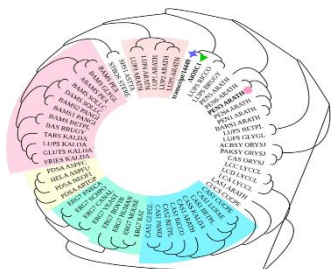




Neem Research Newsletter

Volume 3, Issue 11, 2023



WORLD NEEM ORGANISATION (WNO)



From

The Editor's Desk.....

In this issue of Neem Research Newsletter abstracts of interesting articles published during the last month are presented. Use of neem seed extract has been advocated as a cost-effective solution in tomato pest management in Pakistan based on convincing experimental evidence that it suppresses pests by acting as an antifeedant. Neem oil was found to be a promising candidate for the treatment of infectious diseases in fish. Batch extraction of phenolic compounds from neem was achieved using genetic algorithm and machine learning techniques. Omics studies with reference to the key pathway for triterpenoid biosynthesis in neem were comprehensively reviewed. The suitability of natural neem gum in various composite material applications in place of epoxy resin was assessed. The physico-chemical properties of soil and mineralization were significantly improved by neem. Food packaging films incorporated with neem leaf powder improved tensile properties, biodegradability, as well as antimicrobial activity. Scientific research confirms that neem exhibits relevant physicochemical properties and biological activities that are beneficial for hair care and scalp maintenance. Neem oil was shown to be a viable disinfectant in dental practice. Molecular dynamics simulation studies provide compelling evidence for the potential use of neem compounds in future drug development efforts for the treatment of leishmaniasis. Azadirachtin holds promise as a potential therapeutic in combination with anti-cancer drugs. Neem leaf extract was found to improve nutrient digestibility, growth performance, methane, and blood profile of merino lambs.

S. Nagini

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



Neem in Agriculture & Aquaculture

Managing insect and plant pathogen pests with organic and conventional pesticides in onions.

Constancio N, Higgins D, Hausbeck M, Szendrei Z.

J Econ Entomol. 2023 Nov 1:toad201. doi: 10.1093/jee/toad201. PMID: 37931224

Onion thrips (*Thrips tabaci* Lindeman, Thysanoptera: Thripidae) is a significant insect pest of onions (*Allium cepa* L., Asparagales: Amaryllidaceae). In addition to feeding on onion foliage, they may spread plant pathogens. Currently, onion thrips and pathogens are managed as separate pests with insecticides and fungicides. It may be beneficial to manage these pests simultaneously as limiting onion thrips may reduce pathogen damage. We tested combinations of bio- and conventional pesticides in a season-long management program in Michigan onion fields. From 2020 to 2022, we counted onion thrips weekly and visually estimated plant foliage necrotic damage (%) in experimental plots each year. In 2020, we tested 6 treatment programs including: azadirachtin, spinosad, a copper-based fungicide, azadirachtin + copper-based fungicide, spinosad + copper-based fungicide, and untreated control. The thrips populations were not significantly reduced compared to the control, but necrotic damage was reduced significantly in spinosad-treated plots. In 2021, we tested a combination of 8 bio- and conventional pesticide programs. Compared to the control, the bioinsecticides did not reduce onion thrips populations, but the conventional pesticide programs reduced both onion thrips numbers and necrotic damage. In 2022, we tested only conventional insecticide programs but included 3 different action thresholds for initiation and applied them with or without a fungicide, for 8 treatments. All insecticide programs reduced onion thrips compared to the control, the action threshold did not impact thrips numbers significantly. Overall, the use of action thresholds can lead to fewer insecticide applications and a lower incidence of leaf damage.

Compatibility of pesticides with the predatory mite *Neoseiulus barkeri*.

Matos MC, Silva FWB, Filgueiras RMC, Lima DB, Melo JWS.

Exp Appl Acarol. 2023 Nov 20. doi: 10.1007/s10493-023-00865-5. PMID: 37985607

Multiple arthropod pests can affect the same crop in agricultural systems, requiring the integration of control methods. In the present study, the effects of residual exposure to four broad-spectrum insecticides/acaricides (azadirachtin, abamectin, chlorfenapyr, and fenpyroximate) on immature (development and survival time) and adult females (longevity, fecundity, and fertility life table parameters) of the predatory mite *Neoseiulus barkeri* were evaluated. Additionally, the insecticides/acaricides were categorized according to their selectivity based on the classification proposed by the International Organization for Biological Control (IOBC) for assessing the susceptibility of arthropods in laboratory experiments. Method 004, proposed by the Insecticide Resistance Action Committee (IRAC), was adopted for the bioassays with predators exposed to insecticide-acaricide residues. Among the insecticides/acaricides studied, azadirachtin had minimal effects on immature and adult *N. barkeri* (all non-significant) and was considered harmless based on the classification of toxicity according to the standards/categories proposed by the IOBC.

All other insecticides/acaricides affected immature and adult *N. barkeri* and were considered slightly harmful in terms of toxicity, according to the IOBC.

Botanical biopesticides have an influence on tomato quality through pest control and are cost-effective for farmers in developing countries.

Akhter W, Shah FM, Yang M, Freed S, Razaq M, Mkindi AG, Akram H, Ali A, Mahmood K, Hanif M.

PLoS One. 2023 Nov 28;18(11):e0294775. doi: 10.1371/journal.pone.0294775. eCollection 2023.PMID: 38015916

Synthetic insecticides heavily applied to manage agricultural pests are highly hazardous to the environment and non-target organisms. Their overuse through repeated treatments in smallholder farming communities is frequent. Botanical biopesticides are ideal for sustainable pest management in agricultural environments by keeping synthetic insecticide use at a minimum. Here we evaluated a locally prepared neem seed extract (NSE) alongside emamectin benzoate against both lepidopteran pests *Helicoverpa armigera* (Hübner) and *Spodoptera exigua* (Hübner) on tomato *Lycopersicon esculentum* Mill under natural field conditions in Pakistan. We compared pest severity, fruit injury, quality, marketability, and cost:benefit ratio (CBR) between treatments. The concentration of azadirachtin A in the NSE was 26.5 ppm. NSE at 2% (20 mL/L) and the emamectin benzoate at the recommended field rate in Pakistan were sprayed weekly throughout the fruiting stage. The pest larvae were significantly more abundant on fruits than on flowers and leaves. Fruit injury and losses were significantly more important in untreated control compared to NSE and emamectin benzoate treatments. NSE efficacy varied with respect to the cultivars used and the seasons. Cultivar Eden harboured more pests than Adventa, and emamectin benzoate suppressed more pest individuals than NSE. Both the insecticidal treatments were comparable in terms of marketable yield productions as well as unmarketable, uninjured, and recovered fruit yields. NSE generated a higher CBR (1: 9.26) than emamectin benzoate (1: 3.23). NSE suppressed pests by acting as an antifeedant, similar to its synthetic counterpart. Smallholder growers can thus use NSE as a cost-effective solution in tomato pest management in Pakistan.

Trunk injection to control *Xylosandrus germanus* (Coleoptera: Curculionidae) in topworked apple trees.

Wheeler CE, Vandervoort C, Wise JC.

J Econ Entomol. 2023 Nov 27:toad217. doi: 10.1093/jee/toad217. PMID: 38011810

Xylosandrus germanus (Blandford) is an invasive species of ambrosia beetle known to attack apple trees in North America. *Xylosandrus germanus* are attracted to ethanol produced by stressed and injured trees and can be a serious problem when grafting a new cultivar onto established fruit trees (topworking). The objective of this study was to evaluate the efficacy of 2 insecticides (emamectin benzoate and azadirachtin) and injection timing (fall and spring) on their ability to control *X. germanus* colonization in apple trees with simulated topworking. Our study shows evidence that both emamectin benzoate and azadirachtin injections can reduce *X. germanus* infestations; however, our results were inconsistent. The timing of injections influenced *X. germanus*, with spring injected azadirachtin being more effective than fall injections. Residue analyses of emamectin

benzoate and azadirachtin showed the presence of residues in woody tissue comparable to those found in leaves.

Molecular Docking of Nimbolide Extracted from Leaves of *Azadirachta indica* with Protein Targets to Confirm the Antifungal, Antibacterial and Insecticidal Activity.

Navinraj S, Boopathi NM, Balasubramani V, Nakkeeran S, Raghu R, Gnanam R, Saranya N, Santhanakrishnan VP.

Indian J Microbiol. 2023 Dec;63(4):494-512. doi: 10.1007/s12088-023-01104-6. PMID: 38031617

Nimbolide, a tetranortriterpenoid (limonoid) compound isolated from the leaves of *Azadirachta indica*, was screened both in vitro and in silico for its antimicrobial activity against *Fusarium oxysporum* f. sp. *cubense*, *Macrophomina phaseolina*, *Pythium aphanidermatum*, *Xanthomonas oryzae* pv. *oryzae*, and insecticidal activity against *Plutella xylostella*. Nimbolide exhibited a concentration-dependent, broad spectrum of antimicrobial and insecticidal activity. *P. aphanidermatum* (82.77%) was more highly inhibited than *F. oxysporum* f. sp. *cubense* (64.46%) and *M. phaseolina* (43.33%). The bacterium *X. oryzae* pv. *oryzae* forms an inhibition zone of about 20.20 mm, and *P. xylostella* showed about 66.66% mortality against nimbolide. The affinity of nimbolide for different protein targets in bacteria, fungi, and insects was validated by in silico approaches. The 3D structure of chosen protein molecules was built by homology modelling in the SWISS-MODEL server, and molecular docking was performed with the SwissDock server. Docking of homology-modelled protein structures shows most of the chosen target proteins have a higher affinity for the furan ring of nimbolide. Additionally, the stability of the best-docked protein-ligand complex was confirmed using molecular dynamic simulation. Thus, the present in vitro and in silico studies confirm the bioactivity of nimbolide and provide a strong basis for the formulation of nimbolide-based biological pesticides.

Neem oil against *Aeromonas hydrophila* infection by disrupting quorum sensing and biofilm formation.

Li S, Yang Q, Cheng B, Liu Y, Zhou S, Ai X, Dong

J. Biofouling. 2023 Aug-Sep;39(8):867-878. doi: 10.1080/08927014.2023.2279998. PMID: 37968931

Aeromonas hydrophila is an opportunistic pathogen that can cause a number of infectious diseases in fish and is widely distributed in aquatic environments. Antibiotics are the main approach against *A. hydrophila* infections, while the emergence of resistant bacteria limits the application of antibiotics. Here, quorum-sensing (QS) was defined as the target and the inhibitory effects of neem oil against QS of *A. hydrophila* was studied. The results showed that neem oil could dose-dependently reduce aerolysin, protease, lipase, acyl-homoserine lactones (AHLs), biofilm and swarming motility at sub-inhibitory concentrations. Results of real-time PCR demonstrated that neem oil could down-regulate the transcription of *aerA*, *ahyI* and *ahyR*. Moreover, neem oil showed significant protections to A549 cells and a fish infection model. Taken together, these results indicated that neem oil could be chosen as a promising candidate for the treatment of *A. hydrophila* infections.

Neem- Component & Pathway Analysis

Optimization studies on batch extraction of phenolic compounds from *Azadirachta indica* using genetic algorithm and machine learning techniques.

Patil SS, Deshannavar UB, Gadekar-Shinde SN, Gadagi AH, Kadapure SA.

Heliyon. 2023 Nov 4;9(11):e21991. doi: 10.1016/j.heliyon.2023.e21991. PMID: 38027702

Phenolic compounds play a crucial role as secondary metabolites due to their substantial biological activity and medicinal value. These compounds are present in various parts of plant species. This study focused on solid-liquid batch extraction to recover total phenolic compounds from *Azadirachta indica* leaves. The experimental design was based on the Taguchi L₁₆ array, considering four independent factors: extraction time, temperature, particle size, and solid-to-solvent ratio. Among these factors, the particle size exerted the maximum influence. Particle size inversely affects the yield of total phenolic content (TPC), while temperature, time, and solid-to-liquid ratio have a direct impact. The process factors concerned were investigated both experimentally and through machine learning techniques. Support vector regression (SVR) and random forest method (RFM) algorithms were utilized for predicting TPC, while a genetic algorithm (GA) was employed to derive optimal process parameters. The GA predicts the optimal extraction factors, yielding the maximum TPC. During this study, these factors were the following: particle size of 0.15 mm, extraction time of 40 min, solid-to-liquid ratio of 1:25 g/mL, and a temperature of 55 °C, with a predicted value of 23.039 mg GAE/g of plant material. Notably, in this study, the SVR values of TPC yield closely matched the experimental values for the training and test data set when compared with the random forest method values.

Deciphering the key pathway for triterpenoid biosynthesis in *Azadirachta indica* A. Juss.: a comprehensive review of omics studies in nature's pharmacy.

Dave N, Iqbal A, Patel M, Kant T, Yadav VK, Sahoo DK, Patel A.

Front Plant Sci. 2023 Nov 7;14:1256091. doi: 10.3389/fpls.2023.1256091. PMID: 38023910

Since ancient times, *Azadirachta indica*, or Neem, has been a well-known species of plant that produces a broad range of bioactive terpenoid chemicals that are involved in a variety of biological functions. Understanding the molecular mechanisms that are responsible for the biosynthesis and control of terpenoid synthesis is majorly dependent on successfully identifying the genes that are involved in their production. This review provides an overview of the recent developments concerning the identification of genes in *A. indica* that are responsible for the production of terpenoids. Numerous candidate genes encoding enzymes that are involved in the terpenoid biosynthesis pathway have been found through the use of transcriptomic and genomic techniques. These candidate genes include those that are responsible for the precursor synthesis, cyclization, and modification of terpenoid molecules. In addition, cutting-edge omics technologies, such as metabolomics and proteomics, have helped to shed light on the intricate regulatory networks that govern terpenoid biosynthesis. These networks are responsible for the production of terpenoids. The identification and characterization of genes involved in terpenoid biosynthesis in *A. indica* presents potential opportunities for genetic engineering and metabolic engineering strategies targeted at boosting terpenoid production as well as discovering novel bioactive chemicals.

Neem for Sustainable Environment & Green Synthesis

Experimental studies on thermal and FTIR characterisation of bio-degradable neat neem gum and epoxy resin for composite material applications.

SundaraPandian G, K A.

Nat Prod Res. 2023 Nov 7:1-10. doi: 10.1080/14786419.2023.2275266. PMID: 37933601

This article aims to assess the suitability of natural neem gum in various composite material applications in place of epoxy resin. The assessment was done by thermal characterisation, experimental study and comparative analysis of thermal behaviour, Fourier transform IR spectroscopy (FTIR) characterisation and comparison of functional groups and mechanical properties of neat epoxy and neat neem resins. To study and compare thermal behaviour differential scanning calorimetry (DSC), thermogravimetric (TG) and relative derivative TG (DTG) analysis were conducted. The glass transition temperatures, exothermic and endothermic peaks, curing of thermosetting epoxy and crystallisation of polymeric neem, value of % cure and mass change or mass loss concerning temperature of both the resins were experimentally determined and comparative analysis was conducted to find the suitability of neem resin in composite material applications in place of epoxy resin. Functional groups of neem gum were identified and mechanical properties such as bond strength, toughness, rigidity and ductility were characterised and compared with that of epoxy resin by conducting FTIR.

Study on the Isotherms, Kinetics, and Thermodynamics of Adsorption of Crystal Violet Dye Using Ag-NPs-Loaded Cellulose Derived from Peanut-Husk Agro-Waste.

Aljeddani GS, Alghanmi RM, Hamouda RA.

Polymers (Basel). 2023 Nov 13;15(22):4394. doi: 10.3390/polym15224394. PMID: 38006118

A huge amount of textile dyes are released as industrial waste into the environment each year, which alters the water's natural appearance and causes toxicity and carcinogenicity in the human body. Peanut husk is considered an agro-waste and contains many valuable compounds, such as cellulose. Different concentrations of cellulose were extracted from peanut husk and then loaded with bio-silver nanoparticles, which were fabricated using neem leaves (*Azadirachta indica*) as a reducing agent to form Ag-cellulose nanocomposites (Ag-Cell-NCMs). Different devices were used to characterize Ag-Cell-NCMs. The TEM images displayed that the size of Ag-Cell-NCMs ranged between 13.4 and 17.4 nm after dye adsorption. The Ag-Cell-NCMs were used to adsorb toxic dyes such as crystal violet (CV). Different parameters were applied, such as the ratio of cellulose to Ag-NPs, pH, contact time, adsorbent dose, dye concentration, and the temperature required to reach the optimization conditions to remove CV dye from the aqueous solution. Different kinetics and isotherm models were applied to the experimental data to explain the mechanism of the adsorption process. The adsorption of CV on Ag-Cell-NCMs follows the

pseudo-second order, and the best-fit isotherm was the Langmuir isotherm. The new composite was tested for the possibility of dye desorption and ability to be reused several times, and we found that the new nanocomposite can be reused for multiple adsorptions and there is a possibility of dye desorption.

Investigation on the physico-chemical properties of soil and mineralization of three selected tropical tree leaf litter.

Thamizharasan A, Rajaguru VRR, Gajalakshmi S, Lim JW, Greff B, Rajagopal R, Chang SW, Ravindran B, Awasthi MK.

Environ Res. 2023 Nov 24:117752. doi: 10.1016/j.envres.2023.117752. PMID: 38008202

Plant leaf litter has a major role in the structure and function of soil ecosystems as it is associated with nutrient release and cycling. The present study is aimed to understand how well the decomposing leaf litter kept soil organic carbon and nitrogen levels stable during an incubation experiment that was carried out in a lab setting under controlled conditions and the results were compared to those from a natural plantation. In natural site soil samples, *Anacardium occidentale* showed a higher value of organic carbon at surface (1.14%) and subsurface (0.93%) and *Azadirachta indica* exhibited a higher value of total nitrogen at surface (0.28%) and subsurface sample (0.14%). In the incubation experiment, *Acacia auriculiformis* had the highest organic carbon content initially (5.26%), whereas *A. occidentale* had the highest nitrogen level on 30th day (0.67%). The overall carbon-nitrogen ratio showed a varied tendency, which may be due to dynamic changes in the complex decomposition cycle. The higher rate of mass loss and decay was observed in *A. indica* leaf litter, the range of the decay constant is 1.26-2.22. The morphological and chemical changes of soil sample and the vermicast were substantiated using scanning electron microscopy (SEM) and Fourier transmission infrared spectroscopy (FT-IR).

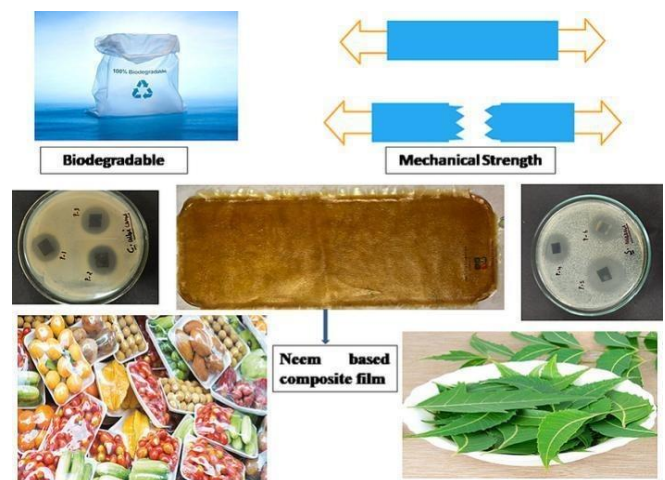
Neem for Food Packaging & Cosmetics

Utilization of marine and agro-waste materials as an economical and active food packaging: Antimicrobial, mechanical and biodegradation studies of O-Carboxymethyl chitosan/pectin/neem composite films.

Rani S, Lal S, Kumar S, ParvinKumar, Nagar JK, Kennedy JF.

Int J Biol Macromol. 2023 Nov 12:128038. doi: 10.1016/j.ijbiomac.2023.128038. PMID: 37963501

The present work deals with the eco-friendly preparation of highly degradable food packaging films consisting of O-CMC (O-Carboxymethyl Chitosan) and pectin, incorporated with neem (*Azadirachta indica*) leaves powder and extract. This study aimed to investigate the tensile properties, antimicrobial activity, biodegradability, and thermal behavior of the composite films. The results of tensile strength and elongation at break, showed that the incorporation of neem leaves powder improved the tensile properties (7.11 MPa) of the composite films compared to the neat O-CMC and pectin films (3.02 MPa). The antimicrobial activity of the films was evaluated against a panel of microorganisms including both gram-positive and gram-negative bacteria as well as fungi. The composite films exhibited excellent antimicrobial activity with a zone of inhibition (12-17.6 mm) against the tested microorganisms. The opacity of the composite films ranges from 1.14 to 4.40 mm⁻¹ and the addition of fiber causes a decrease in opacity value. Biodegradability studies were conducted by Soil burial method and the films demonstrated complete biodegradability within 75 days. The results of thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) of composite films show that they are thermally stable and might be used in food packaging.



Natural alternatives from your garden for hair care: Revisiting the benefits of tropical herbs.

Sang SH, Akowuah GA, Liew KB, Lee SK, Keng JW, Lee SK, Yon JA, Tan CS, Chew YL.

Heliyon. 2023 Nov 7;9(11):e21876. doi: 10.1016/j.heliyon.2023.e21876. PMID: 38034771

Hair shampoos containing botanical ingredients without synthetic additives, such as parabens, petrochemicals, sulfates and silicones are more skin- and environmentally friendly. In recent years, there is a growing demand for shampoo products with botanical extracts. Shampoos with botanical extracts are well-known for their perceived health benefits. They are also generally milder, non-toxic, natural, and less likely to disrupt the hair and scalp's natural pH and oil balance. Many also believe that shampoos with botanical origins have higher standards of quality. Numerous botanical extracts had been used as natural active ingredients in cosmetic formulations to meet consumer demands. In this review, we have revisited six tropical plants commonly added as natural active ingredients in shampoo formulations: *Acacia concinna*, *Camellia oleifera*, *Azadirachta indica*, *Emblica officinalis*, *Sapindus mukorossi*, and *Garcinia mangostana*. These plants have been traditionally used for hair care, and scientific research has shown that they exhibit relevant physicochemical properties and biological activities that are beneficial for hair care and scalp maintenance.

Neem for Human Health

A comparative evaluation of antimicrobial property of traditional and three alternative disinfectants on irreversible hydrocolloid impressions: An *in vitro* study.

Anitha T, Sanketh AK, Kalavathy N, Shetty MM, Kumar PR, Venkataramani A.

J Indian Prosthodont Soc. 2023 Jul-Sep;23(3):294-300. doi: 10.4103/jips.jips_364_22.

PMID: 37929369

Aim: The aim was to compare the efficacy of various herbal disinfectants on irreversible hydrocolloid impressions and to investigate the effectiveness of three herbal disinfectants and a chemical disinfectant against particular pathogens. **Settings and design:** In vitro -a comparative study. **Materials and methods:** The following methodology was followed to achieve the objectives. Four maxillary impressions were made for each selected patient with irreversible hydrocolloid impression material. The preinfection swabs were taken from impression sites of teeth 17, 13, 27, and 23 (FDI system of tooth numbering). The impressions were immersed in all four different disinfectants such as 2% glutaraldehyde, Aloe vera solution, 50% neem oil, and apple vinegar solution, then the postinfection swabs were taken from the same sites 17,13,27,23 and then cultured onto sheep blood agar and examined for growth, and colony forming units (CFUs) of *Streptococcus viridans*, *Streptococcus mutans*, *Streptococcus sanguis*, and *Actinomyces viscosus*. The comparative analysis was done for the preinfection and postinfection values in each study group. **Statistical analysis used:** Descriptive analysis, Kruskal Wallis test, Mann Whitney post hoc test, Wilcoxon signed rank test. **Results:** The results revealed that the mean CFUs of *S. viridans*, *S. mutans*, *S. sanguis*, and *A. viscosus* during postinfection samples were statistically significant when compared to preinfection samples. Multiple comparison of the mean CFUs of all 4 microorganisms in the control group and in 50% Neem oil group was significantly lesser compared to A. vera and Apple Vinegar group. **Conclusion:** CFUs of *S. viridans*, *S. mutans*, *S. sanguis*, and *A. viscosus* significantly decreased in the 50% neem oil group as well as the control group. As a result, 50% Neem oil was a viable option for disinfecting alginate impressions.

Screening of potential inhibitors of *Leishmania major* N-myristoyltransferase from *Azadirachta indica* phytochemicals for leishmaniasis drug discovery by molecular docking, molecular dynamics simulation and density functional theory methods.

Tewari D, Rawat K, Bisht A, Almoyad MAA, Wahab S, Chandra S, Pande V.

J Biomol Struct Dyn. 2023 Nov 3:1-18. doi: 10.1080/07391102.2023.2279281.

PMID: 37922151

Leishmaniasis is one of the most neglected parasitic diseases worldwide. The toxicity of current drugs used for its treatment is a major obstacle to their effectiveness, necessitating the discovery and development of new therapeutic agents for better disease control. In *Leishmania* parasites, N-Myristoyltransferase (NMT) has been identified as a promising target for drug development. Thus, exploring well-known medicinal plants such as *Azadirachta indica* and their phytochemicals can offer a diverse range of treatment

options, potentially leading to disease prevention and control. To assess the therapeutic potential of these compounds, their ADMET prediction and drug-likeness properties were analyzed. The top 4 compounds were selected which had better and significantly low binding energy than the reference molecule QMI. Based on the binding energy score of the top compounds, the results show that Isonimocinolide has the highest binding affinity (-9.8 kcal/mol). In addition, a 100 ns MD simulation of the four best compounds showed that Isonimocinolide and Nimbolide have good stability with LmNMT. These compounds were then subjected to MMPBSA (last 30 ns) calculation to analyze protein-ligand stability and dynamic behavior. Nimbolide and Meldenin showed lowest binding free energy i.e. -84.301 kJ/mol and -91.937 kJ/mol respectively. DFT was employed to calculate the HOMO-LUMO energy gap, global reactivity parameters, and molecular electrostatic potential of all hit molecules. The promising results obtained from MD simulations and MMPBSA analyses provide compelling evidence for the potential use of these compounds in future drug development efforts for the treatment of leishmaniasis.

Exploring Medicinal Herbs' Therapeutic Potential and Molecular Docking Analysis for Compounds as Potential Inhibitors of Human Acetylcholinesterase in Alzheimer's Disease Treatment.

Farihi A, Bouhrim M, Chigr F, Elbouzidi A, Bencheikh N, Zrouri H, Nasr FA, Parvez MK, Alahdab A, Ahami AOT.

Medicina (Kaunas). 2023 Oct 12;59(10):1812. doi: 10.3390/medicina59101812.PMID: 37893530

Background and Objectives: Alzheimer's disease (AD) stands as a pervasive neurodegenerative ailment of global concern, necessitating a relentless pursuit of remedies. This study aims to furnish a comprehensive exposition, delving into the intricate mechanistic actions of medicinal herbs and phytochemicals. Furthermore, we assess the potential of these compounds in inhibiting human acetylcholinesterase through molecular docking, presenting encouraging avenues for AD therapeutics. *Materials and Methods:* Our approach entailed a systematic exploration of phytochemicals like curcumin, gedunin, quercetin, resveratrol, nobiletin, fisetin, and berberine, targeting their capability as human acetylcholinesterase (AChE) inhibitors, leveraging the PubChem database. Diverse bioinformatics techniques were harnessed to scrutinize molecular docking, ADMET (absorption, distribution, metabolism, excretion, and toxicity), and adherence to Lipinski's rule of five. *Results:* Results notably underscored the substantial binding affinities of all ligands with specific amino acid residues within AChE. Remarkably, gedunin exhibited a superior binding affinity (-8.7 kcal/mol) compared to the reference standard. *Conclusions:* These outcomes accentuate the potential of these seven compounds as viable candidates for oral medication in AD treatment. Notably, both resveratrol and berberine demonstrated the capacity to traverse the blood-brain barrier (BBB), signaling their aptitude for central nervous system targeting. Consequently, these seven molecules are considered orally druggable, potentially surpassing the efficacy of the conventional drug, donepezil, in managing neurodegenerative disorders.

Antimicrobial properties of green synthesized silver and chitosan nanocomposites.

S D, Parameswari BD, Annapoorni H, Shankar MS, S RK.

Bioinformation. 2023 Jun 30;19(6):745-748. doi: 10.6026/97320630019745. eCollection 2023.PMID: 37885782

An eco-friendly and simple approach was carried out for the synthesis of silver-chitosan nanocomposites using *Azadirachta indica* and fluconazole-mediated aqueous extract. This extract acted as a reducing agent as well as a capping agent for the green synthesis of silver nanoparticles. Chitosan nanoparticles on the other hand were synthesized from the deacetylation of the chitin matrix. To confirm the nanoparticle synthesis, a UV- A visible spectrophotometer was used and FTIR analysis confirmed the presence of functional groups in the prepared extract. The morphological characteristics of silver and chitosan nanoparticles and as nano-composites were studied and confirmed using scanning electron microscopy (SEM) analysis. The synthesized silver-chitosan nanocomposites were subjected to well-loaded agar plates for the evaluation of antibacterial properties against the *Streptococcus mutans* and *Candida albicans* for their antifungal properties. The synthesized silver and chitosan nanoparticles showed antibacterial and antifungal activities against common oral micro flora such as *Streptococcus mutans* and *Candida albicans* which were measured using the zone of inhibition method. This approach is a one-step, economical and eco-friendly, biocompatible, and effective alternative for nanoparticle synthesis for various prosthetic applications.

Computational Approaches to Designing Antiviral Drugs against COVID-19: A Comprehensive Review.

Singh MP, Singh N, Mishra D, Ehsan S, Chaturvedi VK, Chaudhary A, Singh V, Vamanu E.

Curr Pharm Des. 2023 Nov 1. doi: 10.2174/0113816128259795231023193419. PMID: 37916490

The global impact of the COVID-19 pandemic caused by SARS-CoV-2 necessitates innovative strategies for the rapid development of effective treatments. Computational methodologies, such as molecular modelling, molecular dynamics simulations, and artificial intelligence, have emerged as indispensable tools in the drug discovery process. This review aimed to provide a comprehensive overview of these computational approaches and their application in the design of antiviral agents for COVID-19. Starting with an examination of ligand-based and structure-based drug discovery, the review has delved into the intricate ways through which molecular modelling can accelerate the identification of potential therapies. Additionally, the investigation extends to phytochemicals sourced from nature, which have shown promise as potential antiviral agents. Noteworthy compounds, including gallic acid, naringin, hesperidin, *Tinospora cordifolia*, curcumin, nimbin, azadironic acid, nimbionone, nimbionol, and nimocinol, have exhibited high affinity for COVID-19 Mpro and favourable binding energy profiles compared to current drugs. Although these compounds hold potential, their further validation through in vitro and in vivo experimentation is imperative. Throughout this exploration, the review has emphasized the pivotal role of computational biologists, bioinformaticians, and biotechnologists in driving rapid advancements in clinical research

and therapeutic development. By combining state-of-the-art computational techniques with insights from structural and molecular biology, the search for potent antiviral agents has been accelerated. The collaboration between these disciplines holds immense promise in addressing the transmissibility and virulence of SARS-CoV-2.

Mitigating the Public Health Issues Caused by the Filarial Vector, *Culex quinquefasciatus* (Diptera: Culicidae) Through Phytocontrol and Larval Source Marker Management.

Chatterjee S, Sarkar B, Bag S, Biswal D, Mandal A, Bandyopadhyay R, Sarkar Paria D, Chatterjee A, Saha NC.

Appl Biochem Biotechnol. 2023 Nov 24. doi: 10.1007/s12010-023-04747-9. PMID: 37999898

Failure of conventional mosquito control strategies to curb the population of vectors have made the humans vulnerable to serious medical problems transmitted by them. This effect has been compounded by global climate change enabling the mosquitoes to cross geographical boundaries and cause trouble in regions where they were initially not found. As such, the scientific community has been compelled to devise alternative and innovative strategies of mosquito control that can be integrated with the conventional practices to implement multi-phasic approach of vector management. *Culex quinquefasciatus* is one such mosquito species that is reported to be one of the primary vectors of lymphatic filariasis and many other diseases of global health concern. However, not much is known about its breeding habitat ecology and microbial properties that have enabled the species to achieve reproductive success in urbanized habitats. The current investigation was carried out at Digha, West Bengal, India. The region, despite being endemic for lymphatic filariasis, has rarely been explored for its mosquito diversity and/or their breeding habitat characteristics. Therefore, these were attempted. For survey and sampling, seven villages were chosen, namely, Duttapur, Jatimati, Champabani, Padima, Gobindabasan, Bhagibahampur and Palsandapur. The study showed that *Cx. quinquefasciatus* is the dominant mosquito species at the sampling sites with the highest density of their larvae being recorded from man-made structures like drains and pools close to human habitations and livestock. The study was, therefore, restricted to *Cx. quinquefasciatus*. Seasonal abundance showed that they were most prevalent in the monsoon followed by summer. The physicochemical characterization showed their larvae to prefer almost neutral pH (6.9 to 7.3), low chloride concentration (98 to 258 ppm) and turbidity. As far as other parameters are concerned, they were tolerant towards a wide range allowing them to adapt varied habitats in the study areas. The bacterial profiling of their natural habitat waters revealed the presence of *Paenibacillus nanensis* DGX1(OQ690670), *Bacillus cereus* DGX2(OQ690675), *Bacillus* sp. DGX3(OQ690700) and *Escherichia coli* DGX4(OQ690701). *Bacillus cereus* was found to have high oviposition attractant properties in oviposition assays. *Bacillus cereus* was also obtained from the midgut of third instar larvae indicating that they had entered from the surrounding medium and colonized the larval gut. Subsequent tests exhibited the roles of *B. cereus* in larval development. Numerous plant products have been reported either as insecticides for killing larvae or adult mosquitoes or as repellents for mosquito biting and the best alternatives for mosquito control. Larvicidal potential of emulsified neem oil formulation against the field collected

3rd instar larvae of *Culex quinquefasciatus* mosquito under laboratory conditions was also evaluated. The information thus obtained can be pooled to generate larval source markers and larval source management practices by altering their habitats that cannot be removed. Furthermore, the time of implementation of these strategies can also be planned.

Azadirachtin Attenuates Carcinogen Benzo(a) Pyrene-Induced DNA Damage, Cell Cycle Arrest, Apoptosis, Inflammatory, Metabolic, and Oxidative Stress in HepG2 Cells.

John A, Raza H.

Antioxidants (Basel). 2023 Nov 14;12(11):2001. doi: 10.3390/antiox12112001. PMID: 38001854

Azadirachtin (AZD), a limonoid from the versatile, tropical neem tree (*Azadirachta indica*), is well known for its many medicinal, and pharmacological effects. Its effects as an antioxidant, anti-inflammatory, and anti-cancer agent are well known. However, not many studies have explored the effects of AZD on toxicities induced by benzo(a)pyrene (B(a)P), a toxic component of cigarette smoke known to cause DNA damage and cell cycle arrest, leading to different kinds of cancer. In the present study, using HepG2 cells, we investigated the protective effects of Azadirachtin (AZD) against B(a)P-induced oxidative/nitrosative and metabolic stress and mitochondrial dysfunction. Treatment with 25 μ M B(a)P for 24 h demonstrated an increased production of reactive oxygen species (ROS), followed by increased lipid peroxidation and DNA damage presumably, due to the increased metabolic activation of B(a)P by CYP 450 1A1/1A2 enzymes. We also observed intrinsic and extrinsic apoptosis, alterations in glutathione-dependent redox homeostasis, cell cycle arrest, and inflammation after B(a)P treatment. Cells treated with 25 μ M AZD for 24 h showed decreased oxidative stress and apoptosis, partial protection from DNA damage, and an improvement in mitochondrial functions and bioenergetics. The improvement in antioxidant status, anti-inflammatory potential, and alterations in cell cycle regulatory markers qualify AZD as a potential therapeutic in combination with anti-cancer drugs.

Azadiradione, a Component of Neem Oil, Behaves as a Superoxide Dismutase Mimic When Scavenging the Superoxide Radical, as Shown Using DFT and Hydrodynamic Voltammetry.

Sakib R, Caruso F, Belli S, Rossi M.

Biomedicines. 2023 Nov 18;11(11):3091. doi: 10.3390/biomedicines11113091. PMID: 38002091

The neem tree, *Azadirachta indica*, belongs to the Meliaceae family, and its use in the treatment of medical disorders from ancient times to the present in the traditional medical practices of Asia, Africa and the Middle East is well-documented. Neem oil, extracted from the seeds of the fruit, is widely used, with promising medicinal benefits. Azadiradione, a principal antioxidant component of the seeds of *A. indica*, is known to reduce oxidative stress and has anti-inflammatory effects. To directly measure the antioxidant ability of neem oil, we used Rotating Ring Disk Electrode (RRDE) hydrodynamic voltammetry to quantify how it can scavenge superoxide radical anions. The results of these experiments show that neem oil is approximately 26 times stronger than other natural products, such as olive oil, propolis and black seed oil, which were previously measured using this method.

Next, computational Density Functional Theory (DFT) methods were used to arrive at a mechanism for the scavenging of superoxide radical anions with azadiradione. Our work indicates that azadiradione is an effective antioxidant and, according to our DFT study, its scavenging of the superoxide radical anion occurs through a reaction mechanism in which azadiradione mimics the antioxidant action of superoxide dismutase (SOD). In this mechanism, analogous to the SOD enzymatic reaction, azadiradione is regenerated, along with the production of two products: hydrogen peroxide and molecular oxygen. This antioxidant process provides an explanation for azadiradione's more general and protective biochemical effects.

In vivo antiangiogenic effect of nimbolide, trans-chalcone and piperine for use against glioblastoma.

Senrung A, Tripathi T, Yadav J, Janjua D, Chaudhary A, Chhokar A, Aggarwal N, Joshi U, Goswami N, Bharti AC.

BMC Cancer. 2023 Nov 30;23(1):1173. doi: 10.1186/s12885-023-11625-4.PMID: 38036978

Background: Angiogenesis is an important hallmark of Glioblastoma (GBM) marked by elevated vascular endothelial growth factor-A (VEGF-A) and its receptor 2 (VEGFR-2). As previously reported nimbolide (NBL), trans-chalcone (TC) and piperine (PPR) possess promising antiangiogenic activity in several cancers however, their comparative efficacy and mechanism of antiangiogenic activity in GBM against VEGFR-2 has not been elucidated. **Methods:** 2D and 3D spheroids cultures of U87 (Uppsala 87 Malignant Glioma) were used for evaluation of non-cytotoxic dose for anti-angiogenic activity. The antiangiogenic effect was investigated by the GBM U87 cell line bearing chick CAM model. Excised U87 xenografts were histologically examined for blood vascular density by histochemistry. Reverse transcriptase polymerase chain reaction (RT-PCR) was used to detect the presence of avian and human VEGF-A and VEGFR-2 mRNA transcripts. **Results:** Using 2D and 3D spheroid models, the non-cytotoxic dose of NBL, TC and PPR was $\leq 11 \mu\text{M}$. We found NBL, TC and PPR inhibit U87-induced neoangiogenesis in a dose-dependent manner in the CAM stand-alone model as well as in CAM U87 xenograft model. The results also indicate that these natural compounds inhibit the expression of notable angiogenic factors, VEGF-A and VEGFR-2. A positive correlation was found between blood vascular density and VEGF-A as well as VEGFR-2 transcripts. **Conclusion:** Taken together, NBL, TC and PPR can suppress U87-induced neoangiogenesis via a reduction in VEGF-A and its receptor VEGFR-2 transcript expression at noncytotoxic concentrations. These phytochemicals showed their utility as adjuvants to GBM therapy, with Piperine demonstrating superior effectiveness among them all.

Neem in Veterinary Science

The Effect of Monensin vs. Neem, and Moringa Extracts on Nutrient Digestibility, Growth Performance, Methane, and Blood Profile of Merino Lambs.

Preez DAD, Akanmu AM, Adejoro FA, Hassen A.
Animals (Basel). 2023 Nov 14;13(22):3514. doi: 10.3390/ani13223514.PMID: 38003132

Plant secondary compounds are potential rumen modifiers that can improve nutrient utilization in ruminant animals. This study evaluated the effect of Moringa (*Moringa oleifera*) and Neem (*Azadirachta indica*) leaf extracts on nutrient digestibility, growth performance, and enteric methane production in South African Mutton Merino lambs. Forty 4-month-old ram lambs with a mean body weight of 35 ± 2.2 kg were blocked by weight and from each block, lambs were randomly allocated into one of the following treatments: (i) diet only (fed a total mixed ration TMR-negative control), (ii) Monensin (fed TMR containing Monensin sodium, 15 mg/kg DM), (iii) Moringa (fed TMR, drenched with Moringa extract 50 mg/kg feed DM intake), and (iv) Neem (fed TMR, drenched with Neem extract 50 mg/kg DM intake). Extracts were administered via oral drenching at a concentration determined based on the previous week's feed intake. There were no differences in dry matter intake, average daily gain, feed conversion efficiency, digestibility, and nitrogen retention across the treatments. However, the extracts tended to reduce methane emitted both in g/head/day ($p < 0.08$) and g/ kg dry matter intake ($p < 0.07$). Extracts did not influence any of the blood metabolites in the ram lambs. Although the benefits of utilizing these medicinal plants as rumen modifiers under prolonged feeding conditions is justified, further evaluation is recommended to test Moringa and Neem leaf extracts at higher inclusion levels. Our research group is currently exploring a variety of phyto-genic tools for the identification and standardization of key bioactive compounds linked to methane inhibition, in these leaf extracts.