdelgaber AA, Darwish M, Al-Hakami AM, Alqahtani AJ, Dyab AK.Front Vet Sci. 2025 Mar 31;12:1543162. doi: 10.3389/fvets.2025.1543162. eCollection 2025.PMID: 40230792

Introduction: Tick-borne diseases represent a major threat to both animal and human health globally. This study explores the prevalence of tick infestation and associated piroplasm infections specifically *Theileria* and *Babesia* species in cattle, in addition to evaluating the acaricidal effectiveness of *Chrysanthemum* extract (*Dendranthema grandiflora*) and neem oil emulsion (*Azadirachta indica*).
Methods: Among 130 cattle examined, 61 were infested with ticks and subsequently screened for piroplasm infections. Molecular analysis identified infections caused by *Theileria annulata* and *Babesia bigemina*.

Results: A strong association was found between tick infestation and *Babesia* species, while *T. annulata* infection showed a slight correlation. Hemolymph examination confirmed the critical role of ticks in the life cycle of piroplasm infection. *Chrysanthemum* extract and neem oil were tested for their acaricidal properties against adult ticks (*Rhipicephalus annulatus*). *Chrysanthemum* extract (0.5 mg/mL) caused tick mortality within 24 h. However, neem oil induced rapid and significant tick mortality at (20 mg/L) and (15 mg/L), achieving 100% mortality within the same time frame. Both treatments demonstrated high effectiveness, with results indicating strong dose-and time-dependent effects compared to controls. Scanning electron microscopy (SEM) revealed extensive morphological damage to treated ticks. This damage included destruction of the hypostome, loss of surface striations, wrinkling with pore formation, and cracking following exposure to neem oil and *Chrysanthemum* extract.
Discussion: These findings highlight the potential of *D. grandiflora* extract and neem oil emulsion as effective natural acaricides for controlling tick infestations and reducing tick-borne diseases.

Antiviral activity of **Azadirachta indica** A. Juss and Melia azedarach extracts during the replication cycle of small ruminant lentiviruses.
de Sousa ALM, Pinheiro RR, Araújo JF, Peixoto RM, Lima AMC, de Morais SM, Souza SCR, Amaral GP, da Silva Teixeira MF, Andrioli A.Braz J Microbiol. 2025 Apr 26. doi: 10.1007/s42770-025-01659-0. Online ahead of print.PMID: 40287599

This study aimed to evaluate the in vitro antiviral activity of ethanolic extracts from Azadirachta indica and Melia azedarach during the replication cycle of the CAEV-Cork and MVV-K1514 strains, both part of the small ruminant lentivirus (SRLV) group, in ovine third eyelid (OTE) cells. The crude extracts (CE), along with the ethyl acetate (EAF) and methanol (MF) organic fractions from these plants, were tested in treatments applied before, during, and after viral inoculation of the CAEV-Cork and MVV-K1514 strains in separate OTE cell cultures. Following these treatments, the most effective results were subjected to viral titration analysis. The findings indicate that the EAF of A. indica and M. azedarach may have reduced the viral titer of the CAEV-Cork strain by 316-fold after inoculation and by 1.995-fold when applied concomitantly with inoculation, respectively. For the MVV-K1514 strain, the EAF of A. indica achieved a 1,000-fold inhibition when applied simultaneously with viral inoculation. These results suggest that extracts from Meliaceae plants influenced all phases of the SRLV replication cycle, significantly inhibiting the activity of both viral strains, although complete viral elimination was not achieved.