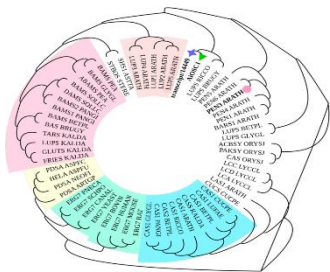




Neem Research Newsletter

Volume 4, Issues 1-3, 2024



WORLD NEEM ORGANISATION (WNO)

From
The Editor's Desk

The year 2024 has started with sustained interest in neem research on various fronts. This newsletter combines three issues in one, covering the effects of neem in agriculture, environment, food and cosmetic industry and human health.

Introduction of salt stress as an elicitor was found to enhance the synthesis of azadirachtin. Proteomics analysis revealed that key proteins related to defence, energy, cell structure, redox, transcriptional and photosynthesis were predominantly differentially regulated. A field study carried out in the subsequent wet (2021) and dry (2022) seasons in a double-cropped rice system showed that application of neem-coated urea during the wet season resulted in the highest economic yield. The decolorization of cottonseed oil with activated carbons from neem and cotton husks was shown to eliminate undesirable pigments in oil in addition to managing by-products of neem and cottonseed processing, which would otherwise cause environmental pollution. A microfluidic paper-based analytical device was developed to detect azadirachtin by a colorimetric assay. Neem oil was shown to be a strong oviposition deterrent and useful in the pest control of moths. Application of neem leaf extract together with gibberelins and serine improved wheat growth and yield. Neem leaf extract exerted antihelminthic effects against parasites of fishes.

The potential of neem tree waste as an adsorbent for wastewater treatment has been reviewed. Combination of neem, sisal, and glass fiber was found effective in environmental remediation. A low-cost, environmentally friendly method for producing tungsten trioxide and tantalum doped nanoparticles using neem leaf extract has been developed. The potential applicability of lemon peel pectin-chitosan-neem leaf extract blend films in biodegradable food packaging has been reported. Combination of neem and rosemary showed superior efficacy compared to ketoconazole against hair loss and dandruff.

Eleven phytochemicals from neem were demonstrated to exert inhibitory effects against multidrug resistance induced by *Pseudomonas aeruginosa*. The antimicrobial activity of a nanoemulsion containing neem and lavender oils with polycaprolactone was found to be effective against airborne bacteria. Neem leaf extract mitigated bacterial infection following head and neck surgery. A large-scale study was conducted to assess community and health worker perspectives on malaria in Meghalaya, India in order to cover the last mile of elimination by 2030. In an interesting rare clinical case of a 77-year-old man neem oil was effective against arthritis and lower back pain. 1 Primary Wound Dressing© as an active composed of neem oil and the oily extracts of *Hypericum perforatum* (L.) flowers, showed therapeutic efficacy as wound dressings. Chitosan and neem gum-based polysaccharide polyelectrolyte complex-based allantoin-loaded biocomposite film was designed for improved wound healing. Novel iron nanoparticles from neem and betel leaves extract combination were synthesized and characterized using response surface methodology-central composite design and coated with chitosan-curcumin as a biocompatible and contrast agent for magnetic resonance imaging. Neem was effective when used as a as a reducing and stabilizing agent to prepare protective sheets against x-radiation. Neem and tamarind gum-based extended-release matrix tablets were designed and found to be effective in drug delivery. Zinc oxide with neem is promising as root canal filling material in primary teeth. The neem phytochemical, epoxyazadiradione exerted synergistic effects in combination with the chemotherapeutic drug, paclitaxel against triple-negative breast cancer cells. The neem compound azadiradione was demonstrated to restore synaptic function in neurological disorders. Nimbolide, a neem limonoid modulated key components of DNA damage response signaling in cellular and animal models of oral cancer. The immunomodulatory effect of neem leaf glycoprotein was demonstrated in a preclinical model of oral cancer.

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



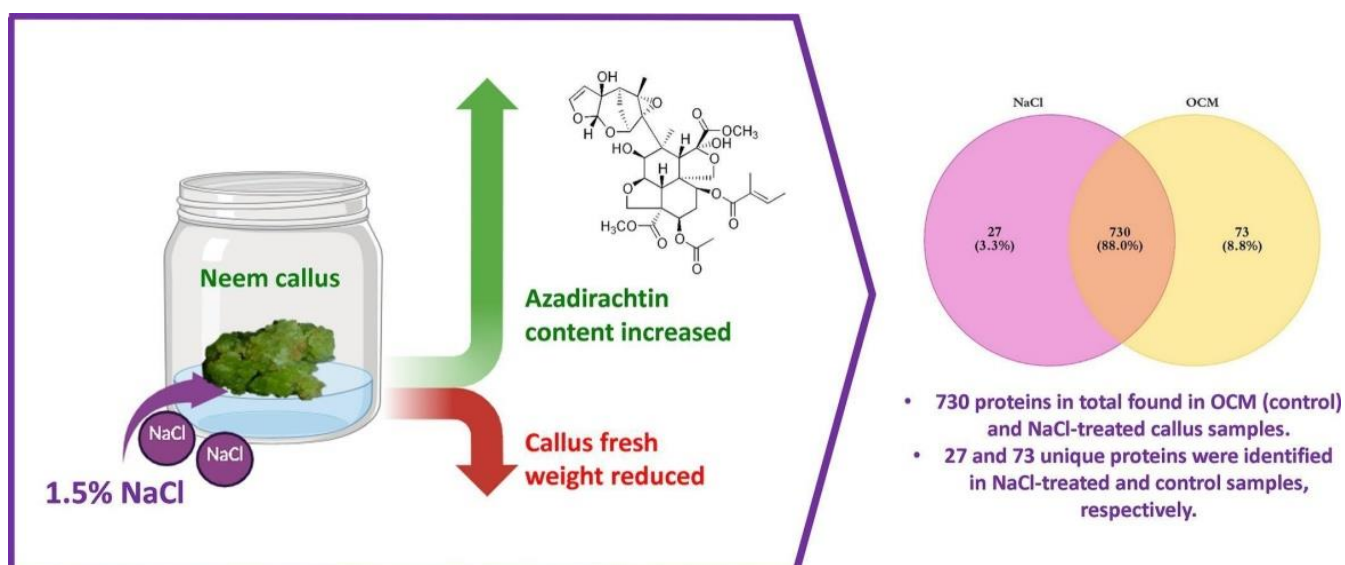
Neem in Agriculture & Aquaculture

Enhanced azadirachtin production in neem (*Azadirachta indica*) callus through NaCl elicitation: Insights into differential protein regulation via shotgun proteomics.

Omar SA, Ashokhan S, Abdul Majid N, Karsani SA, Lau BYC, Yaacob JS.

Pestic Biochem Physiol. 2024 Feb;199:105778. doi: 10.1016/j.pestbp.2024.105778. Epub 2024 Jan 11. PMID: 38458685

With their remarkable bioactivity and evolving commercial importance, plant secondary metabolites (PSMs) have gained significant research interest in recent years. Plant tissue culture serves as a credible tool to examine how abiotic stresses modulate the production of PSMs, enabling clear insights into plant stress responses and the prospects for controlled synthesis of bioactive compounds. *Azadirachta indica*, or neem has been recognized as a repository of secondary metabolites for centuries, particularly for the compound named azadirachtin, due to its bio-pesticidal and high antioxidant properties. Introducing salt stress as an elicitor makes it possible to enhance the synthesis of secondary metabolites, specifically azadirachtin. Thus, in this research, *in vitro* callus cultures of neem were micro-propagated and induced with salinity stress to explore their effects on the production of azadirachtin and identify potential proteins associated with salinity stress through comparative shotgun proteomics (LCMS/MS). To induce salinity stress, 2-month-old calli were subjected to various concentrations of NaCl (0.05-1.5%) for 4 weeks. The results showed that the callus cultures were able to adapt and survive in the salinity treatments, but displayed a reduction in fresh weight as the NaCl concentration increased. Notably, azadirachtin production was significantly enhanced in the salinity treatment compared to control, where 1.5% NaCl-treated calli produced the highest azadirachtin amount (10.847 ± 0.037 mg/g DW). The proteomics analysis showed that key proteins related to primary metabolism, such as defence, energy, cell structure, redox, transcriptional and photosynthesis, were predominantly differentially regulated (36 upregulated and 93 downregulated). While a few proteins were identified as being regulated in secondary metabolism, they were not directly involved in the synthesis of azadirachtin. In conjunction with azadirachtin elicitation, salinity stress treatment could therefore be successfully applied in commercial settings for the controlled synthesis of azadirachtin and other plant-based compounds. Further complementary omics approaches can be employed to enhance molecular-level modifications, to facilitate large-scale production of bioactive compounds in the future.



Thinking green: Insecticidal effect of biorational solutions against *Triatoma pallidipennis* Stal (Hemiptera: Triatominae).

Vargas-Abasolo R, Rivera-Duarte JD, Almaraz-Valle VM, Mejia-Mandujano M, Aguilar-Marcelino L, Córdoba-Aguilar A.

Acta Trop. 2024 Apr;252:107152. doi: 10.1016/j.actatropica.2024.107152. Epub 2024 Feb 19. PMID: 38382592

The control of triatomine vectors depends almost exclusively on conventional insecticides. These compounds can, nevertheless, cause negative effects on environmental and human health as well as induce resistance in triatomines. Therefore, we need to look for more sustainable alternatives. *Triatoma pallidipennis* is one of the main chagasic vectors in Mexico. We evaluated the insecticidal effectiveness of two oils (neem and cinnamon), and two desiccants (potassium salts of fatty acids and diatomaceous earth), on 3rd instar nymphs of *T. pallidipennis*. The laboratory test involved direct exposure of the treatments to the insects. We found that diatomaceous earths caused 80 % mortality of nymphs after 30 days. Meanwhile, the cumulative mortality for the other treatments did not exceed 50 %. When applied to inert surfaces, the powder formulation of diatomaceous earth demonstrated greater effectiveness than the aqueous suspension. Thus, diatomaceous earth could be a promising alternative for an environmentally friendly control of triatomines.

Reducing the environmental impact of rice production in subtropical India by minimising reactive nitrogen loss.

Chatterjee D, Das SR, Mohanty S, Muduli BC, Bhatia A, Nayak BK, Rees RM, Drewer J, Nayak AK, Adhya TK, Parameswaran C, Meher J, Mondal B, Sutton MA, Pathak H.

J Environ Manage. 2024 Mar;354:120261. doi: 10.1016/j.jenvman.2024.120261. Epub 2024 Feb 13. PMID: 38354608

The future of reactive nitrogen (N) for subtropical lowland rice to be characterised under diverse N-management to develop adequate sustainable practices. It is a challenge to increase the efficiency of N use in lowland rice, as N can be lost in various ways, e.g., through nitrous oxide (N₂O) or dinitrogen (N₂) emissions, ammonia (NH₃) volatilization and nitrate (NO₃⁻) leaching. A field study was carried out in the subsequent wet (2021) and dry (2022) seasons to assess the impacts of different N management strategies on yield, N use efficiency and different N losses in a double-cropped rice system. Seven different N-management practices including application of chemical fertilisers, liquid organic fertiliser, nitrification inhibitors, organic nutrient management and integrated nutrient management (INM) were studied. The application of soil test-based neem-coated urea (NCU) during the wet season resulted in the highest economic yield, while integrated nutrient management showed the highest economic yield during the dry season. Total N losses by volatilization of NH₃, N₂O loss and leaching were 0.06-4.73, 0.32-2.14 and 0.25-1.93 kg ha⁻¹, corresponding to 0.06-5.84%, 0.11-2.20% and 0.09-1.81% of total applied N, respectively. The total N-uptake in grain and straw was highest in INM (87-89% over control) followed by the soil test-based NCU (77-82% over control). In comparison, recovery efficiency of N was maximum from application of NCU + dicyandiamide during both the seasons. The N footprint of paddy rice ranged 0.46-2.01 kg N-eq. t⁻¹ during both seasons under various N management. Ammonia volatilization was the process responsible for the largest N loss, followed by N₂O emissions, and NO₃⁻ leaching in these subtropical lowland rice fields. After ranking the different N management practices on a scale of 1-7, soil test-based NCU was considered the best N management approach in the wet year 2021, while INM scored the best in the dry year 2022.

Activated carbons from open air and microwave-assisted impregnation of cotton and neem husks efficiently decolorize neutral cotton oil.

Chetima A, Nde Bup D, Kewir F, Wahaboua A.

Heliyon. 2024 Jan 5;10(1):e24060. doi: 10.1016/j.heliyon.2024.e24060. eCollection 2024 Jan 15. PMID: 38283249

The decolorization of cottonseed oil with activated carbons (ACs) from neem and cotton husks has a dual interest: elimination of undesirable pigments in oil and valorization of the husks; by-products of neem and cottonseed processing, which would otherwise be dumped along riverbanks and farms causing environmental pollution. ACs were produced from neem and cottonseed husks after acid impregnation assisted by microwave heating and in ambient air for the decolorization of neutral cottonseed oil. The experimental data were analyzed by the intraparticle diffusion and the pseudo-second-order kinetic models as well as the Langmuir and Freundlich isotherm models. The method of impregnation and carbonization time had dramatic effects on the specific surface area (800-1500 g/m²), the quantity of burn-off (50-70 %), and methylene blue index (300-5000 mg/g) values which indicated the potential of the prepared activated carbons in the bleaching of vegetable oil and in other applications such as environmental clean-up and in agriculture. Pigment adsorption increased with temperature for all ACs indicating that the decolorization process was endothermic. The quantity of adsorbent equally had a significant effect on the pigment adsorption process for all ACs. All the activated carbons prepared in this work were 30-80 % more efficient in pigment adsorption than bleaching earth that is normally used in decolorizing neutral cotton seed oil in industries. All tested models are adequate to describe pigment adsorption by the ACs. Both methods of preparation of ACs were effective for oil decolorization, but microwave impregnation is more appealing because it requires only 1 h compared to 6 h for ambient air. Optimum decolorization conditions were 90 °C for 40min and adsorbent concentration of 2 %.

Detection of azadirachtin from neem kernels using a paper-based sandwich sensor.

Sinu K, Savitha R, Ranjit B, Pushpavanam S.

Anal Methods. 2024 Feb 15;16(7):1034-1042. doi: 10.1039/d3ay02030d. PMID: 38265638

In this work, a microfluidic paper-based analytical device (μ PAD) was developed to detect the biopesticide azadirachtin (Aza) through a colorimetric assay. High precision estimation of Aza is classically carried out using high performance liquid chromatography (HPLC), which requires highly skilled personnel. Acidified vanillin is a commonly used colorimetric indicator in thin layer chromatography for detection of various phytochemicals. However, the assay involves concentrated acid, which limits the choice of paper substrates for paper-based sensors and raises safety concerns. In this work, we show how the assay can be extended from the liquid phase to a paper substrate. Glass microfiber (GMF) filter paper was found to be suitable paper as it was acid resistant; besides, its hydrophilicity enabled smooth flow of reagents. A microfluidic paper-based sensor (μ PAD) was developed by sandwiching 5 mm sized GMF dots between two parafilm sheets. We demonstrate the use of colorimetric assay on the μ PAD for on-site detection of Aza in neem kernels. The magenta color developed upon the reaction of acidified vanillin with Aza was captured using a smart-phone and analysed using RGB levels in the image. Calibration was established using neem kernel extract of known concentration. Linearity was seen in the concentration range of 5 to 25 mg L⁻¹ Aza. A limit of detection of 2.3 mg L⁻¹ was obtained using this method. The colorimetric assay showed a relative recovery of >85% when compared with the values obtained from HPLC. The stability of the reagents on the GMF sensor was investigated to understand the storage conditions and shelf life of the reagents and sensor. The present work demonstrates the development of a portable sensor for on-site detection of phytochemicals that can be an integral part of the agricultural supply chain.

Ovipositional responses of tortricid moths to sugars, salts and neem oil.

Amat C, Prasad R, Gemeno C.

Sci Rep. 2024 Jan 19;14(1):1677. doi: 10.1038/s41598-024-51972-1.PMID: 38243066

Oviposition is essential in the life history of insects and is mainly mediated by chemical and tactile cues present on the plant surface. Oviposition deterrents or stimulants can modify insect oviposition and be employed in pest control. Relatively few gustatory oviposition stimuli have been described for tortricid moths. In this study the effect of NaCl, KCl, sucrose, fructose and neem oil on the number of eggs laid by *Cydia pomonella* (L.), *Grapholita molesta* (Busck) and *Lobesia botrana* (Dennis & Schifermüller) was tested in laboratory arenas containing filter papers loaded with 3 doses of a given stimulus and solvent control. In general, salts increased oviposition at the mid dose (10^2 M) and sugars reduced it at the highest dose (10^3 mM), but these effects depended on the species. Neem oil dramatically reduced the number of eggs laid as the dose increased, but the lowest neem oil dose (0.1% v/v) increased *L. botrana* oviposition relative to solvent control. Our study shows that ubiquitous plant chemicals modify tortricid moth oviposition under laboratory conditions, and that neem oil is a strong oviposition deterrent. The oviposition arena developed in this study is a convenient tool to test the effect of tastants on the oviposition behavior of tortricid moths.

Role of gibberellins, neem leaf extract, and serine in improving wheat growth and grain yield under drought-triggered oxidative stress.

Hameed S, Atif M, Perveen S.

Physiol Mol Biol Plants. 2023 Nov;29(11):1675-1691. doi: 10.1007/s12298-023-01402-9. Epub 2023 Dec 21.PMID: 38162918

The foliar application of gibberellins (GA_3), neem leaf extract (NLE) and serine can be proven as effective growth regulating agents to counter drought stress-related deleterious effects. The literature about the collaborative role of these substances in foliar spray application under drought stress is not available to this date. No single report is available in literature on combine foliar application of GA_3 , NLE, and serine in improving wheat growth and yield under drought-triggered oxidative stress. The objective of this study was to induct tolerance against drought stress in order to sustain maximum growth and yield of wheat varieties (Anaj-2017 and Galaxy-2013) with foliar applications of GA_3 , NLE, and serine. The current field trial was designed to disclose the protective role of these substances in wheat varieties (Anaj-2017 and Galaxy-2013) under water-deficit stress. Two irrigation levels, i.e., control (normal irrigation) and water stress (water deficit irrigation), and 5 levels of GA_3 , NLE and serine i.e., control (water spray), GA_3 (10.0 ppm), NLE (10.0%), serine (9.5 mM), and mixture (GA_3 + NLE + serine) in a 1:1:1 ratio was applied. Application of these substances improved the pigments (Chlorophyll a, b), carotenoids, growth, biomass, and grain yield traits of both wheat varieties under water-deficit stress. Activities of antioxidant enzymes (POD, CAT and SOD), and non-enzymatic antioxidants (proline, total phenolic contents, anthocyanin and free amino acids) were up-regulated under drought stress and with foliar spray treatments. The foliar applications of these substances reduced the drought triggered overproduction of lipid peroxidation (MDA) and H_2O_2 . The study found that Galaxy-2013 variety is more tolerant to drought stress than Anaj-2017, while co-applied treatments (GA_3 + NLE + serine) were shown to be the most effective among all applications.

Phytochemical profiling and anthelmintic potential of extracts of selected tropical plants on parasites of fishes in Epe Lagoon.

Ukwa UD, Saliu JK, Akinsanya B.

Sci Rep. 2023 Dec 20;13(1):22727. doi: 10.1038/s41598-023-48164-8.PMID: 38123590

This research aims to study the anthelmintic properties of selected five (5) tropical plant extracts, ascertained margin of fish host safety in reference with praziquantel, a commonly used chemotherapeutics. Qualitative and quantitative analysis of Alligator pepper seeds (*Aframomum melegueta*), Moringa leaves (*Moringa oleifera*), Neem leaves (*Azadirachta indica*), Ginger bulbs (*Zingiber officinale*) and Garlic (*Allium sativum*) and their potencies in reference to praziquantel against *Clarias gariepinus* and different classes of helminth parasites were investigated. The results obtained show that the 70% ethanol extract had 80 to 100% presence of the phytochemical content, compared with the 100% aqueous and 100% ethanol extracts with 50 to 80% and 50 to 90%, respectively. Among the five tropical plants, the richest in saponin and flavonoids are alligator pepper and neem with alkaloids, tannin, flavonoid and saponin in ratios 1:1:3:9 and 1:1:4:3 respectively. While, moringa, garlic and ginger are rich in alkaloids with alkaloids, tannin, flavonoid and saponin in ratios, 8:1:10:1, 6:2:1:4 and 6:3:2:1, respectively. *Aframomum melegueta* and praziquantel showed above 70% potency (at 96 h LC₅) against all the classes of parasites; *Wenyonia* spp (cestode), *Procamallanus* spp (nematode), *Tenuisentis* spp (acanthocephalan), and *Electrotaenia* sp (cestode) as compared to the other plant extracts that showed above 70% potency (at 96 h LC₅) only against *Electrotaenia* spp. Sub-lethal Concentrations (96 h LC₅) of praziquantel and *Aframomum melegueta* on the juvenile fish host (12.36 mg/l and 9.9 mg/l respectively) were found to be 90.9% and 93.5% effective against adult *Electrotaenia* spp after 8 to 10 min of exposure. These concentrations were 78 to 85.7% and 89.7 to 88.4%, respectively, effective against the other classes of parasites after 18 to 25 min and 15 to 21 min of exposure. These concentrations were tested on the post juvenile of the fish to determine behavioral changes; there were no significant behavioral responses after 24 h of exposure. The effective concentrations indicate the widest margin of safety for the fish host.

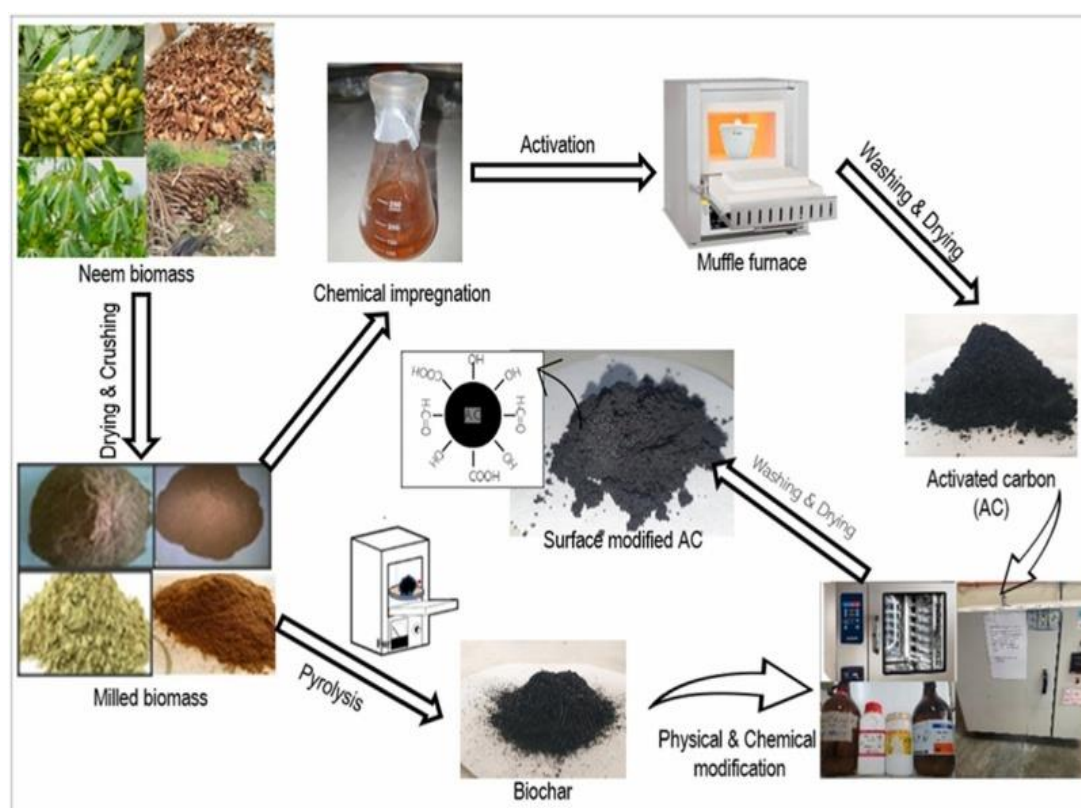
Neem for Sustainable Environment & Green Synthesis

A review of pre- and post-surface-modified neem (*Azadirachta indica*) biomass adsorbent: Surface functionalization mechanism and application.

Karim AR, Danish M, Alam MG, Majeed S, Alanazi AM.

Chemosphere. 2024 Mar;351:141180. doi: 10.1016/j.chemosphere.2024.141180. PMID: 38218237

In contemporary wastewater treatment industry, advanced oxidation techniques, membrane filtration, ion exchange, and reverse osmosis are used to treat chemically loaded wastewater. All these methods required highly toxic oxidizing chemicals, high capital investment in membrane/filter materials, and the installation of sophisticated equipment. Wastewater treatment through an adsorption process using biomass-based adsorbent is economical, user-friendly, and sustainable. Neem tree waste has been explored as an adsorbent for wastewater treatment. The chemical components in the neem biomass include carbohydrates, fat, fiber, cellulose, hemicellulose, and lignin, which support the functionalization of neem biomass. Moreover, adsorbent preparation from renewable resources is not only cost-effective and environmentally friendly but also helps in waste management for sustainable growth. Contemporary researchers explored the pre- and post-surface-modified neem biomass adsorbents in scavenging the pollutants from contaminated water. This review extensively explores the activation process of neem biomass, physical and chemical methods of surface modification mechanism, and the factors affecting surface modification. The pollutant removal through pre and post-surface-modified neem biomass adsorbents was also summarized. Furthermore, it also provides a comprehensive summary of the factors that affect the adsorption performance of the neem biomass-derived adsorbents against dyes, metal ions, and other emerging pollutants. Understanding the surface-modification mechanisms and the adsorption efficiency factor of adsorbents will help in harnessing their potential for more efficiently combatting environmental pollution and making strides toward a greener and more sustainable future.

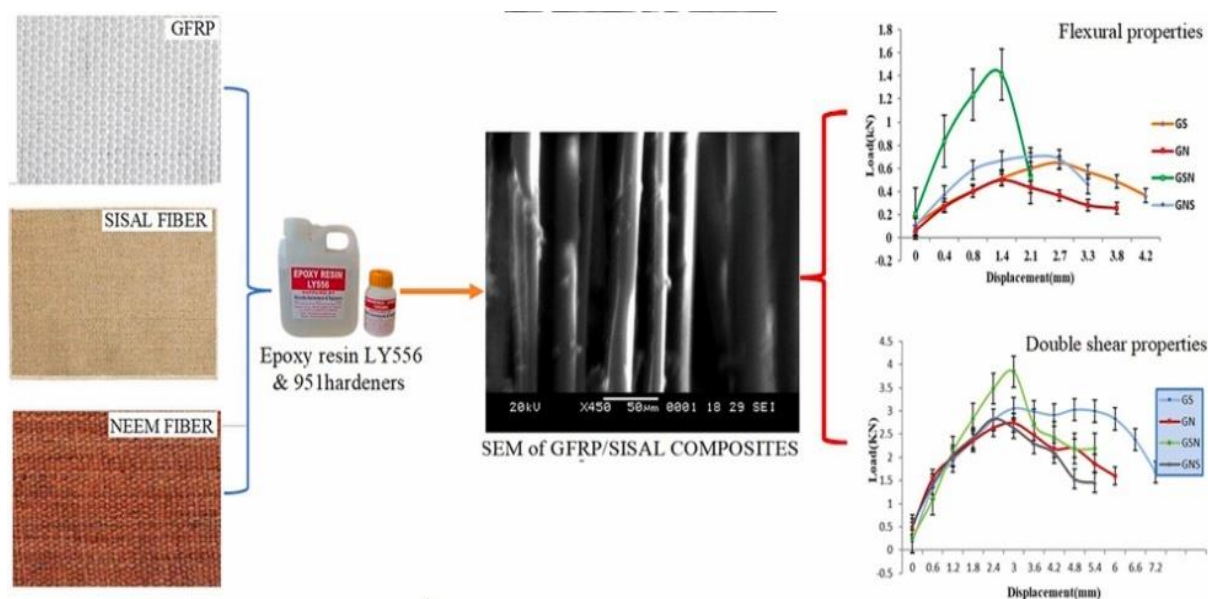


Bo-derived waste neem to enriching reinforced hybrid composite for environmental remediation.

Anbucheziyan G, Mubarak NM, Hussain Siddiqui MT, Malafaia G, Abnisa F.

Chemosphere. 2024 Feb;350:141055. doi: 10.1016/j.chemosphere.2023.141055. Epub 2024 Jan 2. PMID: 38176589

The utilization of natural fibres often entails a lesser environmental impact when compared to synthetic fibres. Biodegradable natural fibres minimize waste and pollution, and promote sustainability, but their weaker bonds limit their resilience. These issues can be addressed by customizing the composite's mechanical properties with natural and synthetic fibres. In this study, hybrid composites were created using the hand layup method with a novel dissimilar layer arrangement of neem (N), sisal (S), and glass (G) fibre and analyze its mechanical and thermal properties. Experimental observation shows that the GN composite had a higher maximum ultimate tensile strength of 26 N/mm² than the GS, GNS, and GSN composites. The GN composite had a percentage elongation of 6.33%, similar to the percentage elongation of the GS composite (6.833%), and it also had a higher ultimate shear strength of 50 MPa. The composite GS absorbed 6.6 J energy, higher than the composites GN, GNS, and GNS, which absorbed 6.1 J, 4.5 J, and 4.5 J, respectively. The fractured surface's SEM images were obtained and analyzed for failure. The results demonstrated that the hybridization was effective, and better properties can be obtained by combining neem, sisal, and glass fiber, and it can be used for other requirements, including strength, weight, cost, and ecological impact.



Proportional impact prediction model of coating material on nitrate leaching of slow-release Urea Super Granules (USG) using machine learning and RSM technique.

Swain SS, Khura TK, Sahoo PK, Chobhe KA, Al-Ansari N, Kushwaha HL, Kushwaha NL, Panda KC, Lande SD, Singh C.

Sci Rep. 2024 Feb 6;14(1):3053. doi: 10.1038/s41598-024-53410-8. PMID: 38321086

An accurate assessment of nitrate leaching is important for efficient fertiliser utilisation and groundwater pollution reduction. However, past studies could not efficiently model nitrate leaching due to utilisation of conventional algorithms. To address the issue, the current research employed advanced machine learning algorithms, viz., Support Vector Machine, Artificial Neural Network, Random Forest, M5 Tree (M5P), Reduced Error Pruning Tree (REPTree) and Response Surface Methodology (RSM) to predict and optimize nitrate leaching. In this study, Urea Super Granules

(USG) with three different coatings were used for the experiment in the soil columns, containing 1 kg soil with fertiliser placed in between. Statistical parameters, namely correlation coefficient, Mean Absolute Error, Willmott index, Root Mean Square Error and Nash-Sutcliffe efficiency were used to evaluate the performance of the ML techniques. In addition, a comparison was made in the test set among the machine learning models in which, RSM outperformed the rest of the models irrespective of coating type. Neem oil/ Acacia oil(ml): clay/sulfur (g): age (days) for minimum nitrate leaching was found to be 2.61: 1.67: 2.4 for coating of USG with bentonite clay and neem oil without heating, 2.18: 2: 1 for bentonite clay and neem oil with heating and 1.69: 1.64: 2.18 for coating USG with sulfur and acacia oil. The research would provide guidelines to researchers and policymakers to select the appropriate tool for precise prediction of nitrate leaching, which would optimise the yield and the benefit-cost ratio.

Facile green synthesis of novel tantalum doped tungsten trioxide for photocatalytic degradation: Correlation with COMSOL simulation.

Maryam I, Iqbal T, Syed A, Bahkali AH, Tehseen A, Afsheen S, Sultan MS.

Spectrochim Acta A Mol Biomol Spectrosc. 2024 Mar 26;314:124191. doi: 10.1016/j.saa.2024.124191. Online ahead of print. PMID: 38565046

The facile green synthesis technique is becoming more and more important, and it has been proposed as a potential substitute for chemical techniques. The current study describes a low-cost, environmentally friendly method for producing tungsten trioxide (WO_3) and tantalum (Ta) doped WO_3 nanoparticles that uses 15 % (w/v) *Azadirachta indica* (Neem) leaf extract and different concentrations of Ta dopant (1 to 5 %) due to its well-matched ionic radius with WO_3 . Various techniques FESEM, TEM, EDX, BET, UV-Vis and PL, XRD, and FTIR were used to illustrate the morphological, elemental, optical, structural, and vibrational analysis of the synthesized nanoparticles respectively. Interestingly, the band gap was significantly reduced to 1.88 eV by the addition of a dopant element. For 3 % Ta/ WO_3 , the average particle size was also reduced to 31.6 nm. The synthesized WO_3 nanoparticles employed in the current study have been used for photocatalytic activity purposes. Methylene blue (MB), one of the principal water pollutants, was degraded more quickly by the synthesized Ta/ WO_3 nanoparticles when exposed to UV radiation. Among them, 3 % Ta/ WO_3 gives significantly higher photodegradation 89 % attributed to the Burstein-Moss effect. The significant output of optimized nano-photocatalyst has been observed from the trapping experiment and reusability test. Furthermore, Zeta potential and TOC analysis have been taken to check the stability and mineralization performance. Additionally, the results of the simulation that was carried out using the finite element analysis approach in the RF module of COMSOL Multiphysics 5.3a are quite similar to the experimental findings. This simulation method made it easier for readers to understand the numerous aspects of the photocatalytic process that has been discussed here.

Neem for Food & Cosmetic Industry

Preparation and characterization of biodegradable food packaging films using lemon peel pectin and chitosan incorporated with neem leaf extract and its application on apricot fruit.

Firdaus S, Ahmad F, Zaidi S.

Int J Biol Macromol. 2024 Apr;263(Pt 2):130358. doi: 10.1016/j.ijbiomac.2024.130358. Epub 2024 Feb 25. PMID: 38412939

The present study aims to develop and characterize biodegradable packaging films from lemon peel-derived pectin and chitosan incorporated with a bioactive extract from neem leaves. The films (PCNE) contained varying concentrations of neem leaf extract and were comprehensively assessed for their physical, optical, mechanical, and antimicrobial attributes. The thickness, moisture content, water solubility, and water vapor permeability of the biodegradable packaging films increased with the increasing concentration of neem leaf extract. Comparatively, the tensile strength of the films decreased by 42.05 % compared to the control film. The Scanning Electron Microscopy (SEM) confirmed that the resultant blended pectin-chitosan films showed a uniform structure without cracks. Furthermore, the analysis targeting *Staphylococcus aureus* and *Aspergillus niger* indicated that the films had potent antimicrobial activity. Based on these results, the optimum films were selected and subsequently applied on apricot fruits to increase their shelf life at ambient temperature. The findings, after examining factors such as colour, firmness, total soluble solids, shrinkage, weight loss, and appearance, concluded that the apricots coated by PCNE-5 had the most delayed signs of spoilage and increased their shelf life by 50 %. The results showed the potential applicability of lemon peel pectin-chitosan-neem leaf extract blend films in biodegradable food packaging.

Starch-based antibacterial food packaging with ZnO nanoparticle.

Kumar P, Gautam S, Bansal D, Kaur R.

J Food Sci Technol. 2024 Jan;61(1):178-191. doi: 10.1007/s13197-023-05834-9. Epub 2023 Sep 28. PMID: 38192709

Starch-based biofilms with embedded nanoparticles (NPs) are used to wrap food in biodegradable packaging system that has high antibacterial action against a variety of microorganisms. In this study, ZnO NPs were synthesised using both a green synthesis approach utilising *Azadirachta indica* (Neem) and a chemical synthesis approach using the sol-gel technique. The structural and morphological properties of all synthesised NPs were characterized through XRD, UV-VIS, UV-DRS, FTIR, and FESEM analysis. Further, these NPs were employed in the development of starch-based biodegradable films. A meticulous comparative analysis was performed to evaluate the functional properties of the nanocomposites, encompassing crucial parameters such as film thickness, moisture content, swelling index, opacity, solubility, water vapor permeability, and tensile strength. In comparison to films embedded with chemically synthesised NPs (F1), nanocomposite with green synthesised NPs (F2) showed 15.27% greater inhibition against *Escherichia coli* growth and 22.05% stronger inhibition against *Staphylococcus aureus* bacterial strains. Based on the biodegradability analysis, the nanocomposite film-F2 showed a 53.33% faster degradation rate compared to the film-F1. The developed films were utilized to assess the quality of both wrapped and unwrapped grapes, leading to the generalization of the research for the development of starch-based antibacterial and environmentally friendly food packaging material.

Rosemary and neem: an insight into their combined anti-dandruff and anti-hair loss efficacy.

Hashem MM, Attia D, Hashem YA, Hendy MS, AbdelBasset S, Adel F, Salama MM.

Sci Rep. 2024 Apr 2;14(1):7780. doi: 10.1038/s41598-024-57838-w.PMID: 38565924

Dandruff, a common scalp disorder characterized by flaking dead skin, is often treated with conventional topical products. However, limitations exist due to potential side effects and high costs. Therefore, searching for natural, cost-effective solutions for dandruff and hair loss is crucial. Rosemary herb and neem tree, both cultivated in Egypt, possess well-documented anti-inflammatory properties derived from their rich phenolic phytoconstituents. This study formulated a standardized combined extract of rosemary and neem (RN-E 2:1) into hair gel and leave-in tonic formats. This extract demonstrated superior efficacy against *Malassezia furfur* (a causative agent of dandruff) and *Trichophyton rubrum* (associated with scalp disorders) compared to the conventional antifungal agent, ketoconazole. The combined extract (RN-E 2:1) also exhibited potent anti-inflammatory activity. Additionally, the suppression of iNOS expression is considered concentration-dependent. Quality control verified formulation stability, and ex-vivo studies confirmed effective ingredient penetration into the epidermis, the primary site of fungal presence. Remarkably, both formulations outperformed the standard treatment, minoxidil in hair growth trials. These findings highlight the potential of natural extracts for scalp and hair health.

Neem for Human Health

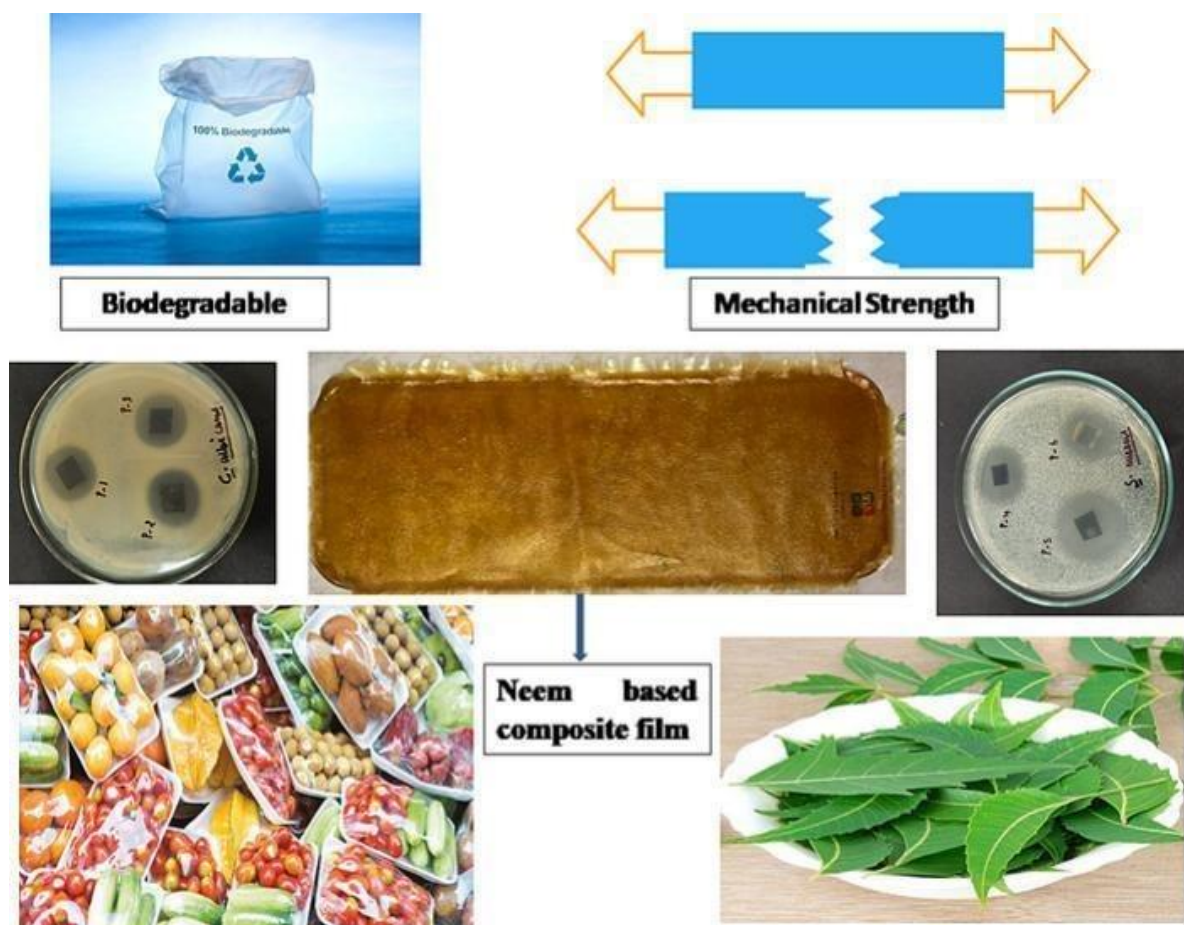
Antimicrobial activity

Antimicrobial phytoconstituents from *Azadirachta indica* (neem) with potential inhibitor against FtsZ protein of *Pseudomonas aeruginosa*.

Orozco-Ugarriza ME, Arrieta Caldera NP, Olivo-Martínez Y.

Nat Prod Res. 2024 Mar 22;1-6. doi: 10.1080/14786419.2024.2332946. Online ahead of print. PMID: 38516734

Pseudomonas aeruginosa is a well-known pathogen for its rapid development of multi-drug antibiotic resistance. This pathogen is responsible for numerous human diseases, particularly affecting immunocompromised and elderly patients. Hence, discovering novel therapeutics has become necessary in the fight against antimicrobial resistance. This study is focused on evaluating the potential inhibitory activity of eleven phytoconstituents from *Azadirachta indica* against the nucleotide-binding site of the FtsZ protein of *P. aeruginosa* through a cheminformatics approach. FtsZ is an indispensable and highly conserved protein in prokaryotic cell division. Docking studies revealed favourable binding energies ($\Delta G = -8.3$ to -5.4 kcal/mol) for all selected phytoconstituents. Finally, we selected Nimbiol (CID 11119228), as a lead compound, exhibiting a binding energy ($\Delta G = -7.8$ kcal/mol) for the target. Based on our findings, Nimbiol shows potential as an anti-FtsZ compound, making it a promising candidate for further *in vitro* and *in vivo* investigations to assess its antimicrobial activity.



Antimicrobial Activity of Polycaprolactone Nanofiber Coated with Lavender and Neem Oil Nanoemulsions against Airborne Bacteria.

Rahman MM, Kotturi H, Nikfarjam S, Bhargava K, Ahsan N, Khandaker M.

Membranes (Basel). 2024 Jan 29;14(2):36. doi: 10.3390/membranes14020036.PMID: 38392663

The development of efficient, eco-friendly antimicrobial agents for air purification and disinfection addresses public health issues connected to preventing airborne pathogens. Herein, the antimicrobial activity of a nanoemulsion (control, 5%, 10%, and 15%) containing neem and lavender oils with polycaprolactone (PCL) was investigated against airborne bacteria, including *Escherichia coli*, *Bacillus subtilis*, and *Staphylococcus aureus*. Various parameters such as the physicochemical properties of the nanoemulsion, pH, droplet size, the polydispersity index (PDI), the minimum inhibitory concentration (MIC), the minimum bacterial concentration (MBC), and the color measurement of the emulsion have been evaluated and optimized. Our results showed that the antimicrobial activity of PCL combined with neem and lavender oil was found to be the highest MIC and MBC against all tested bacteria. The droplet sizes for lavender oil are 21.86-115.15 nm, the droplet sizes for neem oil are 23.92-119.15 nm, and their combination is 25.97-50.22 nm. The range of pH and viscosity of nanoemulsions of various concentrations was found to be 5.8 to 6.6 pH and 0.372 to 2.101 cP. This study highlights the potential of nanotechnology in harnessing the antimicrobial properties of natural essential oils, paving the way for innovative and sustainable solutions in the fight against bacterial contamination.

Comparative Extraction and Bioactive Potential of the Leaf Extracts of *Azadirachta indica* for Combatting Postoperative Head and Neck Infections: An In Vitro Study.

S PV, Neralla M, V B, Satheesh T.

Cureus. 2023 Dec 29;15(12):e51303. doi: 10.7759/cureus.51303. eCollection 2023 Dec.PMID: 38288224

Introduction: Surgical site infections (SSIs) following head and neck cancer surgery are very common postoperative sequelae. Delayed wound healing leads to a poor aesthetic outcome, delay in restarting oral intake, and delay in getting or starting adjuvant therapy. Antibiotic resistance is on the rise necessitating studies that use alternatives to combat the rising antibiotic resistance. Many plant compounds have been studied to explore the possibility. Neem (*Azadirachta indica*), a high medicinal value plant, possesses a vast array of phytochemicals, which are broadly grouped into isoprenoids and non-isoprenoids. These phytochemicals are crucial for its anti-inflammatory, antioxidant, antimicrobial, antipyretic, and various other pharmacological activities. **Materials and methods:** In this study, we examined the impact of the extraction solvents on the bioactive potential of neem. Neem leaf samples were extracted with water and ethanol; followed by their biological activities like extraction yield, antioxidant, antimicrobial, and cytotoxicity studies were performed. The extraction yield was found to be higher in the ethanolic extract than in the aqueous extract, which also corroborates with increased antioxidant and antibacterial activity. Both the aqueous and ethanolic extracts of neem exhibited antibacterial activities against dental biofilm-producing pathogens like *Staphylococcus aureus*, *Streptococcus mutans*, *Pseudomonas aeruginosa*, and *Escherichia coli*. Results: Extraction yield was higher in the ethanolic extract of neem. Antioxidant activity was found to be higher in the ethanolic extract than in the aqueous extract. Neem extract has no toxicity, which was observed through hemolytic and zebrafish embryo toxicity assays. The ethanolic extract of neem was shown to be more effective against the Gram-positive and Gram-negative drug-resistant bacterial pathogen. **Discussion and conclusion:** Thus, the utilization of neem extracts is certainly useful in controlling pathogenic bacterial growth in clinical applications. Further, a detailed mechanism of action of neem extract in bacterial growth inhibition at the molecular level is warranted to utilize their potential in disease management.

Antimalarial activity

Community and health worker perspectives on malaria in Meghalaya, India: covering the last mile of elimination by 2030.

Nengnong CB, Passah M, Wilson ML, Bellotti E, Kessler A, Marak BR, Carlton JM, Sarkar R, Albert S.

Malar J. 2024 Mar 18;23(1):83. doi: 10.1186/s12936-024-04905-2.PMID: 38500097

Background: Malaria remains a public health problem in regions of Northeastern India because of favourable bio-geographic transmission conditions, poor access to routine healthcare, and inadequate infrastructure for public health and disease prevention. This study was undertaken to better understand community members' and health workers' perceptions of malaria, as well as their knowledge, attitudes, and prevention practices related to the disease in Meghalaya state. **Methods:** The study included participants from three malaria endemic districts: West Khasi Hills, West Jaiñtia Hills, and South Garo Hills from 2019 to 2021. A total of 82 focus group discussions (FGD) involving 694 community members and 63 in-depth interviews (IDI) with health personnel and traditional healers residing within the three districts were conducted. A thematic content analysis approach was employed, using NVivo12 software for data management. **Results:** Most participants reported a perceived reduction in malaria during recent years, attributing this to changes in attitudes and behaviours in health seeking, and to more effective government interventions. Local availability of testing and treatment, and an improved, more responsive health system contributed to changing attitudes. Long-lasting insecticidal nets (LLINs) were largely preferred over indoor residual spraying (IRS), as LLINs were perceived to be effective and more durable. Community members also reported using personal protective measures such as applying repellents, burning neem tree leaves, straw/egg trays, wearing long sleeve clothes, and applying ointments or oils to protect themselves from mosquito bites. While most participants acknowledged the role of mosquitoes in malaria transmission, other conditions that are not mosquito-borne were also attributed to mosquitoes by some participants. The communities surveyed have largely shifted from seeking treatment for malaria from traditional healers to using public facilities, although some participants reported switching between the two or using both simultaneously. Improved understanding of cerebral malaria, which some participants previously attributed to mental illness due to 'bad spirits', is an example of how cultural and ritualistic practices have changed. **Conclusion:** The findings reveal diverse perceptions among community members regarding malaria, its prevention, practices to prevent mosquito-transmitted diseases, and their opinions about the healthcare system. A key finding was the shift in malaria treatment-seeking preferences of community members from traditional healers to the public sector. This shift highlights the changing dynamics and increasing acceptance of modern healthcare practices for malaria treatment and prevention within tribal and/or indigenous communities. By recognizing these evolving attitudes, policymakers and healthcare providers can better tailor their interventions and communication strategies to more effectively address ongoing needs and concerns as India faces the 'last mile' in malaria elimination.

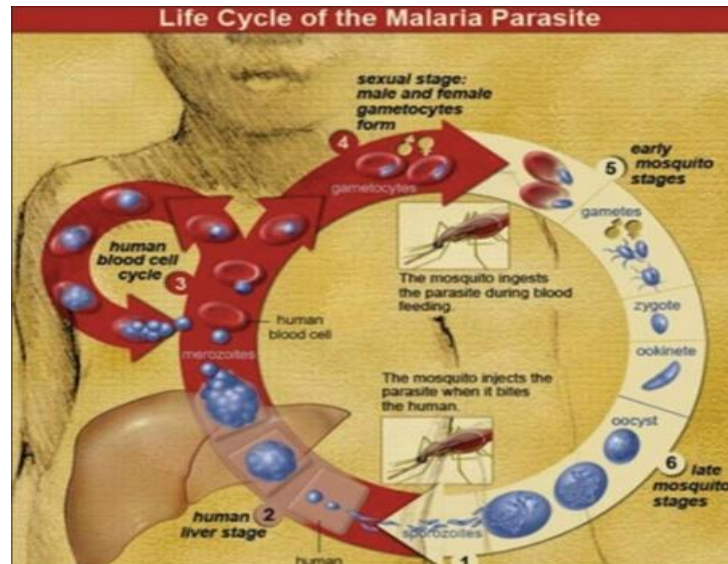
Alternative first-line malaria treatment.

Maafoh C, Onyedibe K.

Ann Afr Med. 2024 Jan-Mar;23(1):5-12. doi: 10.4103/aam.aam_35_23.PMID: 38358164

Malaria is a disease affecting millions of people, especially in Africa, Asia, and South America, and has become a substantial economic burden. Because malaria is contracted through the bite of a mosquito vector, it is very challenging to prevent. Bed nets and insect repellents are used in some homes; others do not have or use them even when available. Thus, treatment measures are crucial to controlling this disease. Artemisinin-based combination therapy (ACT) is currently the first-line treatment for malaria. ACT has been used for decades, but recently, there has been evidence of potential resistance. This threat of resistance has led to the search for possible alternatives to ACT. In sub-Saharan Africa, *Azadirachta indica*, or simply neem, is a plant used to

treat a variety of ailments, including malaria. Neem is effective against one of the more deadly malaria parasites *Plasmodium falciparum*. Reports show that neem inhibits microgametogenesis of *P. falciparum* and interferes with the parasite's ookinete development. Although there is substantial *in vitro* research on the biological activity of *A. indica* (neem), there is limited *in vivo* research. Herein, we discuss the *in vivo* effects of neem on malaria parasites. With *A. indica*, the future of malaria treatment is promising, especially for high-risk patients, but further research and clinical trials are required to confirm its biological activity.



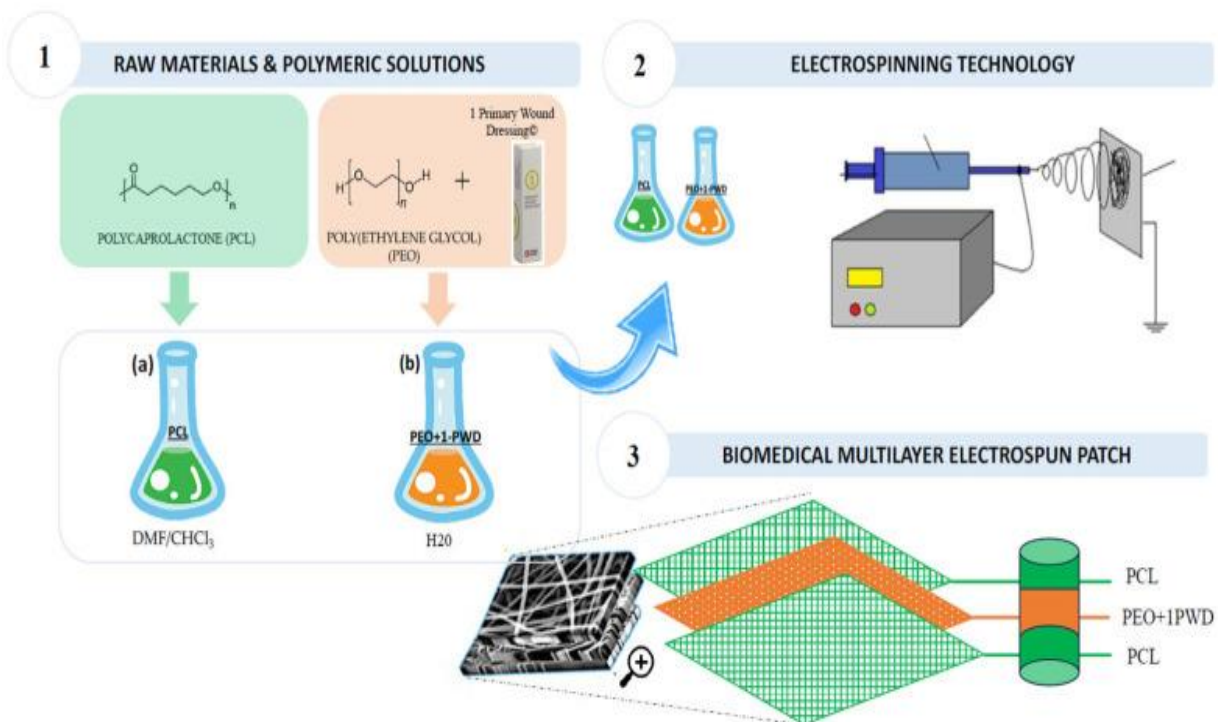
Wound healing & Anti-inflammatory activity

Innovative Multilayer Electrospun Patches for the Slow Release of Natural Oily Extracts as Dressings to Boost Wound Healing.

Fiaschini N, Carnevali F, Van der Esch SA, Vitali R, Mancuso M, Sulli M, Diretto G, Negroni A, Rinaldi A.

Pharmaceutics. 2024 Jan 24;16(2):159. doi: 10.3390/pharmaceutics16020159.PMID: 38399220

Electrospinning is an advanced manufacturing strategy used to create innovative medical devices from continuous nanoscale fibers that is endowed with tunable biological, chemical, and physical properties. Innovative medical patches manufactured entirely by electrospinning are discussed in this paper, using a specific plant-derived formulation "1 Primary Wound Dressing®" (1-PWD) as an active pharmaceutical ingredient (API). 1-PWD is composed of neem oil (*Azadirachta indica* A. Juss.) and the oily extracts of *Hypericum perforatum* (L.) flowers, according to the formulation patented by the ENEA of proven therapeutic efficacy as wound dressings. The goal of this work is to encapsulate this API and demonstrate that its slow release from an engineered electrospun patch can increase the therapeutic efficacy for wound healing. The prototyped patch is a three-layer core-shell membrane, with a core made of fibers from a 1-PWD-PEO blend, enveloped within two external layers made of medical-grade polycaprolactone (PCL), ensuring mechanical strength and integrity during manipulation. The system was characterized via electron microscopy (SEM) and chemical and contact angle tests. The encapsulation, release, and efficacy of the API were confirmed by FTIR and LC-HRMS and were validated via *in vitro* toxicology and scratch assays.

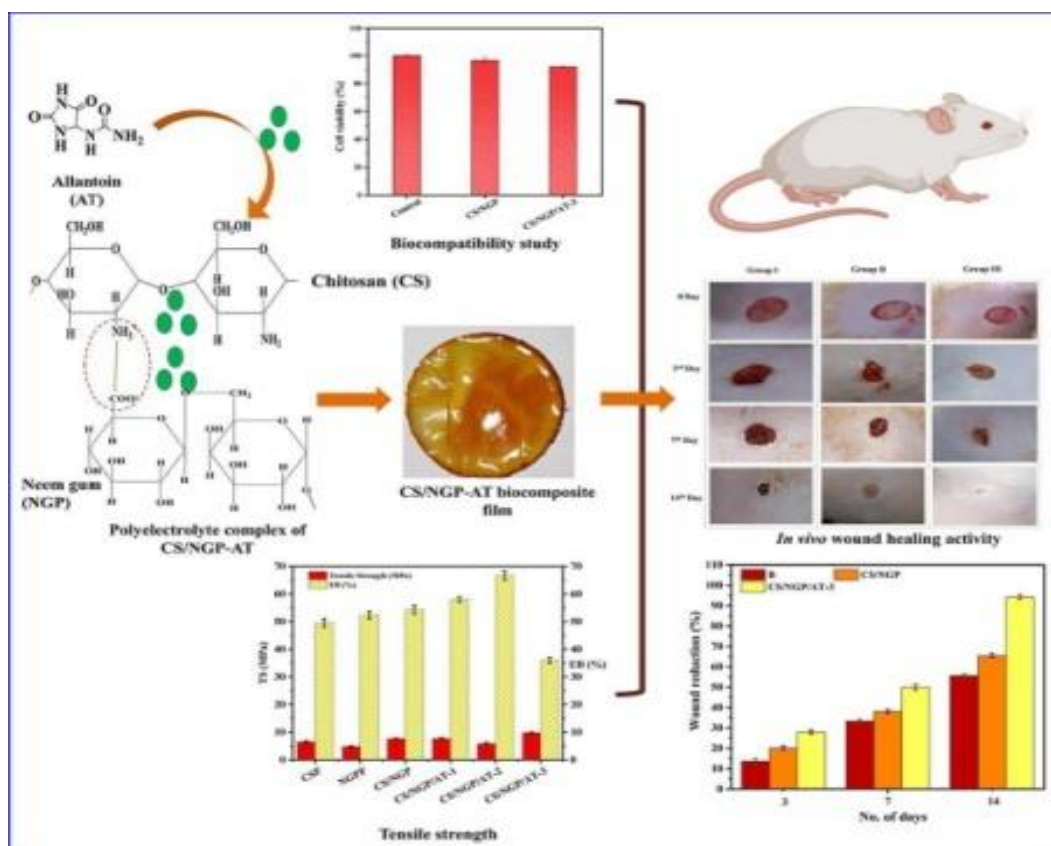


Chitosan and neem gum-based polyelectrolyte complex for design of allantoin loaded biocomposite film: In-vitro, ex-vivo, and in-vivo characterization.

Patil A, Nangare S, Mahajan P, Jain P, Zawar L.

Int J Biol Macromol. 2024 Apr;263(Pt 1):130280. doi: 10.1016/j.ijbiomac.2024.130280. Epub 2024 Feb 18. PMID: 38378120

Presently, the preference for chitosan (CS) and gum polysaccharides in biomedical applications including drug delivery and wound healing has been extensively documented. Despite this, the demerits of CS and gum polysaccharides such as poor mechanical properties, degradation rate, swelling, etc., limit their applications for designing biocomposite films for drug delivery. Therefore, the anticipated work aims to design a CS and neem gum polysaccharides (NGP) polyelectrolyte complex-based allantoin (AT)-loaded (CS/NGP-AT) biocomposite film for improved wound healing. In brief, CS, NGP, and CS/NGP-AT-based biocomposite films were prepared using the solvent-casting method, and in-vitro, ex-vivo, and in-vivo characterizations were performed to assess the performance of these biocomposite films compared to their counterparts. In this, diffractogram and thermogram analysis assured the conversion of crystalline AT into an amorphous form. The optimized CS/NGP/AT-3 formulation exhibited controlled water absorption, appropriate water uptake capacity, good water retention ability, excellent water vapor transmission rate, controlled degradation rate, enhanced mechanical properties, cell and blood biocompatibility, etc. Furthermore, it offered improved antimicrobial, anti-inflammatory, and antioxidant potential. The optimized film provided a modified release ($88.3 \pm 0.3\%$) of AT from the film for up to 48 h. Wound healing experiments on rats and their histopathology studies confirmed a significantly higher rate of wound recovery within 14 days compared to the control and CS/NGP film, attributable to the combined effects of CS, NGP, and AT. In conclusion, the fabricated CS/NGP-based biocomposite film presents promising prospects as an excellent candidate for wound healing applications.



Botanical Briefs: Neem Oil (*Azadirachta indica*).

Patel N, Knabel M, Speiser J.

Cutis. 2024 Jan;113(1):22-24. doi: 10.12788/cutis.0928.PMID: 38478934

Azadirachta indica, commonly known as neem, has many uses as a natural remedy. We review and discuss the pharmacologic, biologic, and medicinal properties of neem in disease management. We also report a rare clinical case of a 77-year-old man who presented with a hypopigmented rash on the lower back, bilateral flanks, and buttocks after 6 months of repeated application of neem oil to treat persistent arthritis and lower back pain.

Radioprotection & Drug delivery

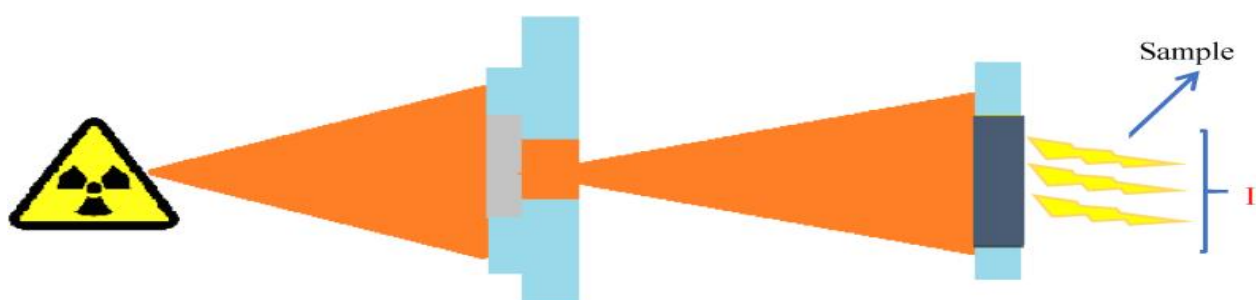
A new method in the production of protective sheets against X-ray radiation.

Teymoori M, Pourshamsian K.

Heliyon. 2023 Dec 5;10(1):e23301. doi: 10.1016/j.heliyon.2023.e23301. eCollection 2024 Jan 15.PMID: 38205301

Today, the use of X-rays in diagnosing and sometimes treating patients is inevitable. Despite the many benefits of using X-rays in medical and other sciences, the harmful effects of this radiation on human tissue should not be neglected. One of the best ways to prevent the harmful effects of X-rays on the human body is to use appropriate covers against these rays. It seems that it is necessary to find effective particles to weaken X-rays and choose a suitable substrate with high mechanical resistance to scatter particles in it. In this study, the synthesis of SnO₂ nanoparticles from SnCl₂·2H₂O precursor and BaSO₄ nanoparticles from BaCl₂·2H₂O precursor using neem tree extract (*Azadirachta indica*) as a reducing and stabilizing agent is reported. After the synthesis of

nanoparticles, their structure was investigated by X-ray diffraction, scanning electron microscopy and energy dispersive X-ray analysis. Then the desired composite and nanocomposite were prepared in the polymer substrate. The sheets were prepared using an extruder and then a hot hydraulic press. The output sheets had a thickness of 1 mm. The structural characteristics of the produced sheets such as surface morphology, density of prepared composites, mechanical properties, thermal gravimetric analysis and retention of loaded particles after three times washes were investigated. The X-ray attenuation capability of each sample was evaluated by calculating the linear attenuation coefficient for each prepared sample. The results show that all sheets filled with tin and barium micro and nano particles have more X-ray attenuation capabilities than pure polymer. Among the prepared sheets, the nanocomposite prepared from low-density polyethylene (77 %) + SnO₂ (10 %) + BaSO₄ (10 %) + multi-walled carbon nanotubes (3 %) showed the highest X-ray attenuation.

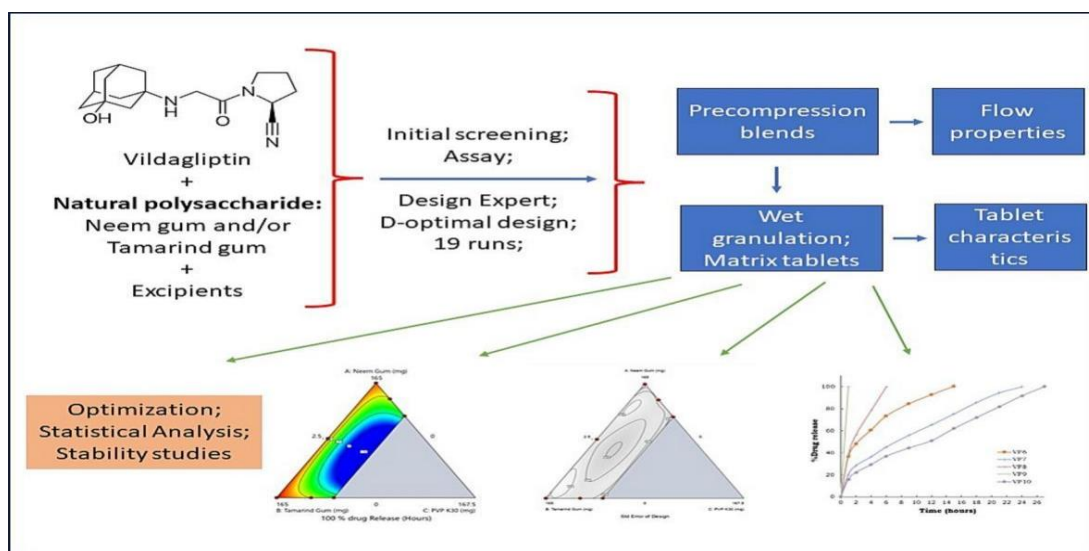


Exploring the potential of neem and tamarind gum as release retardants: Design and statistical optimisation of vildagliptin extended release matrix systems using D-optimal quadratic mixture design.

Kumar NR, Rao GSNK, Ratna JV, Murthy KVR.

Int J Biol Macromol. 2024 Feb;259(Pt 1):129136. doi: 10.1016/j.ijbiomac.2023.129136. Epub 2024 Jan 3. PMID: 38181924

Exploring the significant role of natural polymers in developing drug delivery systems has been a promising area of research interest. The current investigation uses a D-optimal quadratic mixture design to design and evaluate neem and tamarind gum-based vildagliptin extended-release matrix tablets. Studying the combination effect of gums is one of the major objectives. Initial screening studies were performed to select the factors and their levels. The variables selected at different levels in mg/tablet are neem gum, tamarind gum, polyvinylpyrrolidone, and lactose monohydrate. Based on the screening experiments with both gums, the polymer content of 165 mg was chosen as the highest level in the DOE. Nineteen runs were generated to screen the desired parameters as responses. The total weight of the formulation was kept constant at 275 mg. Time (hours) required for 50 %, 90 % and 100 % of drug release and tablet hardness were selected as the responses for each run. The wet granulation method was adopted, and the critical variables were optimised using the design of experiments following Design Expert software. Statistical analysis was conducted, and the optimised formulations were prepared and evaluated to compare with the predicted responses. Stability studies were performed for the optimised batches. Results indicated that the prepared batches met the compendial limits and confirmed the application of neem and tamarind gum in the development of extended-release tablets of vildagliptin for 24 h. An optimised formulation comprising of 16.52 mg of neem gum and 148.48 mg of tamarind gum with a hardness of 7.5-8.5 kp produced 50 %, 90 % and 100 % drug release in 12, 22 and 25 h.



Optimization and chemical free fabrication of green synthesized iron nanoparticles as potential MRI contrast agent.

S Y, N P, M C.

Biotechnol Appl Biochem. 2024 Feb 1. doi: 10.1002/bab.2561. Online ahead of print. PMID: 38298147

The current research article has investigated the synthesis and characterization of novel iron nanoparticles (INPs) from neem and betel leaves extract combination using response surface methodology-central composite design and coated with chitosan-curcumin (CCINPs) as a biocompatible and contrast agent for magnetic resonance imaging (MRI). The coating of INPs with chitosan and curcumin (CCINPs) was carried out using a simple, easy, chemical-free ultrasonication method and characteristics were confirmed by UV-visible (Vis) spectrophotometer (UV-Vis), Fourier-transform infrared spectroscopy, X-ray diffraction, scanning electron microscope, atomic force microscopy, and vibrating sample magnetometer. The biocompatibility of the particles was ensured by conducting hemolytic and cell viability assays. The nanoparticle was found to be nonhemolytic (<5%) up to 150 µg/mL for both INPs and CCINPs. The cell viability was stable (peripheral blood mononuclear cells-PBMCs) till 48 h at 150 µg/mL of INPs and CCINPs. Both the test results produced were found to be biocompatible and additionally, an in vitro MRI study of INPs and CCINPs demonstrated the efficiency of the nanoparticle as a negative contrast agent with enhanced contrast nature in CCINPs. Thus, overall results indicate that the green synthesized chemical-free novel CCINPs could be a potential candidate for a wide range of applications such as MRI, drug delivery, and in magnetic fluid hyperthermia.

Neem leaves mediated synthesis of CeO₂ nanoparticles for X/gamma ray absorption applications.

Munirathnam R, Seenappa L, Manjunatha HCS, Vidya YS, Sridhar KN, Manjunath S, Murugan VR, Nagaiah N.

Radiat Prot Dosimetry. 2023 Dec 21;199(20):2499-2505. doi: 10.1093/rpd/ncad230. PMID: 38126863

Cerium oxide (CeO₂) nanoparticles (NPs) exhibit a variety of properties, which have prompted researchers to explore CeO₂ NPs in various applications such as biomedical, electrochemical, gas sensing and display applications. CeO₂ NPs capabilities were impacted by the type of synthesis mechanism. CeO₂ NPs were synthesized by solution combustion method using neem leaves

extract as a reducing agent. The synthesized sample is characterized with different techniques. The Bragg reflections confirm the formation of cubic spinel structure. The surface morphology consists of agglomerated NPs. The direct energy band gap was found to be 2.9 eV. X-ray radiation absorption properties were studied within 1 keV-100GeV range. The results indicate that CeO₂ NPs found to be potential in radiation applications.

Dental Disorders

Clinical and Radiographic Evaluation of Various Herbal Products Used with Zinc Oxide as an Obturating Material in Primary Teeth: An *In Vivo* Study.

Sunil, Anand S, Ahmad A, Prakash R, Singh A, Megha V.

J Contemp Dent Pract. 2023 Sep 1;24(9):692-699. doi: 10.5005/jp-journals-10024-3559.PMID: 38152944

Aim: To compare the clinical and radiographically mixture of zinc oxide with *Aloe vera*, *Curcumin* and neem as an obturating material for pulpectomy. **Materials and methods:** The study comprised of age group 4-8 years children requiring endodontic treatment for at least a single primary molar tooth. Sixty primary molar teeth from 43 children were divided equally and randomly into four study groups. The materials used for obturation were zinc oxide powder (ZnO) and Eugenol (ZOE) (group I), ZnO and *Aloe vera* Gel (group II), ZnO and *Curcumin* Powder (group III), ZnO and neem extract (group IV). They were evaluated clinically and radiographically at immediate postoperative and then at 1-, 3-, 6-, and 9-month intervals. **Results:** At the end of 9 months, the Chi-square test revealed 100% success rate for recovery of pain in group I and III, 66.66% in group II and 93.3% in group IV. The success rates for absence of abscess and for periradicular radiolucency in group I, III, and group IV were 100% and 66.6% for group II. The success rate for periapical radiolucency in group I and group III was 100%, in group II 66.6% and in group IV 93.35%. The success rate for all the groups shows 100% success in terms of pathological root resorption. **Conclusion:** Zinc oxide eugenol has proven to be the best obturating material. ZnO with *Aloe vera* showed a success rate which is significantly lower than the other medicaments. ZnO with *Curcumin* and ZnO with neem had shown promising clinical and radiographical results. **Clinical significance:** ZnO with *Curcumin* and ZnO with neem can be used as a root canal filling material in primary teeth with further follow-up studies.

Neuroprotection

Azadiradione up-regulates the expression of parvalbumin and BDNF via Ube3a.

Jana S, Giri B, Das S, Manna A, Mandal SC, Ranjan Jana N.

Gene. 2024 Mar 1;897:148081. doi: 10.1016/j.gene.2023.148081. Epub 2023 Dec 13.PMID: 38101713

Azadiradione is a small bioactive limonoid found in the seed of *Azadirachta Indica*, an Indian medicinal plant commonly known as Neem. Recently, it has been shown to ameliorate the disease pathology in fly and mouse model of Huntington's disease by restoring impaired proteostasis. Here we report that the azadiradione could be involved in modulating the synaptic function through increased expression of Ube3a, a dual function protein having ubiquitin ligase and co-activator functions and associated with Angelman syndrome and autism. Treatment of azadiradione to HT22 hippocampal cell line and in adult mice induced the expression of Ube3a as well as two important synaptic function and plasticity regulating proteins, parvalbumin and brain-derived neurotrophic factor (BDNF). Interestingly, another synaptic plasticity modulating protein Arc (activity-regulated cytoskeletal associated protein) was down-regulated by azadiradione. Partial knockdown of Ube3a

in HT22 cell abrogated azadiradione induced expression of parvalbumin and BDNF. Ube3a-maternal deficient mice also exhibited significantly decreased expression of parvalbumin and BDNF in their brain and treatment of azadiradione in these animals did not rescue the altered expression of either parvalbumin or BDNF. These results indicate that azadiradione-induced expression of parvalbumin and BDNF in the brain is mediated through Ube3a and suggest that azadiradione could be implicated in restoring synaptic dysfunction in many neuropsychiatric/neurodegenerative disorders.

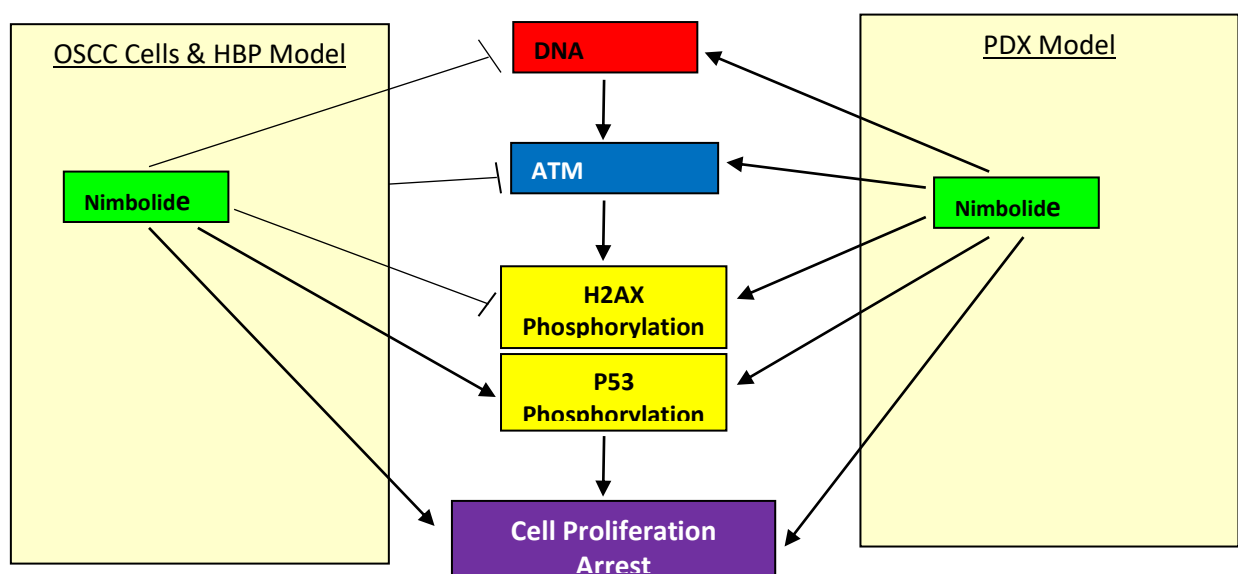
Anticancer activity

The Neem Limonoid Nimbolide Modulates Key Components of the DNA Damage Response Signalling in Cellular and Animal Models of Oral Squamous Cell Carcinoma.

Arvindh S, Priyadarshini M, Baba AB, Veeravarmal V, Mishra R, Dash R, Nagini S.

Curr Pharm Biotechnol. 2024 Mar 28. doi: 10.2174/0113892010291998240321074920. Online ahead of print. PMID: 38561609

Background: Deregulated DNA damage response (DDR) network is implicated in cancer progression and therapy resistance. **Objective:** The present study was designed to investigate whether nimbolide, an anticancer neem limonoid, targets key components of the DDR signalling pathway in cellular and animal models of oral squamous cell carcinoma (OSCC). **Methods:** OSCC cells (SCC-4 and SCC-9), 7,12-dimethylbenz[a]anthracene (DMBA)-induced hamster buccal pouch (HBP) carcinoma model, chemoresistant OSCC patient-derived xenograft (PDX) model established in athymic nude mice, and tissue sections from patients with oral premalignant/malignant disease were used for the study. Key molecules that orchestrate the DDR, including the MRN complex, ATM, DNA-PKcs, H2AX, and p53, were analysed by qRTPCR, immunoblotting, immunofluorescence, and immunohistochemistry. Cell proliferation and apoptosis indices were evaluated. **Results:** Nimbolide significantly reduced 8-oxodG levels, expression of MRN, ATMS1891, and g- H2AX, with an increase in p-p53S15 in OSCC cells as well as in the HBP model. Nimbolide potentiated the effect of KU-55933 in ATM inhibition. In the PDX model, nimbolide suppressed tumor formation, stimulated DDR and apoptosis, inhibited cell proliferation, and enhanced sensitivity to cisplatin. Analysis of p-ATM expression revealed a significant increase during the sequential progression of hamster and human OSCC. **Conclusions:** This study provides compelling evidence that nimbolide functions as a DDR inhibitor in cellular and hamster OSCC models and as a DDR activator in the PDX model primarily by targeting ATM. Small molecules like nimbolide that modulate DDR are of immense benefit in cancer therapy. The study has also unveiled p-ATM as a promising biomarker of tumour progression in human OSCCs.

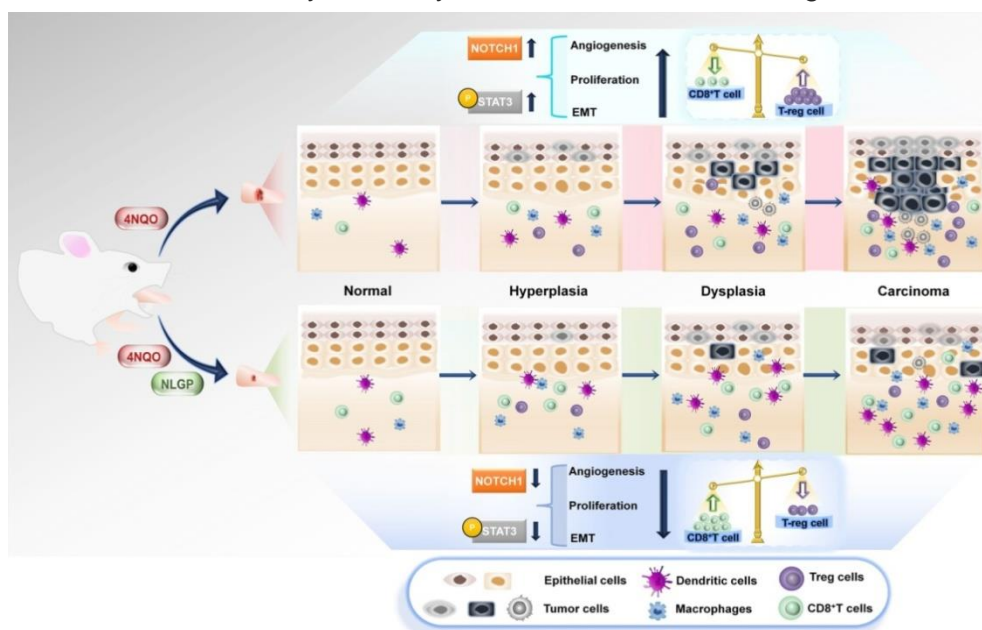


The immunomodulatory impact of naturally derived neem leaf glycoprotein on the initiation progression model of 4NQO induced murine oral carcinogenesis: a preclinical study

Das J, Bera S, Ganguly N, Guha I, Ghosh Halder T, Bhuniya A, Nandi P, Chakravarti M, Dhar S, Sarkar A, Das T, Banerjee S, Ghose S, Bose A and Baral R

Front. Immunol. 2024; 15:1325161. doi: 10.3389/fimmu.2024.1325161

Introduction: Murine tumor growth restriction by neem leaf glycoprotein (NLGP) was established in various transplanted models of murine sarcoma, melanoma and carcinoma. However, the role of NLGP in the sequential carcinogenic steps has not been explored. Thus, tongue carcinogenesis in Swiss mice was induced by 4-nitroquinoline-1-oxide (4NQO), which has close resemblance to human carcinogenesis process. Interventive role of NLGP in initiation-promotion protocol established during 4NQO mediated tongue carcinogenesis in relation to systemic immune alteration and epithelial-mesenchymal transition (EMT) is investigated. **Methods:** 4NQO was painted on tongue of Swiss mice every third day at a dose of 25 μ l of 5mg/ml stock solution. After five consecutive treatment with 4NQO (starting Day7), one group of mice was treated with NLGP (s.c., 25 μ g/mice/week), keeping a group as PBS control. Mice were sacrificed in different time-intervals to harvest tongues and studied using histology, immunohistochemistry, flow-cytometry and RT-PCR on different immune cells and EMT markers (e-cadherin, vimentin) to elucidate their phenotypic and secretory status. **Results:** Local administration of 4NQO for consecutive 300 days promotes significant alteration in tongue mucosa including erosion in papillae and migration of malignant epithelial cells to the underlying connective tissue stroma with the formation of cell nests (exophytic-hyperkeratosis with mild dysplasia). Therapeutic NLGP treatment delayed pre-neoplastic changes promoting normalization of mucosa by maintaining normal structure. Flow-cytometric evidences suggest that NLGP treatment upregulated CD8⁺, IFN γ ⁺, granzyme B⁺, CD11c⁺ cells in comparison to 4NQO treated mice with a decrease in Ki67⁺ and CD4⁺FoxP3⁺ cells in NLGP treated cohort. RT-PCR demonstrated a marked reduction of MMP9, IL-6, IL-2, CD31 and an upregulation in CCR5 in tongues from 4NQO+NLGP treated mice in comparison to 4NQO treated group. Moreover, 4NQO mediated changes were associated with reduction of e-cadherin and simultaneous up-regulation of vimentin expression in epithelium that was partially reversed by NLGP. **Discussion:** Efficacy of NLGP was tested first time in sequential carcinogenesis model and proved effective in delaying the initial progression. NLGP normalizes type 1 immunity including activation of the CD8⁺T effector functions, reduction of regulatory T cell functions, along with changes in EMT to make the host systemically alert to combat the carcinogenic threat.



Zeolitic Imidazole Framework/Silica Nanocomposite for Targeted Cancer Therapeutics: Comparative Study of Chemo-Drug Cisplatin (CpT) and Green Platinum (GPt) Efficacy.

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A chemo-drug such as cisplatin is effective for cancer treatment but remains non-specific, is susceptible to drug resistance, and induces several side effects on organ systems. Zeolitic imidazolate framework-8, a type of MOF, has gained attention, including as a drug delivery method for targeted cancer therapeutics. In this study, ZIF-8/Silica nanocomposite was synthesized using a one-pot hydrothermal technique using the Stober technique. We studied the effect of phyto-synthesized GPt and chemo-drug cisplatin CpT on ZIF-8/Silica for targeted efficacy of cancer therapy. The texture, morphology, and chemical environment of Pt on ZIF-8/Silica were analyzed using different characterization techniques such as XRD, FT-IR, BET, diffuse reflectance spectroscopy, SEM-EDX, TEM, zeta potential, and TGA analysis. The isothermal behavior of CpT and GPt adsorption was investigated using isotherm models like Langmuir, Freundlich, and Temkin isotherm. The adsorption kinetics indicating the adsorption efficiency of GPt and CpT are influenced by the concentration of Pt complex and the adsorption sites of ZIF-8/Silica. A high entrapment efficiency and loading capacity of GPt (86% and 4.3%) and CpT (91% and 4.5%) were evident on ZIF-8/Silica. The nanocomposite showed a pH-sensitive Pt release using a dialysis membrane technique. For instance, a high release of GPt (93%) was observed under pH = 6.6 in 72 h, while the release reduced to 50% at pH 7.4 in 72 h. The anti-cancer activity of nanoformulations was studied in vitro using MCF7 (breast cancer cells) and HFF-1 (human foreskin fibroblast) cells. The findings demonstrated that GPt is as effective as CpT; the EC₅₀ value for MCF7 cells treated with ZIF-8/Silica/Cp/PEG was 94.86 µg/mL, whereas for ZIF-8/Silica/GPt/PEG it was 60.19 µg/mL.

Synergistic effects of epoxyzadiradione (EAD) and paclitaxel against triple-negative breast cancer cells.

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Background: Triple-negative breast cancer (TNBC) is the most aggressive and chemo-resistant form of breast cancer subtype, and chemotherapy is a vital treatment option for that. Paclitaxel is an effective chemo drug for TNBC. However, in clinical settings, paclitaxel has adverse side effects. The synergistic combination is the most promising method for overcoming undesirable toxicity and achieving a beneficial therapeutic outcome. Previous reports, including our study, showed certain anticancer potential of epoxyzadiradione (EAD), the neem limonoid, in different types of cancer cells, including TNBC. **Objective:** This study was designed to investigate the possible synergistic effects of EAD and paclitaxel against TNBC cells. **Methods:** We examined the effects of EAD and paclitaxel alone and in combination in MDA-MB 231 cells, and the percentage cytotoxicity was used to calculate synergism. Characteristic apoptotic changes were observed by visualizing cellular morphology, nuclear fragmentation and membrane integrity. We further estimated anti-migratory potential of experimental compounds by wound healing assay. The reduction in inflammation during combinatorial treatment was evaluated by observing NF-κB translocation. **Results:** The combined treatment with EAD (5 µM) and paclitaxel (5 nM), which were used at doses lower than their individual IC₅₀ concentrations, showed a synergistic effect in MDA-MB-231 cells. This combination effectively induced apoptosis and antimigration and reduced the inflammatory reactions induced by the higher dose of paclitaxel. **Conclusion:** To conclude, EAD could be the drug of choice for combined treatment with paclitaxel in a chemotherapy regimen.

Eco-friendly Synthesis of Azadirachta indica-based Metallic Nanoparticles for Biomedical Application & Future Prospective.**Kumari P, Devi L, Kadian R, Waziri A, Alam MS.***Pharm Nanotechnol. 2024 Feb 22. doi: 10.2174/0122117385262947240206055107. Online ahead of print.PMID: 38409695*

The process of producing the metallic nanoparticles (MNPs) in a sustainable and environment-friendly process is very desirable due to environmental hazards posed by climatic changes. Biomedical one of the fields classified under nanoscience, nanoparticles have a potential synthetic application, which makes it a vast area of research. These particles can be prepared using chemical, physical, and biological methods. One of the methods of synthesis of nanoparticles is by the use of plant extracts, known as green synthesis. Because of its low cost and nontoxicity, it has gained attention in recent times. This review was conducted to find the possible outcomes and uses of metallic nanoparticles synthesized using different parts like gum, root, stem, leaf, fruits, etc. of *Azadirachta indica* (AI). AI, a popular medicinal plant commonly known as neem, has been studied for the green synthesis of NPs by using the capping and reducing agents secreted by the plant. Various phytochemicals identified in neem are capable of metal ion reduction. Green synthesis of NPs from neem is an eco-friendly and low-cost method. These NPs are reported to exhibit good antimicrobial activity. The review covers the preparation, characterization, and mechanism associated with the antibacterial, anticancer, and neurological diseases of the MNPs. Furthermore, the limitations associated with the existing NPs and the prospects of these NPs are also examined.