Neem Research Newsletter

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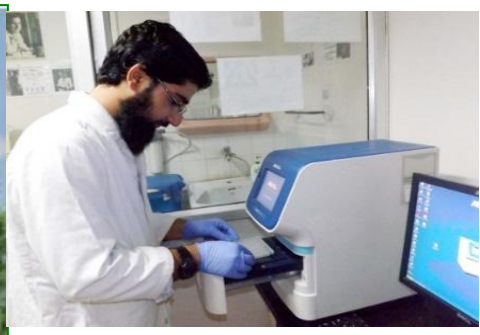

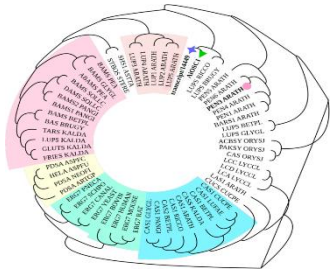

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WORLD NEEM ORGANISATION (WNO)

From

The Editor's Desk……

The interest in researching neem continues unabated. Endophytic fungi were isolated and identified from the leaves of young and mature plants of neem. The study concluded that the endophytes of neem can be harnessed and optimized to secrete cellulase enzymes for commercial use. The lethal and transgenerational effects of botanical and synthetic insecticides were investigated on the egg parasitoid *Trichogramma atopovirilia*, an important natural enemy of *Spodoptera frugiperda* in Brazil and beyond. Azamax® [limonoids (azadirachtin + 3-tigloilazadirachtol)] caused substantial reductions (99.13% and 92.36%, respectively) in the parasitism rate without causing transgenerational effects.

The effects of neem biochar and cow manure as additives during direct vermicomposting of sewage sludge using two earthworm species significantly improved vermicompost quality, increasing total nitrogen, phosphorus, reducing total organic carbon and yielded the best outcomes for earthworm growth and nutrient enhancement. These findings underscore the potential of integrating neem biochar and cow manure into direct sewage sludge vermicomposting as a sustainable solution for waste management and soil amendment. The co-pyrolysis of neem seed cake in combination with plastic waste yielded an optimal oil production of 69.4 wt% with maximum positive synergy of 6.25% at 500°C. The physicochemical characteristics of the resulting co-pyrolysis oil demonstrated a striking resemblance to those of conventional fossil diesel. Green synthesized zinc oxide nanoparticles from neem flower has emerged as a promising option for therapeutic, antimicrobial, and bioengineering applications. Neem methyl ester- petrol blend showed good performance in engines.

Silver nanoparticles synthesized using neem leaf extract exhibited potential in the treatment of periodontal diseases. Neem was also found to be useful as a root canal irrigant. Neem oil was tested for efficacy as a functional food ingredient. From the library of 235 neem-derived phytocompounds screened for activity against key Ebola virus proteins, daucosterol emerged as the most efficacious antiviral agent. A review article highlighted the potential of neem as a potent antimalarial agent. Using a novel approach, neem oil-loaded biocomposite film was demonstrated to be highly promising as a rapid means to stop bleeding and promote wound healing. In an in silico study, natural compounds including azadirachtin were found to be effective against antibiotic-resistant biofilms. A cost-effective predictive modelling and ranking for neem compounds was developed that could provide insights for accelerating drug discovery and development. The neem limonoid, nimbolide was demonstrated to alleviate drug-induced acute liver injury in an animal model. Small molecules from neem are envisaged to confer protection against mechanisms that lead to Alzheimer's disease. In a review article, the potential of the neem compound gedunin to induce death of cancer cells has been highlighted. It is also noteworthy that integrative genomic and in silico analysis revealed the immense potential of neem derived compounds in inhibiting breast cancer. In the area of veterinary science, research findings supported the use of neem leaf as effective phytogenic additive for improving rumen fermentation and mitigating methane production.

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Evaluation of cellulase production by endophytic fungi isolated from young and mature leaves of medicinal plants using maize cob substrate.

Mwendwa PK, Omwenga GI, Maingi JM, Karanja AW.Sci Rep. 2025 May 22;15(1):17842. doi: 10.1038/s41598-025-94864-8.PMID: 40404787

Endophytic fungi in medicinal plants aid in producing useful therapeutic compounds and enzymes. Among the most useful enzymes are cellulases. However, cellulase enzyme production in endophytic fungi of Azadirachta indica and Aloe secundiflora has not been comprehensively explored. The objective of this study was to; isolate and identify endophytic fungi from the leaves of young and mature plants of A. indica and A. secundiflora, determine colonization frequency of the endophytic fungi, and evaluate and optimize the cellulase production by the endophytic fungi on maize cob media. Eleven fungal endophytic isolates were obtained from the leaves of both A. secundiflora and A. indica, collected in Kitui and Kiambu Counties in total: Six from Kitui County and five from Kiambu County. Penicillium Sp. had highest colonization frequency in Kitui, while Candida sp. had highest in Kiambu. For enzyme optimization, isolates Candida boidinii, Galactomyces candidum, and Candida stellimalicola produced the highest amounts of Fpases and endoglucanases on third, sixth and ninth days. High exoglucanase producers were Colletotrichum gloeosporioides, Galactomyces candidum, and Candida stellimalicola. The endophytic communities within the leaves of A. indica and A. secundiflora are diverse. Maize cob agrowaste media can be used to cultivate the production of cellulases successfully in fungal endophytic isolates of A. indica and A. secundiflora. The study concluded that the endophytes of A. indica and A. secundiflora can be harnessed and optimized to secrete cellulase enzymes for commercial use, and especially isolates G. candidum and C. stellimalicola which yield significantly high amounts of total cellulases, endoglucanases and exoglucanases.

Harmful to Parents, Harmless to Offspring: Lethal and Transgenerational Effects of Botanical and Synthetic Insecticides on the Egg Parasitoid *Trichogramma atopovirilia*.

Santana EDR, Thiesen LV, Ribeiro LDP, Takahashi TA, Parra JRP, Yamamoto PT.Insects. 2025 May 5;16(5):493. doi: 10.3390/insects16050493.PMID: 40429206

This study investigated the lethal and transgenerational effects of botanical and synthetic insecticides on the egg parasitoid *Trichogramma atopovirilia*, an important natural enemy of *Spodoptera frugiperda* in Brazil and beyond. The treatments were assessed for their impact on parasitism, emergence, sex ratio, and flight capacity of adults exposed to contaminated eggs. The botanical insecticide ESAM (ethanolic seed extract of *Annona mucosa*) significantly reduced the parasitism in the F_0 generation by 99.76%, categorizing it as toxic. Anosom® [acetogenins (annonin as a major component)] and Azamax® [limonoids (azadirachtin + 3-tigloilazadirachtol)] also caused substantial reductions (99.13% and 92.36%, respectively) in the parasitism rate. EFAMON (ethanolic leaf extract of *Annona montana*) reduced the parasitism by 62%, while the synthetic

insecticide Premio® (chlorantraniliprole) resulted in a 28.21% reduction. In the F_1 generation, emergence rates for EFAMON, Azamax®, and Premio® exceeded 70%, showing no significant differences from the negative control (82%), while Anosom® resulted in a lower emergence rate of 61.39%. No significant effects were observed on sex ratio or parasitism in the F_1 and F_2 generations. Most adults reached high flight capacity (above 80%). These results indicate that while ESAM was toxic, the other treatments showed no transgenerational effects. Our findings contribute to understanding insecticide selectivity and highlight the importance of such studies for the sustainable management of *S. frugiperda* within integrated pest management programs.

Neem for Sustainable Environment & Green Synthesis

Neem biochar and cow manure as additives enhanced earthworm productivity and vermicompost quality during sewage sludge vermicomposting.

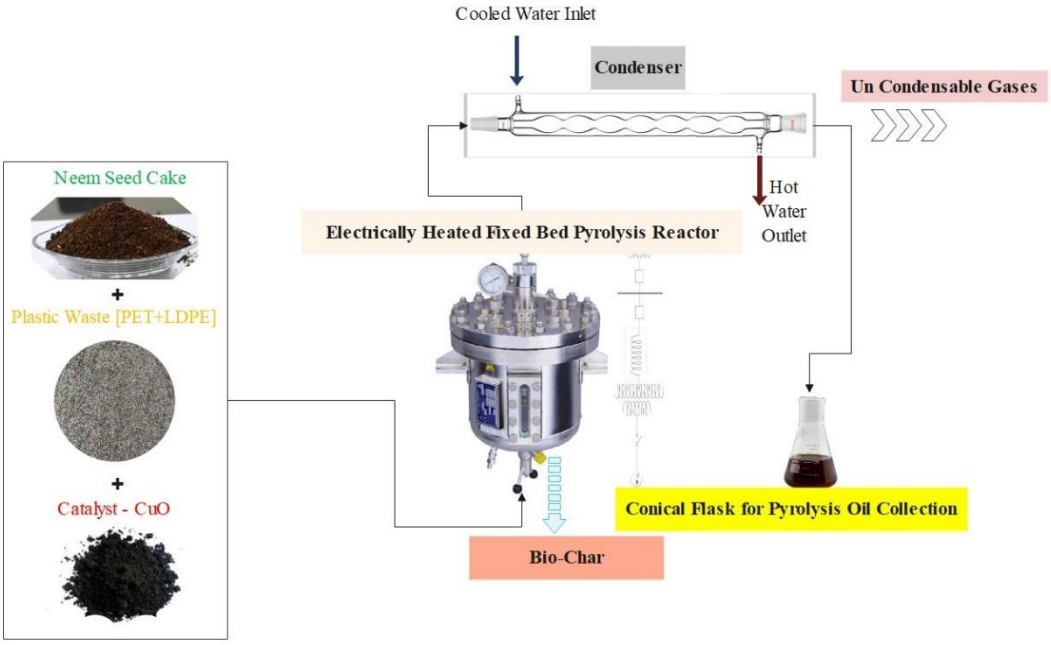
Madhubala S, Pravinkumar P, Karthikeyan K, Karmegam N, Hussain N.J Environ Manage. 2025 May 21;387:125870. doi: 10.1016/j.jenvman.2025.125870. Online ahead of print. PMID: 40403655

Vermicomposting has proven to be an effective technique for organic waste management, including sewage sludge. While previous studies have demonstrated its feasibility, the direct vermicomposting of sewage sludge-bypassing pre-composting-remains underexplored, particularly regarding the incorporation of additives like biochar combined with cow manure. Moreover, most research has predominantly utilized single earthworm species, leaving a gap in understanding species-specific responses and their interactions with these amendments. This study evaluates the effects of neem (Azadirachta indica) biochar and cow manure as additives during direct vermicomposting of sewage sludge using two earthworm species, Eudrilus eugeniae and Eisenia fetida. Over seven weeks, the impact of these additives on earthworm biomass, reproduction, and vermicompost quality was assessed. Biochar and cow manure improved vermicompost quality, increasing total nitrogen by up to 85%, available phosphorus by 58%, and reducing total organic carbon by 45%. FTIR analyses indicated accelerated organic matter decomposition, while scanning electron microscopy revealed biochar's role in stabilizing large organic molecules. Earthworm biomass increased by 47%, juvenile production by 157 % and cocoon production rose by 115% compared to untreated sludge. Phytotoxicity tests confirmed the non-toxicity of vermicompost, with germination indices exceeding 80 %. The treatment combining equal quantities of cow manure and sewage sludge with biochar (BCM_{50}) yielded the best outcomes for earthworm growth and nutrient enhancement. These findings underscore the potential of integrating biochar and cow manure into direct sewage sludge vermicomposting as a sustainable solution for waste management and soil amendment.

Non-catalytic and catalytic co-pyrolysis of **neem** seed cake and plastic waste: an experimental investigation on product distribution, synergistic interaction and characterization.

Livingston TPS, Madhu P, Dhanalakshmi CS, Ayyakkannu V.An Acad Bras Cienc. 2025 May 12;97(2):e20241284. doi: 10.1590/0001-3765202520241284. eCollection 2025.PMID: 40366932

This investigation elucidates the co-pyrolysis of neem seed cake in combination with plastic waste across a spectrum of mass ratios namely, 0:1, 3:1, 2:1, 1:1, 1:2, 1:3, and 1:0 subjected to varying pyrolytic temperatures from 350°C to 650°C, employing a CuO catalyst as a facilitating agent. The research concentrated on elucidating the effect of reaction temperature and the blend ratio of neem seed cake to plastic waste on the distribution of products and the chemical composition of the resultant pyrolysis oil. The co-pyrolysis performed at a 1:2 ratio of neem seed cake to plastic waste yielded an optimal oil production of 69.4 wt% with maximum positive synergy of 6.25% at 500°C. The physicochemical characteristics of the resulting co-pyrolysis oil demonstrated a striking resemblance to those of conventional fossil diesel. Further analysis through FT-IR revealed the presence of a different range of aromatic components. Quantitative analysis utilizing chromatographic peak area evaluations was undertaken to elucidate the compositional profile of the pyrolysis oils, thereby accentuating the presence of synergistic effects. Furthermore, GC-MS analysis provided empirical validation of the interaction between neem seed cake and waste plastics during co-pyrolysis, as indicated by discernible decrease in the concentration of oxygenated compounds.



Binding properties and biological applications of green synthesized ZnO nanoparticles from **neem** flower.

Mohanasundaram P, Saral A M.Sci Rep. 2025 May 22;15(1):17727. doi: 10.1038/s41598-025-02157-x.PMID: 40399393

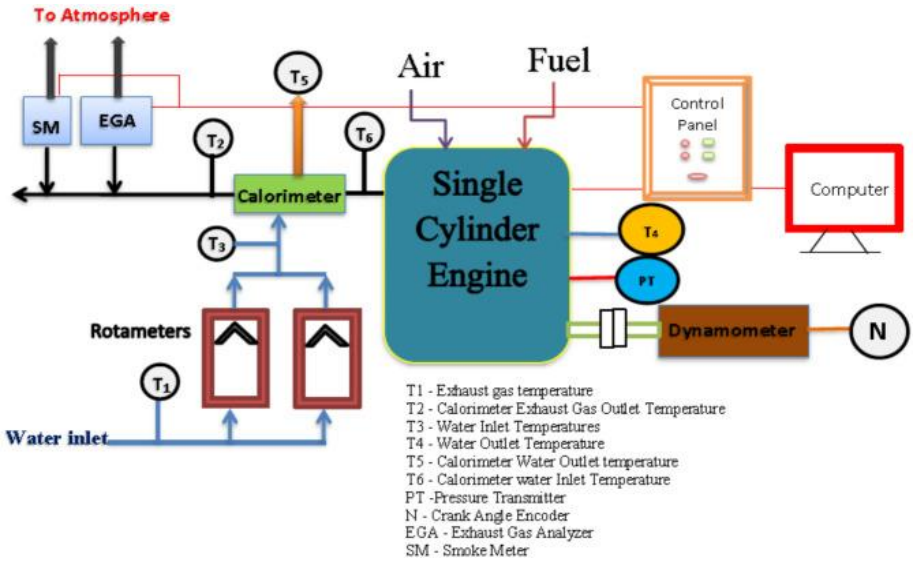
Zinc oxide (ZnO) nanoparticles exhibit distinctive electronics, sensors, and biomedical applications. The present work aims to synthesize an eco-friendly, cost-effective, and sustainable approach for the fabrication of zinc oxide nanoparticles (ZnO NPs). An

aqueous extract of neem flowers was used to fabricate the ZnO NPs as a natural reducing and capping agent. Analytical techniques, including UV-Vis, TEM, FTIR, FESEM, XRD, zeta potential analysis, and TGA confirmed the successful formation, crystalline nature, and stability of the ZnO NPs. The synthesized ZnO NPs were confirmed by the peak at 363 nm in the UV-Vis spectrum. The average particle size was found between 30 ~ 60 nm by FESEM, TEM, and Particle Size Analysis. The ZnO NP shows the highest % of inhibition was found to be > 80% in antioxidant activity. The antimicrobial assays show promising activity against pathogens. Moreover, their interaction with biomolecules such as DNA and bovine serum albumin (BSA) demonstrated strong binding affinity, highlighting their potential for biomedical applications. Cytotoxicity analysis using HEK-293 cells revealed minimal toxicity, suggesting that these nanoparticles are safe for normal cells. This study highlights the potential of green-synthesized ZnO nanoparticles as a promising option for therapeutic, antimicrobial, and bioengineering applications.

Investigation on diesel engine with biodiesel - gasoline fuel blends at a distinguished injection pressure.

Basem A, Smaisim GF, Prabu NM.Sci Rep. 2025 May 22;15(1):17812. doi: 10.1038/s41598-025-91163-0.PMID: 40404792

Due to the design challenges and low performance of engines in green fuels, the researchers started to investigate fuel blends. The inlet parameters also will influence the performance and, emission characteristics of the engines. Considering the effect of injection pressure, the current study revealed the clarity of distinct feedstocks that may be used effectively with esterified petrol blends at different injection pressure. This study has considered the various non-edible vegetable oil-based fuels such as Pongamia methyl ester-Gasoline blend [PME-5G], Jatropha methyl ester- petrol blend [JME-5G], Neem methyl ester- petrol blend [NME-5G], Mahua methyl ester- petrol blend [MME-5G], Dairy scum methyl ester - petrol blend [DME-5G], and Used cooking oil methyl ester - petrol blend [UME-5G] for investigation. The entire test is carried out in the CI engine of irrigation water pumping systems under the distinct injection pressures of 210, 230, and 250 bar with respective loading conditions of 0%, 20%, 40%, 60%, 80%, and 100%. The output parameters such as Brake power, Thermal efficiency, Specific fuel consumption, heat release rate, cylinder pressure and emission stanadrds are elaborately discussed. The final results show the maximum performance at higher injection pressure which is reverse in the case of emissions that exhibited.



Neem for Human Health

[Therapeutic Potential of AgNP-Infused Patches in Periodontal Disease: An Observational Study in Albino Rats.]

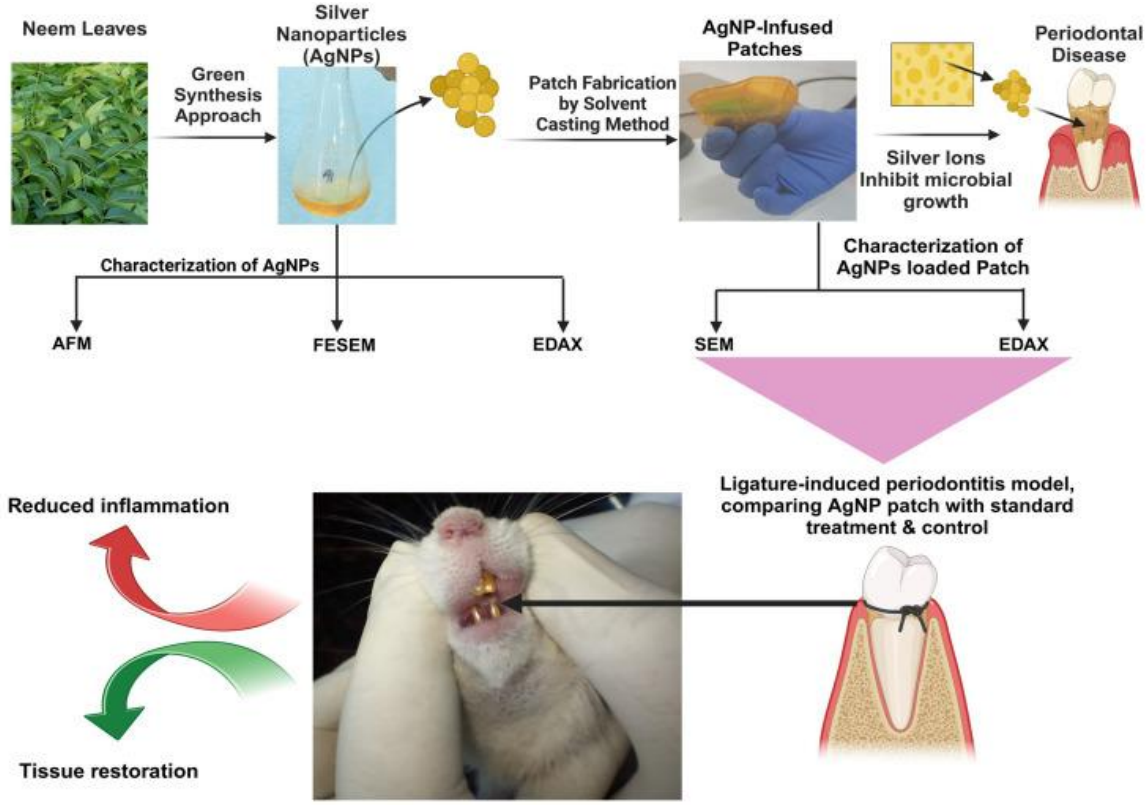
Barik B, Satapathy BS, Acharya B, Pattnaik G, Sillanpää M, Al-Farraj SA, Alkahtane AA.Int J Nanomedicine. 2025 Apr 26;20:5337-5352. doi: 10.2147/IJN.S515396. eCollection 2025.PMID: 40308646

Introduction: Silver nanoparticles (AgNPs) have emerged as a promising therapeutic modality in periodontal disease management due to their potent antimicrobial activity and ability to promote tissue regeneration. This study aimed to evaluate the efficacy of AgNP-infused patches in ligature-induced periodontitis rat model.

Methods: AgNPs were synthesized using a green synthesis method with neem (*Azadirachta indica*) leaf extract followed by incorporation into polyvinyl alcohol (PVA)-based patches. In vivo efficacy of experimental AgNP patch was tested in albino rats *vs* marketed formulation and control groups, following ARRIVE guidelines.

Results: Characterization by Atomic Force Microscopy revealed spherical AgNPs with an average size of 85 nm, while Field Emission Scanning Electron Microscopy confirmed uniform morphology and size distribution. Production of microporous AgNP patches with uniform nanoparticle dispersion was also validated by Scanning electron microscopy and Energy Dispersive X-ray Analysis. Observational and histopathological analysis revealed significant improvements in gingival and periodontal tissue restoration, inflammation reduction in the AgNP-treated groups compared to untreated and standard-treated groups.

Discussion: Notably, the high-dose AgNP patch (1000 mg/kg) treated group exhibited near-complete tissue restoration. These findings highlight the potential of AgNP patch as a localized treatment alternative for periodontal disease.



Antibacterial effect of various herbal root canal irrigants.

N V, Bahadur S, Sharma A, Gupta N, Ahmed Almuntashiri AA, Rajan R, Mohapatra A, Gupta A.Bioinformation. 2025 Feb 28;21(2):165-168. doi: 10.6026/973206300210165. eCollection 2025.PMID: 40322710

Root canal irrigation is crucial in endodontics. Therefore, it is of interest to evaluate the antibacterial efficacy of various herbal root canal irrigants (Triphala, Neem (*Azadiracta indica*, green tea and *Curcuma longa* (Turmeric)) against *Enterococcus faecalis*. Antimicrobial efficacy of the herbal irrigants and sodium hypochlorite was done using a brain-heart infusion method. The tested herbal irrigants had antibacterial efficacy against *E faecalis*. Hence, these herbal irrigants are alternative to sodium hypochlorite.

Harnessing the benefits of seed oils: a comprehensive study on their role in functional foods.

Kamel MA, Gamal AA, Abdelhamid SA, El-Said MM, El-Messery TM, Zahran HA.AMB Express. 2025 May 26;15(1):81. doi: 10.1186/s13568-025-01875-9.PMID: 40418264

There has been a growing interest in functional foods in recent years to improve health and boost immunity, particularly since the COVID-19 pandemic, which reflects their significant role in promoting health and preventing various diseases, especially metabolic disorders. This study investigated the antimicrobial, antioxidant, anticoagulant, and prebiotic activities of six different oils: Calotropis procera oil (CPO), Chia seed oil (CSO), Moringa oil (MO), Neem oil (NO), Black seed oil (BSO), and Wheat germ oil (WGO) and their potential applications in health and nutrition. The DPPH and ABTS assays were used to evaluate the antioxidant activity of these oils. A good diffusion assay and minimum inhibitory concentrations (MIC) method were used to investigate the antimicrobial activity against pathogenic bacteria and fungi of human interest. Also, the prebiotic activities of oils were tested on three probiotic strains of Lactobacillus to evaluate their role in promoting the growth of beneficial bacteria against the pathogenic E. coli. Furthermore, the haematological effect of these oils was investigated in vitro through measuring their anticoagulant, and Fibrinolytic activity. The results demonstrated that DPPH assay revealed that CPO and WGO exhibited the highest antioxidant activity with IC50 values of 15.2 µg/mL and 18.7 µg/mL, respectively, while BSO showed the least activity with an IC50 of 45.3 µg/mL. Antimicrobial activity, assessed using inhibition zone diameters, showed that CPO had the strongest effect against Staphylococcus aureus with a zone of 22 mm, followed by CSO at 19 mm. In terms of anticoagulant activity, CSO demonstrated the most potent fibrinolytic effect with a clot lysis percentage of 78%, while MO exhibited weaker activity at 35%. Prebiotic testing revealed that individual oils had limited effects on Lactobacillus growth, but a synergistic blend enhanced growth by 25% compared to controls. Overall, this study highlights the diverse health benefits of these oils and their potential as functional food ingredients that could contribute to improved health.

In-silico evaluation of **Azadirachta indica**-derived Daucosterol against key viral proteins of Ebolavirus using ML and MD simulations approach.

Joshi T, Priyamvada P, Mathpal S, Sriram S, Madaan S, Ramaiah S, Anbarasu A.J Biol Phys. 2025 May 26;51(1):17. doi: 10.1007/s10867-025-09683-9.PMID: 40419736

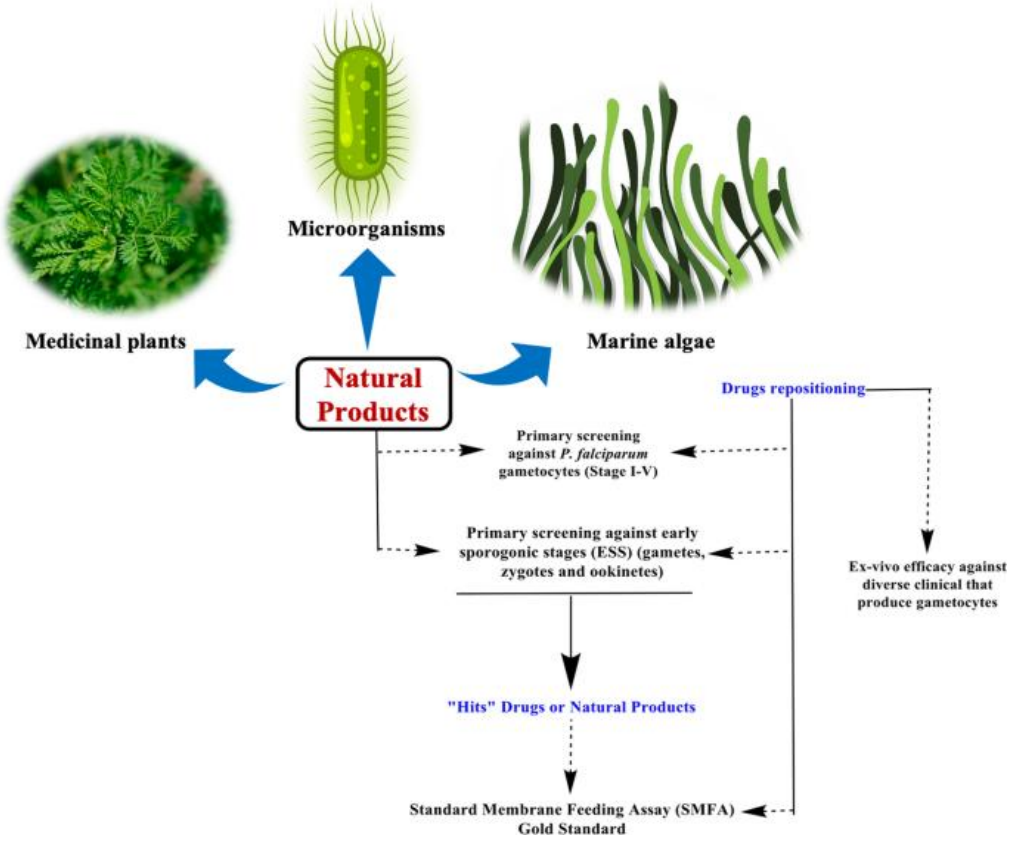
Ebola virus disease (EVD) is an acute life-threatening disease caused by highly pathogenic Ebolavirus (EBOV), with reported case fatality rates reaching 90%. There have been numerous EBOV outbreaks and epidemics since the first outbreak was reported in Africa in 1976. Despite the approval of three vaccines and two monoclonal antibody therapies by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of EVD the urgent need for alternative therapeutic strategies persists. In the present study, we screened a library of 235 phytocompounds derived from Azadirachta indica against the key EBOV viral protein 24 (VP24), VP30, VP35 and VP40 through a random forest-based machine learning model with an accuracy of 84.5%. Initially, 48 compounds were identified as active, and subsequent toxicity assessment refined the selection to a promising candidate, daucosterol. Molecular docking studies indicated that daucosterol exhibited significant binding affinity to all four viral proteins. Subsequent validation through molecular dynamics simulations confirmed the stability of daucosterol protein complexes. These results imply that daucosterol acts as a potential multitarget inhibitor against EBOV proteins and could serve as a promising lead compound for future therapeutic development against EVD.

Natural products as transmission-blocking agents against malaria: a comprehensive review of bioactive compounds and their therapeutic potential.

Fokou PVT, Tali MBT, Mbouna CDJ, Yamthe LRT, Sharifi-Rad J, Calina D, Radha, Kumar M, Tchouankeu JC, Boyom FF.Malar J. 2025 May 26;24(1):164. doi: 10.1186/s12936-025-05395-6.PMID: 40420292

Malaria eradication is hindered by the persistence of transmission stages of Plasmodium falciparum that enable parasite transfer from humans to mosquitoes. Current therapeutic strategies, such as artemisinin-based combination therapy (ACT) combined with primaquine, are insufficient due to limited efficacy on mature gametocytes and safety concerns in populations with glucose-6-phosphate dehydrogenase deficiency. This highlights the critical need for innovative, safe, and effective transmission-blocking interventions. This review explores the potential of natural sources, including medicinal plants, marine organisms, and microorganisms-as reservoirs of novel bioactive compounds with anti-malarial properties. A comprehensive literature search identified promising natural products with gametocytocidal and sporontocidal activity, validated through advanced bioassays. The review also evaluates various methodologies, such as colorimetric, microscopy, and flow cytometry assays, for assessing transmission-blocking efficacy. The findings emphasize the potent gametocytocidal effects of certain plant extracts, such as Azadirachta indica and Vernonia amygdalina, and microbial products, including ionophores and proteasome inhibitors. Despite promising in vitro and in vivo data, the transition of these compounds to clinical applications remains limited. Challenges include standardizing assays, addressing resistance to current therapies, and ensuring

drug safety for endemic populations. The current review underscores the untapped potential of natural products as transmission-blocking agents and proposes a systematic, stage-specific screening cascade to identify and optimize these compounds. Addressing these gaps could significantly advance global malaria eradication efforts.

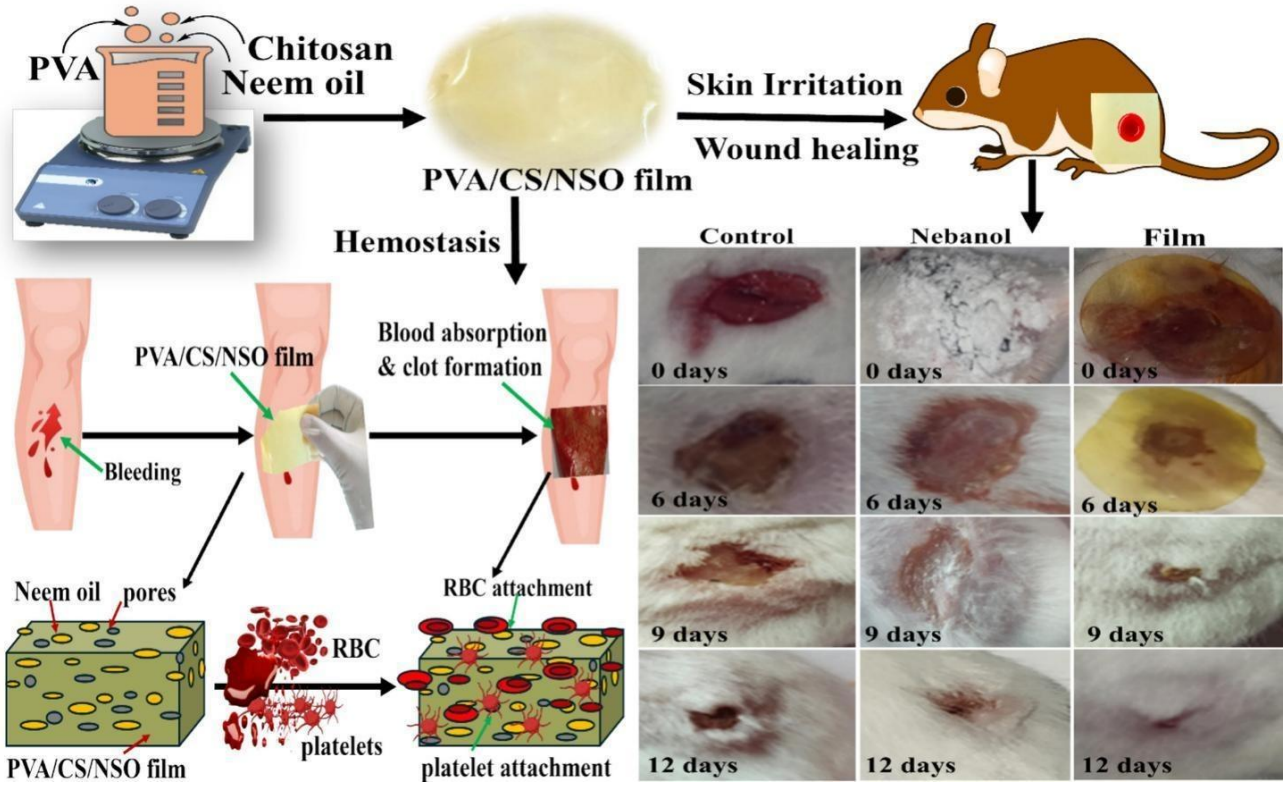


Investigation of **neem**-oil-loaded PVA/chitosan biocomposite film for hydrophobic dressing, rapid hemostasis and wound healing applications.

Rahman MH, Mondal MIH.Int J Biol Macromol. 2025 May 27:144712. doi: 10.1016/j.ijbiomac.2025.144712. Online ahead of print.PMID: 40441574

The present work aims to develop a hydrophobic dressing with a blood-repellent surface that achieves fast clotting without blood loss, having antibacterial properties, clot self-detachment, and superior wound healing activity. For these reasons, a novel approach was applied by producing a hydrophobic film made of PVA, chitosan, and neem seed oil (NSO). The film had the necessary hydrophobicity, mechanical strength, stability and was able to transmit water vapor to be suitable for the wound skin surface and demonstrated faster blood clotting (BCI = 91.44 % in 5 min and 85.22 % in 10 min). The proportion of red blood cells (2.78 %) and platelets (17.33 %) attached to the film proved its excellent hemostatic activity. It was anti-adhesive, created spontaneous clot detachment, and exhibited antibacterial properties at the wound site, as evidenced by in vivo testing. Moreover, in vivo testing and histopathological findings showed enhanced wound healing activity, greater re-epithelialization, and decreased granulation tissue. Additionally, the film's eco-friendliness was evaluated using a soil burial degradation test, and the results show that it deteriorated into the soil but did so slowly because of its hydrophobic property.

Thus, PVA/CS/NSO composite film may be a green biomedical material for hemostasis and wound healing.



[Bioactive Compounds as a Potential Inhibitor of Biofilm Production: An In silico Study to Identify Natural Hindrance Resources.]

Gupta J, Gupta A, Bhattacharya D, Nag M, Lahiri D, Mitra D.Curr Drug Discov Technol. 2025 May 2. doi: 10.2174/0115701638367145250418033053. Online ahead of print.PMID: 40325815

Background: Biofilm formation by microorganisms, specifically bacteria, threatens various fields, including biomedicine and the environment. The development of biofilms has associations with increased resistance to antimicrobial agents and immune responses; it poses a significant threat to human health. ESKAPE pathogens, a group of bacteria known for their multidrug resistance, are particularly adept at biofilm formation. This research explores strategies to combat biofilm-associated infections, with a focus on natural compounds as potential anti-biofilm agents.

Methods: The study investigates 23 natural compounds for their druglike properties in fighting against antibiotic-resistant biofilms. These compounds include flavonoids, terpenes, and alkaloids, and exhibit promising bioavailability and usage potential as ligands. Molecular docking analysis em-ploying AutoDock Vina was used to evaluate the binding affinities of these ligands to key biofilm-forming genes and membrane proteins in ESKAPE pathogens.

Results: Despite a few violations of a variety of established criteria, the overall safety and efficiency of oral drug reception are maintained, emphasizing their potential for further drug development. The results show specific ligands, such as Baicalin, Apigenin, Azadirachtin, Curcumin, Hyperforin, etc., demonstrating high binding energies against biofilm-associated proteins. This approach aligns with the pursuit of sustainable alternatives to combat biofilm-related infections.
Conclusion: Natural compounds like Baicalin, Apigenin, Azadirachtin, Curcumin, Hyperforin not only exhibit broad-spectrum coverage but also show reduced risks of resistance development compared to synthetic antibiotics. The integration of natural compounds into multifaceted strategies considers the complexities of the biofilm matrix, bacterial diversity, and pathogen characteristics, offering a sustainable approach to address biofilm-associated infections.

Predictive modelling and ranking: **Azadirachta indica** compounds through indices and multi-criteria decision-making techniques.

Anuradha DS, Jaganathan B.Front Chem. 2025 Apr 29;13:1580267. doi: 10.3389/fchem.2025.1580267. eCollection 2025.PMID: 40365176

Introduction: *Azadirachta indica* (neem) shows medicinal potential against chronic diseases, but clinical translation is challenging. This study aimed to analyze neem compounds using topological indices (TIs) to predict physicochemical properties.

Methods: Valency-based indices, including Zagreb and atom bond connectivity indices, were used to characterize boiling point, vaporization, enthalpy, mass, and refractivity. Regression analysis and multi-criteria decision-making methods were employed for predictive modeling and compound ranking.

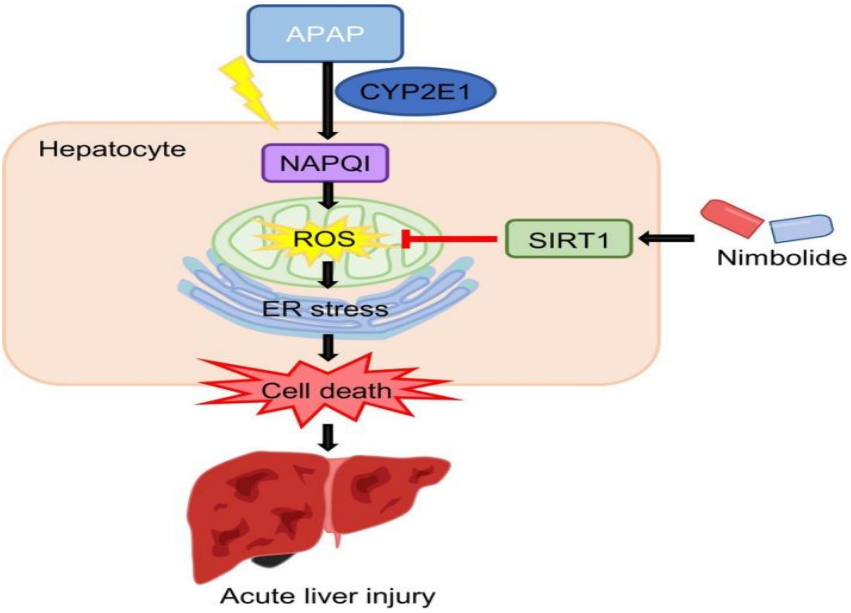
Results: Statistical metrics demonstrated the predictive power of the models. Ranking methods provided a hierarchical ordering of compounds based on therapeutic potential.

Discussion: This study contributes to analogous prediction, optimization, and virtual screening of neem compounds using a cost-effective approach. The findings offer insight into neem compound properties, potentially accelerating drug discovery and development.

Nimbolide Targeting SIRT1 Protects Against Acetaminophen-Induced Acute Liver Injury by Regulating Oxidative Stress and Endoplasmic Reticulum Stress.
Ba J, Lin Y, Zhang J, Wang Y, Wu B.Pharmacol Res Perspect. 2025 Jun;13(3):e70120. doi: 10.1002/prp2.70120.PMID: 40375435

Acetaminophen (APAP) is a major cause of acute liver injury (ALI), and N-acetylcysteine is the only approved detoxification drug. Nimbolide (Nim), which is isolated from the neem tree (Azadirachta indica), possesses protective properties against multiple diseases, including pancreatitis, autoimmune hepatitis, arthritis, and diabetic cardiomyopathy. Here, we investigated the protective effect of nimbolide on APAP-induced ALI. Male C57BL/6J mice were used to establish an ALI model via APAP administration (500 mg/kg, i.p.). All the mice received nimbolide (20 mg/kg, i.p.) or a vehicle 2 h before APAP injection. Blood

and liver samples were collected at the indicated times. As expected, Nim treatment alleviated APAP-induced liver injury and inflammation in the mice. Moreover, Nim inhibited APAP-induced apoptosis by regulating endoplasmic reticulum (ER) stress. We further revealed that Nim improved mitochondrial function and increased Sirtuin 1 (SIRT1) expression. However, the protective effects of Nim were partially blocked by SIRT1 knockdown via siRNA in vitro. Our study revealed that nimbolide alleviated APAP-induced ALI by inhibiting oxidative stress and ER stress via SIRT1 activation.



Small molecule-mediated therapeutic approaches to target Tau and Alzheimer's disease.
Chinnathambi S.Adv Protein Chem Struct Biol. 2025;145:287-304. doi: 10.1016/bs.apcsb.2024.11.010. Epub 2024 Dec 5.PMID: 40324850

Neurodegeneration is marked by the altered proteostasis and protein degradation mechanism. This is caused due to the accumulation of aberrant proteins. Alzheimer's disease is one of the leading causes of neurodegeneration characterized by the aggregation of Tau and Amyloid-β proteins intracellularly and extracellularly, respectively. The intracellular aggregation of Tau triggers accumulation of oxidative stress, loss of ER and mitochondrial function, leading to the aggravation of aggregates formation. Thus, increasing the load of aberrant proteins on chaperones and degradative mechanism, such as autophagy and ubiquitin-proteasome system. Although several small molecules are known to target and prevent Tau aggregation, the detrimental effects in the cell due to aggregates accumulation shall not be overlooked. In such instance, small molecules that effectively target Tau aggregates and the cellular aberrations would be of great importance. Here we have discussed the efficacy of natural molecule, Limonoid, isolated from Azadirachta indica that prevents Tau aggregation and also activates the heat shock protein system. The activated heat shock protein system elevates the levels of Hsp70 that is known to interact with aberrantly folded Tau. Further, the role of Hsp70 in directing Tau clearance by macroautophagy or chaperone-mediated autophagy elucidates the effect of limonoids in overcoming AD pathology due to Tau aggregation.

HSP90 and the cancer transcriptome: a comprehensive review of inhibitors and mechanistic insights.

Shahana MV, Choudhary B.Int J Clin Oncol. 2025 May 18. doi: 10.1007/s10147-025-02782-6. Online ahead of print.PMID: 40383747

This review summarizes the structure, function, expression, and inhibitors of HSP90, the chaperone, in cancers. It systematically investigates the effects of HSP90 inhibitors, including AUY922, B11B021, CCT-018159, D7-gedunin, geldanamycin, and gedunin, across a range of cancer cell lines (HCC151, HT29, MCF7, PC3, VCAP, and A375) and a normal HA1E cell line, using data from the CLUE database. Our analysis reveals that treatment with these HSP90 inhibitors induces significant stress responses in tumor cells, initiating intrinsic and extrinsic apoptotic pathways. The HSP90AA1, HSP90AB1, HSP27, HSP70, VEGF, and NOTCH exhibited notable upregulation at 24 h post-treatment compared to 6 h, indicating a time-dependent increase in cellular stress (heat shock response) and activation of pro-survival signaling mechanisms. Additionally, the study highlights a significant upregulation of immune-related pathways, including those involving IL10, IL3, and IL7, following HSP90 inhibition, indicating that these inhibitors not only directly affect tumor cell viability but also modulate the tumor microenvironment by enhancing immune cell activation and cytokine release. The elevated levels of IL10 point to a dual role, where immune suppression mechanisms are also at play, potentially facilitating immune evasion by the tumor. The findings suggest that HSP90 inhibitors exhibit varying mechanisms of action across different cancer cell lines despite the presence of some common targets. These insights highlight the need for further investigation into the precise mechanisms of HSP90 inhibitors to optimize their therapeutic potential in different cancers.

Integrative Genomic and in Silico Analysis Reveals Mitochondrially Encoded Cytochrome C Oxidase III (MT-CO3) Overexpression and Potential **Neem**-Derived Inhibitors in Breast Cancer.

Agboola OE, Agboola SS, Oyinloye OM, Fadugba AE, Omolayo EY, Ayinla ZA, Osunsanmi FO, Olaiya OE, Olojo FO, Ajiboye BO, Oyinloye BE.Genes (Basel). 2025 Apr 30;16(5):546. doi: 10.3390/genes16050546.PMID: 40428367

Background: The increasing global incidence of breast cancer calls for the identification of new therapeutic targets and the assessment of possible neem-derived inhibitors by means of computational modeling and integrated genomic research.
Methods: Originally looking at 59,424 genes throughout 42 samples, we investigated gene expression data from The Cancer Genome Atlas-Breast Cancer (TCGA-BRCA) dataset. We chose 286 genes for thorough investigation following strict screening for consistent expression. R's limma package was used in differential expression analysis. The leading candidate's protein modeling was done with Swiss-ADME and Discovery Studio. Molecular docking studies, including 132 neem compounds, were conducted utilizing AutoDock Vina.
Results: Among the 286 examined, mitochondrially encoded cytochrome C oxidase III (MT-CO3) turned out to be the most greatly overexpressed gene, showing consistent

elevation across all breast cancer samples. Protein modeling revealed a substantial hydrophobic pocket (volume: 627.3 $Å^3$) inside the structure of MT-CO3. Docking investigations showed five interesting neem-derived inhibitors: 7-benzoylnimbocinol, nimolicinol, melianodiol, isonimocinolide, and stigmasterol. Strong binding affinities ranging from -9.2 to -11.5 kcal/mol and diverse interactions with MT-CO3, mostly involving the residues Phe214, Arg221, and Trp58, these molecules displayed. With hydrophobic interactions dominant across all chemicals, fragment contribution analysis revealed that scaffold percentage greatly influences binding effectiveness. Stigmasterol revealed greater drug-likeness (QED = 0.79) despite minimal interaction variety, while 7-benzoylnimbocinol presented the best-balanced physicochemical profile.
Conclusion: Connecting traditional medicine with current genomics and computational biology, this work proposes a methodology for structure-guided drug design and development using neem-derived chemicals and finds MT-CO3 as a potential therapeutic target for breast cancer.

Neem in Veterinary Science & Medicine

Assessment of different phytogenic-based additives on *in vitro* rumen fermentation profile and methane emissions.
El-Zaiat HM, Masood HA, Al Hinai SS, Al Maamari RH, Al Riyami SS, Al-Kharousi K, Al-Salami AH, Al-Habsi N.Front Vet Sci. 2025 May 1;12:1591700. doi: 10.3389/fvets.2025.1591700. eCollection 2025.PMID: 40376100

Introduction: Phytogenic feed additives have gained increasing attention in ruminant nutrition due to their capacity to modulate ruminal fermentation and reduce methane (CH_4) emissions. This study evaluated the effects of three plant-based additives.
Methods: Neem leaf (*Azadirachta indica*; NL), Indigofera leaf (*Indigofera oblongifolia*; IL), and Pumpkin peel (*Cucurbita pepo*; PP) included at four levels (0, 10, 20, and 30 g/kg DM) on *in vitro* ruminal fermentation, feed degradability, and CH_4 emissions. A total mixed ration (TMR) was incubated with each additive and buffered rumen fluid using the *in vitro* gas production technique for 24 hours.
Results and discussion: NL and IL supplementation significantly ($p < 0.05$) increased gas and carbon dioxide (CO_2) production, organic matter degradability, and total volatile fatty acid concentrations, particularly propionate and butyrate. Simultaneously, acetate concentration, CH_4 emissions, NH_3-N levels, and protozoa abundance were reduced ($p < 0.05$). However, PP had limited effects on these parameters. The phenolic profiles of NL and IL, notably rich in 2-hydroxycinnamic acid and p-coumaric acid, likely contributed to these outcomes. In conclusion, these findings support the use of NL and IL as effective phytogenic additives for improving rumen fermentation and mitigating CH_4 production. Further *in vivo* trials are recommended to validate these *in vitro* results.