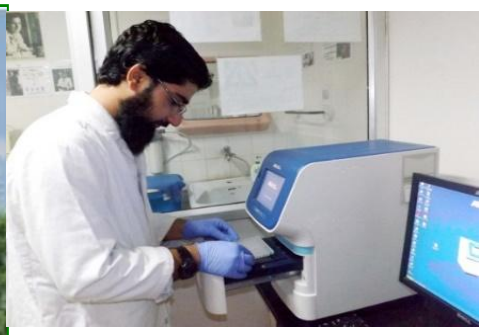
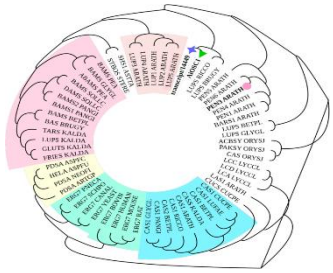
Neem Research Newsletter

Volume 4, Issue 6 & 7, 2024





WORLD NEEM ORGANISATION (WNO)

From

The Editor's Desk……

This issue chronicles some interesting research findings in different areas. Neem essential oil was shown to be an effective sanitizer against fungus infecting fruits in citrus packing houses. The properties of lavender plants showed significant improvement with addition of nano-copper synthesized using neem extract. Silver nanoparticles synthesized using neem leaf extract showed excellent antimicrobial and antioxidant properties against fish pathogens. Carbon dots from neem leaves decorated onto cadmium sulfide were found to be effective for the photocatalytic degradation of ciprofloxacin. Treatment of microalgae with neem-derived silver nanoparticles was found to be a promising strategy to reduce the atmospheric carbon dioxide as well as increasing biomass and production of hydrogen as clean energy. SFS synthesized using neem was shown to be a reliable approach for the quick identification of bacterial contamination in water. Green synthesis of magnetite iron oxide nanoparticles using neem leaf extract loaded on reduced graphene oxide was found to degrade dye pollutants such as methylene blue. Neem leaf extract was found to be effective against fungal infection of the scalp. Neem phytocompounds such as epoxyazadiradione and nimbolide exhibited efficacy against multidrug resistant bacteria. An in silico study identified three neem phytochemicals, quercetin, kaempferol, and cianidanol with antiviral activity against Nipah virus from 418 phytochemicals associated with the neem plant. The anticlotting potential of neem leaf powder-based biocomposite was demonstrated. The addition of neem leaf nanoparticles improved the hardness and hydrophobicity of dental implants. Nimbidiol, a neem phytochemical was found to protect diabetic mice from kidney damage. Another neem phytochemical nimbolide was shown to protect against diabetic cardiomyopathy. Combined treatment with epoxyazadiradione and paclitaxel displayed synergistic chemotherapeutic effects.

S. Nagini

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

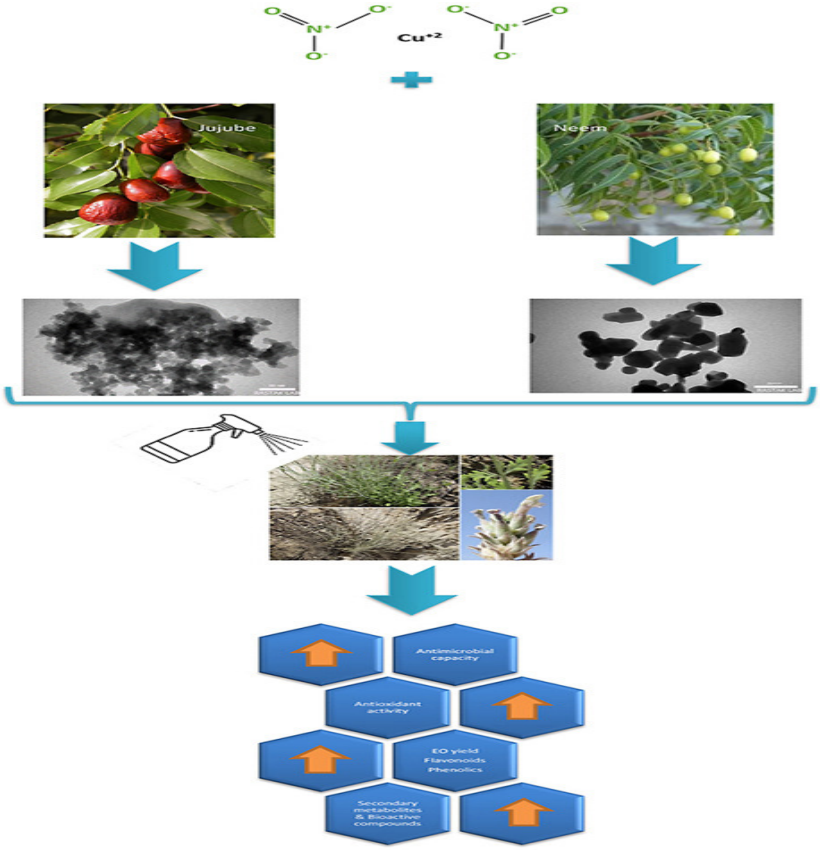
Neem in Agriculture & Aquaculture

Variations in the biochemical characteristics of Lavandula sublepidota Rech.f. in response to the foliar enrichment of green-synthesized copper nano complexes from extract of neem and jujube.

Mazraeh A, Tavallali H, Tavallali V.

Plant Physiol Biochem. 2024 Jun 28;214:108885. doi: 10.1016/j.plaphy.2024.108885. Online ahead of print.PMID: 38971088

Copper (Cu) is an essential micronutrient in plant physiology and biochemistry. This article synthesized copper nano complexes (Cu-NCs) based on aqueous extracts of jujube and neem leaves. The effects of foliar application of Cu-jujube and Cu-neem Cu-NCs at concentrations of 0, 10, 25, and 50 mg L^{-1} on the bioactive compounds, antioxidant capacity, and essential oil of the Iranian native medicinal herb Lavandula sublepidota Rech. f. was investigated. The highest levels of flavonoids and polyphenols were observed in the plants treated with Cu-NCs at 25 mg $L^{-1.}$ However, no superiority was observed between the two types of Cu-NCs. Furthermore, 25 mg L^{-1} nCu-Z and nCu-N foliar application boosted essential oil yield (48 and 52%, respectively) over control. This suggests an ideal threshold beyond which toxicity was found. Similarly, the amount of commercially significant secondary metabolites increased at 25 mg L^{-1} CuNCs compared to 10 and 50 mg L^{-1} concentrations. The maximum antioxidant activity was found in extracts of lavender that had been treated with 25 mg L^{-1} CuNCs. When CuNCs were applied exogenously, the extracts' antibacterial activity (MIC µg mL^{-1}) was substantially increased against the three pathogen strains. The results suggest that CuNCs demonstrate notably greater effectiveness, particularly at an ideal concentration of 25 mg L^{-1}, in enhancing the production of essential oil and bioactive compounds in Lavandula sublepidota Rech. f. Therefore, these findings indicate the importance of the biosynthesis of NCs using plants and measuring the phytochemical changes of lavender plants.



Natural Enemies of the fall armyworm (Spodoptera frugiperda Smith) and comparing Neem aqueous extracts with its larvae, Gurage zone, central Ethiopia.

Degaga AH, Degaga EG.

Heliyon. 2024 May 29;10(11):e32083. doi: 10.1016/j.heliyon.2024.e32083. eCollection 2024 Jun 15.PMID: 38912443

The fall armyworm (*Spodoptera frugiperda* Smith) is an invasive and polyphagous insect pest. It poses a significant threat to maize crops, uncontrolled infestation can result 100 % loss. However, natural enemies play a vital role in regulating the population of this pest. Additionally, botanical sources extracts have the potential to be effective insecticides. The objectives of the study were to investigate the natural enemies of *S. frugiperda* in the Gurage zone and to compare efficacy of Neem seed and leaf aqueous extracts with *S. frugiperda* larvae, central Ethiopia. *S. frugiperda* larvae and egg masses, cocoons and larvae cadavers collected from infested maze farms. From each round collection 25 healthy and inactive larvae were sampled to rear until emerging adults. Observed predator species recorded. Neem seed and leaf aqueous extracts was tested against *S. frugiperda* in laboratory condition. The study found a diverse range of natural enemies associated with *S. frugiperda*, including parasitoids, predators, and entomopathogenic fungi. Three species of parasitoids (*Exorista xanthaspis*, *Tachina* spp., and *Charops annulipes*) were documented in Ethiopia for the first time. Predatory insects belonging to four distinct orders: Hemiptera, Dermaptera, Coleoptera, and Mantodea also identified. In particular, various Hemipterans were observed in the maize farms infested with *S. frugiperda*. In terms of Neem seed and leaf aqueous extracts, they demonstrated similar mortality rates for *S. frugiperda* larvae after 72 h, although differences were observed at 24 and 48 h. For effective management of *S. frugiperda,* more research is needed to fully exploit the potential of natural enemies and botanical source insecticides.

Enhancing productivity and sustainability of ravine lands through horti-silviculture and soil moisture conservation: A pathway to land degradation neutrality.

Jinger D, Kakade V, Bhatnagar PR, Paramesh V, Dinesh D, Singh G, N NK, Kaushal R, Singhal V, Rathore AC, Tomar JMS, Singh C, Yadav LP, Jat RA, Kaledhonkar MJ, Madhu M.

J Environ Manage. 2024 Jun 12;364:121425. doi: 10.1016/j.jenvman.2024.121425. Online ahead of print.PMID: 38870789

Ravine lands are the worst type of land degradation affecting soil quality and biodiversity. Crop production in such lands is impossible without adopting proper conservation measures. In-situ moisture conservation techniques could play an instrumental role in restoring ravine lands by improving soil moisture. We hypothesized that restoring ravine land through a combination of tree planting, fruit crop cultivation, and in-situ moisture conservation practice would result in significant improvements in productivity, profitability, and soil fertility. An experiment was conducted involving the combination of Malabar Neem (Melia dubia) and Dragon fruit (Hylocereus undatus) in conjunction with in-situ soil moisture conservation measures specifically involving half-moon structures (HM). The experiment was conducted under randomized block design (RBD) comprising eight treatments. These treatments include sole Melia cultivation (MD 3m × 3m), sole cultivation

of dragon fruit (DF 3m × 3m), silviculture system (MDF-3m × 3m), horti-silviculture system with larger spacing (MDF-4m × 4m), sole Melia cultivation with in-situ moisture conservation (MDH-3m × 3m), sole Dragon fruit cultivation with in-situ moisture conservation (DFH-3m × 3m), horti-silviculture system of Melia and Dragon fruit with in-situ moisture conservation (MDFH-3m × 3m), and horti-silviculture system with larger spacing and in-situ moisture conservation (MDFH-4m × 4m). Each treatment was replicated thrice to evaluate their impact on productivity, profitability, soil fertility, and carbon sequestration for 8 years (2016-2023). The results revealed that the horti-silviculture system (MDFH-3 × 3 m) exhibited the highest total tree biomass and total carbon sequestration with an increase of 183.2% and 82.8% respectively, compared to sole Melia cultivation without HM and sole Melia with HM. Furthermore, sole Melia with HM augmented soil nutrients (N, P, K, and SOC) by 74.4%, 66.4%, 35.2%, and 78.3%, respectively, compared to control (no planting), with performance at par with MDFH-3 × 3 m. Similarly, sole Melia with HM enhanced SOC stock and SOC sequestration rate by 79.2% and 248% over control. However, it was found at par with MDFH-3 × 3 m. The horti-silviculture system (MDFH-3 × 3 m) consistently produced the highest fruit yield throughout the years surpassing other treatments. This treatment increased the average dragon fruit yield by 115.3% compared to sole dragon fruit without HM. Hence, the adoption of the horti-silviculture system (MDFH-3 × 3 m) could be a promising strategy for achieving enhanced environmental and economic benefits in ravine lands. Therefore, dragon fruit based horti-silviculture system (MDFH-3 × 3 m) could be recommended for restoration of ravine lands, improving land productivity, and mitigating impact of soil erosion particularly in Western India or similar agro-climatic regions of the world.

Compatibility of synthetic and biological pesticides with a biocontrol agent Phytoseiulus longipes (Acari: Phytoseiidae).

Savi PJ, de Moraes GJ, Hountondji FCC, Nansen C, de Andrade DJ.

Exp Appl Acarol. 2024 Jun 13. doi: 10.1007/s10493-024-00926-3. Online ahead of print.PMID: 38869728

Phytoseiulus longipes is a predatory mite of Tetranychus evansi, which is an invasive pest in Africa and elsewhere. The introduction of this predator in Africa has considerable potential, but little is known about the compatibility of P. longipes with commonly used pesticides. Here, we examined lethal and sublethal effects of two pyrethroids (cypermethrin and deltamethrin), two organophosphates (dimethoate and chlorpyrifos), one nicotinoid (imidacloprid), two acaricides (propargite and abamectin), two naturally derived pesticides (oxymatrine and azadirachtin), and one entomopathogenic fungal-based formulation (Hirsutella thompsonii) on P. longipes eggs and adults. The pesticides were sprayed at their maximum recommended concentrations. Topical exposures to azadirachtin, imidacloprid, propargite, abamectin, oxymatrine, and H. thompsonii significantly reduced the net reproductive rate (R_0), intrinsic rate of increase (r) and finite rate of increase (λ)of P. longipes. Pesticide lethal and sublethal effects on the predator were summarized in a reduction coefficient (E_x) for the classification based on IOBC toxicity categories. Results revealed that Azadirachtin and H. thompsonii were slightly harmful effects to adults. Imidacloprid, propargite, abamectin, and oxymatrine were moderately harmful to both eggs and adults. Residual persistence bioassays revealed that

4-day-old residue of azadirachtin had no harmful effect on the predator. Abamectin, oxymatrine, and H. thompsonii became harmless to it 10 days post-spraying, and propargite and imidacloprid were considered harmless after 20 days. Cypermethrin, deltamethrin, dimethoate, and chlorpyrifos were highly harmful to both eggs and adults, persistence remaining high even after 31 days of application. These findings provide valuable insights into decision-making when considering P. longipes for use in IPM programs.

Direct and indirect toxicity mechanisms of the natural insecticide azadirachtin based on in-silico interactions with tubulin, topoisomerase and DNA.

Kutluer F, Özkan B, Yalçin E, Çavuşoğlu K.

Chemosphere. 2024 Aug 2:143006. doi: 10.1016/j.chemosphere.2024.143006. PMID: 39098344

Natural pesticides, which attract attention with safe properties, pose a threat to many non-target organisms, so their toxic effects should be studied extensively. In this study, the toxic effects of Azadirachtin, a natural insecticide derived from Azadirachta indica, were investigated by in-vivo and in-silico methods. In-vivo toxic effects were determined using the Allium test and bulbs were treated with 5 mg/L (0.5x EC_{50}), 10 mg/L (EC_{50}), and 20 mg/L (2xEC_{50}) Azadirachtin. In the groups treated with Azadirachtin, there was a decline in germination-related parameters and accordingly growth was delayed. This regression may be related to oxidative stress in the plant, and the increase in malondialdehyde and proline levels in Azadirachtin-applied groups confirms oxidative stress. Azadirachtin toxicity increased dose-dependently and the most significant toxic effect was observed in the group administered 20 mg/L Azadirachtin. In this group, the mitotic index decreased by 43.4% and sticky chromosomes, vagrant chromosomes and fragments were detected at rates of 83.1±4.01, 72.7±3.46 and 65.1±3.51, respectively. By comet analysis, it was determined that Azadirachtin caused DNA fragmentation, and tail DNA, which was 0.10±0.32% in the control group, increased to 34.5±1.35% in the Azadirachtin -treated groups. These cytotoxic and genotoxic effects of Azadirachtin may be due to direct interaction with macromolecules as well as induced oxidative stress. Azadirachtin has been found to interact in-silico with alpha-tubulin, beta-tubulin, topoisomerase I and II, and various DNA sequences. Possible deteriorations in macromolecular structure and functions as a result of these interactions may cause cytotoxic and genotoxic effects. These results suggest that natural insecticides may also be unreliable for non-target organisms, and the toxic effects of compounds presented as "natural" should also be investigated.

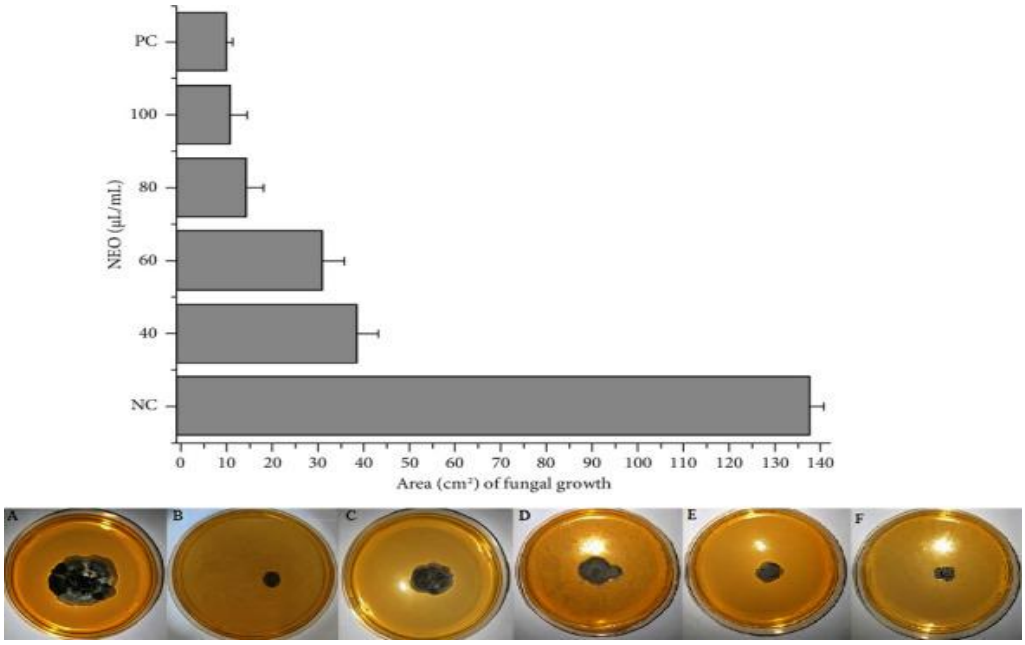
Neem Essential Oil as an Antifungal Agent against Phyllosticta citricarpa.

Schuch JM, Mendes CR, Cardoso GL, André da Veiga Lima Rosa Costamilan C, Matos Lopes PR, Montagnolli RN, Dilarri G, Bidoia ED.

Int J Microbiol. 2024 Jul 19;2024:6251407. doi: 10.1155/2024/6251407. PMID: 39071039

The fungus *Phyllosticta citricarpa* is a quarantine phytopathogen responsible for causing citrus black spot (CBS) disease. To export fruits to CBS-free countries, they must undergo a sanitation process to ensure disease control. In this study, neem essential oil (NEO) was tested against *P. citricarpa* for the first time as an alternative sanitizer. *In vitro* experiments

were conducted to determine the inhibition concentration of NEO for *P. citricarpa*, and the mode of action of the essential oil was evaluated. *In vivo* assays were performed to simulate the sanitization process used in packing houses. NEO was characterized by GC-MS/MS. The results revealed that NEO at 100 $\mu L \cdot mL^{-1}$ exhibited a similar inhibitory effect as copper oxychloride, suppressing 89.68 ± 1.14% of fungal mycelium growth. Fluorescence microscopy experiments demonstrated that NEO functions by disrupting the cytoplasmic membrane of fungal hyphae, leading to their death within 30 minutes of contact with NEO. GC-MS/MS characterization revealed a high presence of phenolic compounds, which serve as the primary antifungal agents responsible for the action against fungal hyphae. *In vivo* assays showed that NEO at 100 $\mu L \cdot mL^{-1}$ also reduced microorganisms (CFU mL^{-1}) by 93.00 ± 3.88% compared to the negative control. Overall, the results demonstrate that NEO can effectively serve as an alternative sanitizer against *P. citricarpa* in citrus packinghouses. Our findings allow future studies to explore the use of NEO for sanitizing other fruits and combating different phytopathogens to broaden its potential application in fruit sanitation for export.



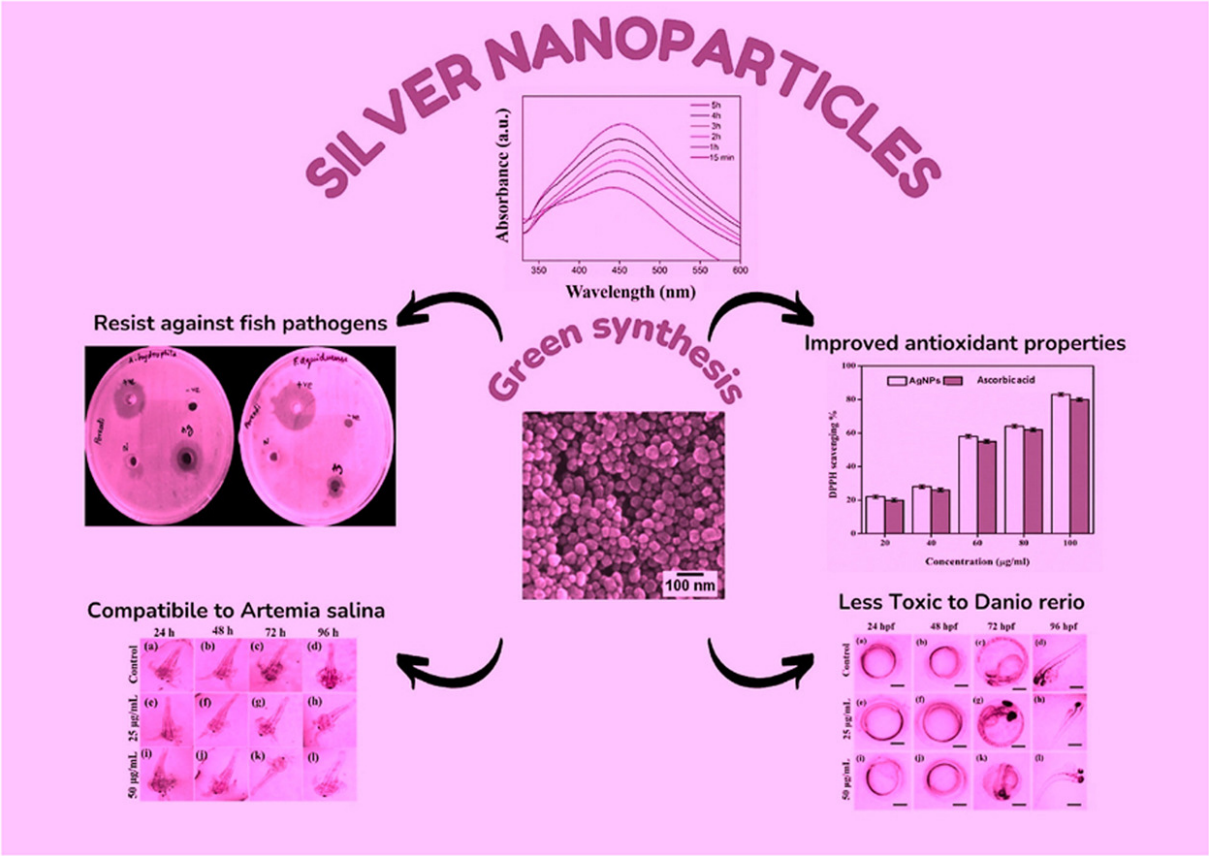
Antimicrobial efficiency against fish pathogens on the green synthesized silver nanoparticles.

Ramya JR, Ali S, ThanigaiArul K, Vijayalakshmi R, Gajendiran J, Gnanam S, Ramachandran K.

Microb Pathog. 2024 Jun 5:106725. doi: 10.1016/j.micpath.2024.106725. Online ahead of print.PMID: 38848933

Fish-borne pathogens such as A. hydrophila and F. aquidurense are the most resistant strains in pisciculture farming. Removing the aforementioned pathogens without antibiotics presents a formidable challenge. To overcome this problem, silver nanoparticles (AgNPs) are synthesized using silver nitrate, water medium, and as an Azadirachta indica leaf extract via the green synthesis route. X-ray diffraction (XRD) pattern results authenticate the synthesized material is the face-centered cubic structure of silver. The optical absorption edge of the synthesized product was found at the wavelength of 440 nm from

the UV-visible spectra, which is confirmed to relate to the Surface Plasmon Resonance peaks of silver particles. In addition, the optical band gap value of the synthesized Ag sample is measured to be 2.81 eV from the obtained optical absorption spectra. EDX spectrum of the synthesized product also supports confirming the silver particle formation. The FT-IR spectra of the neem extract and silver nanoparticles showed their characteristic functional groups, respectively. The presence of bands between 1000 cm^{-1} to 500 cm^{-1} indicates to the formation of silver particles. Spherical particles appeared in the synthesized Ag using Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM). The particle size of Ag NPs was measured as 40 nm and 62 ± 10 nm by TEM and Dynamic Light Scattering (DLS). The zeta potential was also measured as -12 mV showing the synthesized sample's stable nature. Using the DPPH assay, synthesized AgNPs were taken along with the various concentrations of ascorbic acid (20, 40, 60, 80, and 100 µg/mL) to examine the free radical scavenging activity (RSA). RSA value is higher (84±2%) for synthesized AgNPs at higher concentration (100 µg/mL) than 21±2% at low concentration (100 µg/mL). The antimicrobial efficacy of the AgNPs against A. hydrophila and F. aquidurense was performed through the agar diffusion method and its results showed the inhibitory zones of the F.aquidurense and A. hydrophila were measured as 25 ± 3 mm, and 28 ± 4 mm respectively. The synthesized Ag particles showed excellent antimicrobial and antioxidant properties confirmed by antimicrobial and DPPH experiments. It implies that the green synthesized silver nanoparticles could be a good alternative for antibiotics in aquaculture farms. The exposure of low concentrations of silver nanoparticles to zebrafish and brine shrimp does not affect the viability and morphology. The exposure of silver nanoparticles in the fisheries in optimized concentration and time could control the fish-borne pathogens without antibiotics.



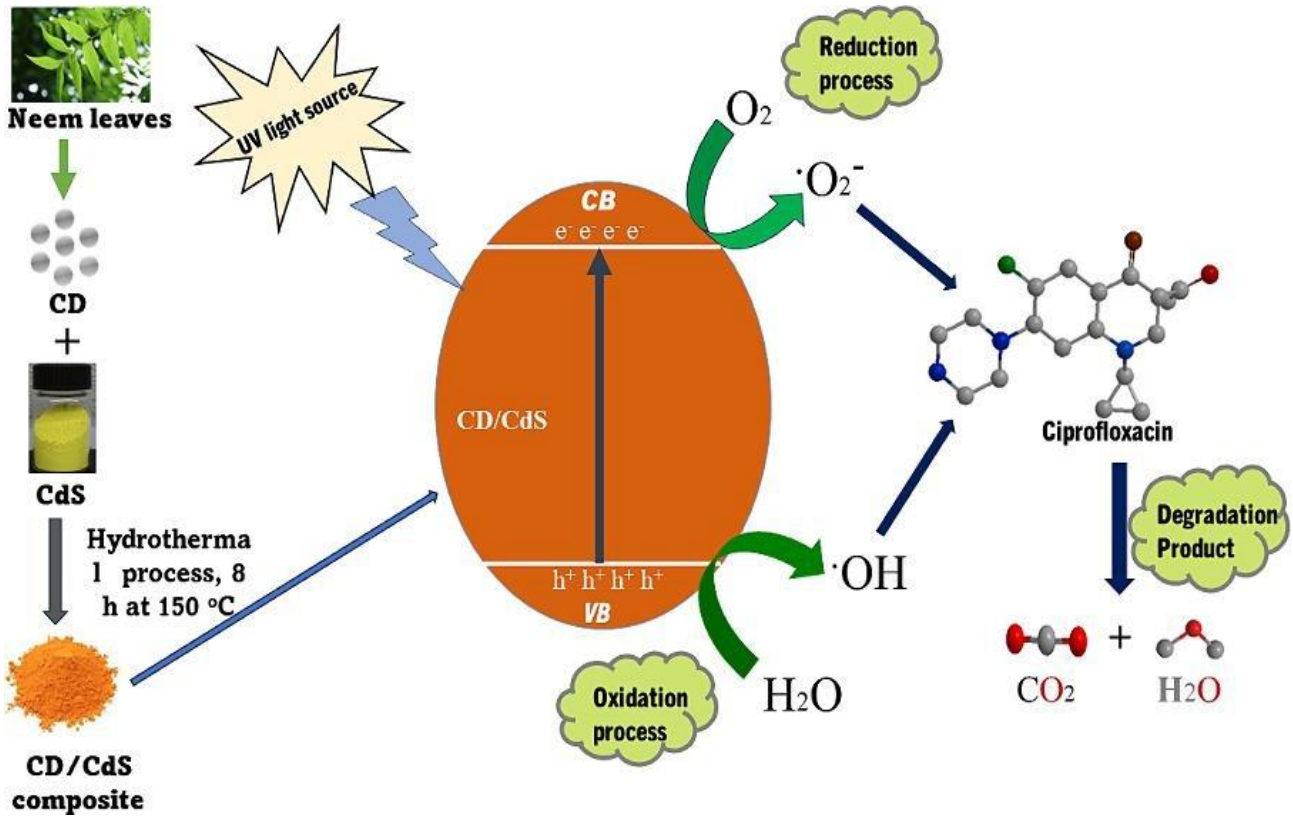
Neem for Sustainable Environment & Green Synthesis

Carbon dots decorated cadmium sulfide nanomaterials for boosting photocatalytic activity for ciprofloxacin degradation.

Choudhary M, Saini P, Chakinala N, Surolia PK, Gupta Chakinala A.

Spectrochim Acta A Mol Biomol Spectrosc. 2024 May 31;319:124572. doi: 10.1016/j.saa.2024.124572. Online ahead of print.PMID: 38830330

This study investigates the utilization of carbon dots (CDs) from neem leaves (Azadirachta indica) decorated onto cadmium sulfide (CdS) for the photocatalytic degradation of ciprofloxacin. A comparative study of ciprofloxacin degradation with pristine CdS and CD decorated CdS demonstrated high degradation of ~ 75 % with CD/CdS when compared to bare CdS (~68 %). Process optimization studies were further carried out with CD/CdS catalysts at different solution pH (4-10), feed concentrations (10-50 mg/L), catalyst loadings (25-125 mg/L), temperatures (10 - 30 °C), and lamp power (25, 50, 250 W and sunlight). Higher temperatures, combined with a solution pH of 7 and catalyst loading of 100 mg/L favored the enhanced degradation of 20 mg/L of ciprofloxacin. The ciprofloxacin degradation rate increased linearly with temperature with an apparent activation energy of 27 kJ mol^{-1}. The CD/CdS photocatalyst demonstrated maximum degradation rates with higher lamp powers while it also showed remarkable performance under natural sunlight achieving the same degradation within 3 h.

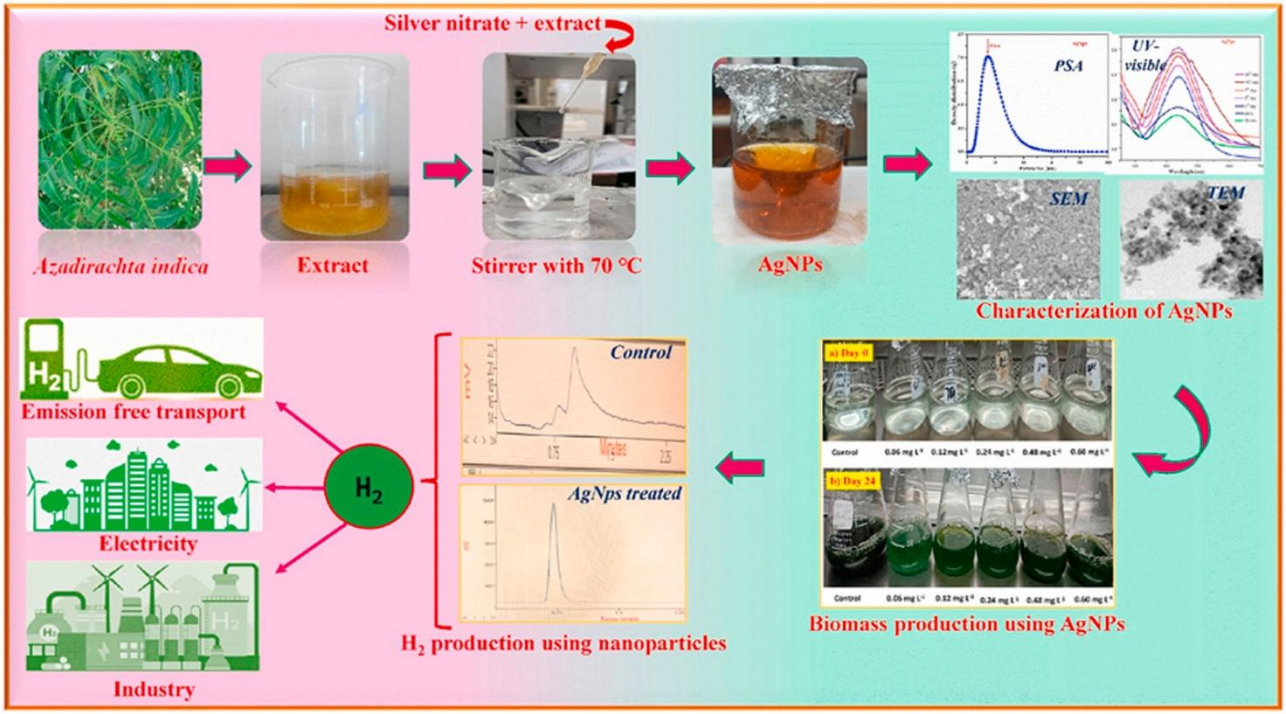


Characterization and potentiality of plant-derived silver nanoparticles for enhancement of biomass and hydrogen production in Chlorella sp. under nitrogen deprived condition.

Subramani K, Wutthithien P, Saha R, Lindblad P, Incharoensakdi A.

Chemosphere. 2024 Jun 1;361:142514. doi: 10.1016/j.chemosphere.2024.142514. Online ahead of print. PMID: 38830468

Energy is a crucial entity for the development and it has various alternative forms of energy sources. Recently, the synthesis of nanoparticles using benign biocatalyst has attracted increased attention. In this study, silver nanoparticles were synthesized and characterized using Azadirachta indica plant-derived phytochemical as the reducing agent. Biomass of the microalga Chlorella sp. cultivated in BG11 medium increased after exposure to low concentrations of up to 0.48 mg L^{-1} AgNPs. In addition, algal cells treated with 0.24 mg L^{-1} AgNPs and cultivated in $BG11_0$ medium which contained no nitrogen source showed the highest hydrogen yield of 10.8 mmol L^{-1}, whereas the untreated cells under the same conditions showed very low hydrogen yield of 0.003 mmol L^{-1}. The enhanced hydrogen production observed in the treated cells was consistent with an increase in hydrogenase activity. Treatment of $BG11_0$ grown cells with low concentration of green synthesized AgNPs at 0.24 mg L^{-1} enhanced hydrogenase activity with a 5-fold increase of enzyme activity compared to untreated $BG11_0$ grown cells. In addition, to improve photolytic water splitting efficiency for hydrogen production, cells treated with AgNPs at 0.24 mg L^{-1} showed highest oxygen evolution signifying improvement in photosynthesis. The silver nanoparticles synthesized using phytochemicals derived from plant enhanced both microalgal biomass and hydrogen production with an added advantage of CO_2 reduction which could be achieved due to an increase in biomass. Hence, treating microalgae with nanoparticles provided a promising strategy to reduce the atmospheric carbon dioxide as well as increasing production of hydrogen as clean energy.



Optimized microwave-assisted azadirachtin extraction using response surface methodology.

Martínez-Castro R, Flórez-Santiago J, Valle-Molinares R, Cabrera-Barraza J, Espitia-Almeida F.

Heliyon. 2024 May 18;10(10):e31504. doi: 10.1016/j.heliyon.2024.e31504. PMID: 38831827

The neem tree (*Azadirachta indica* A. Juss) is grown mainly for shade, fuel, and numerous non-timber forest products using its leaves, fruit, and bark. It produces an essential oil that is used as a source for obtaining bioinsecticides, with a broad spectrum of action in agricultural production. Its bioinsecticidal activity is due to the presence of triterpenes, such as azadirachtin, a product in continued growth of the global biopesticide market. Optimal conditions for neem oil extraction using response surface methodology (RSM) and microwave-assisted extraction (MAE) methods have been defined. However, the extraction conditions for these methods tend to consume high volumes of organic solvent and long extraction times. The aim of the present study is to determine the optimal conditions for the extraction of azadirachtin from neem seeds in a hydroalcoholic medium using MAE and RSM with a Box-Behnken design (BBD). A BBD was applied to evaluate the effects of the factors, magnetron voltage (X_1), extraction time (X_2), and pH of the extraction medium (X_3), on the yield of the azadirachtin extraction process. The effect of each variable on the extraction yield was studied independently, considering the pure coefficients (linear and quadratic) on the three levels that were studied in the experiments. Moreover, the study experiments were conducted in triplicate, data were presented as mean and standard deviation, homogeneity of variances was estimated using Levene's test, and a two-way ANOVA with Tukey's post hoc analysis was performed to identify the experimental conditions that allowed us to find the highest extraction yield and to analyze whether the response surface model adequately described our data. The most significant effects of the model correspond to quadratic and interaction effects ($p < 0.0001$); the quadratic terms voltage (X_1), extraction time (X_2), and pH (X_3); and the interaction effects between voltage-pH (X_1*X_3) and time-pH (X_2*X_3), which had a significant influence on the model. Moreover, a canonical analysis was performed. The optimal conditions were as follows: 69.22 V, 6.89 min, and a pH value of 4.35, coinciding with the zones shown in the contour plots. Furthermore, the response obtained at the optimal conditions was 37.5 µg of azadirachtin per gram of pretreated seed.

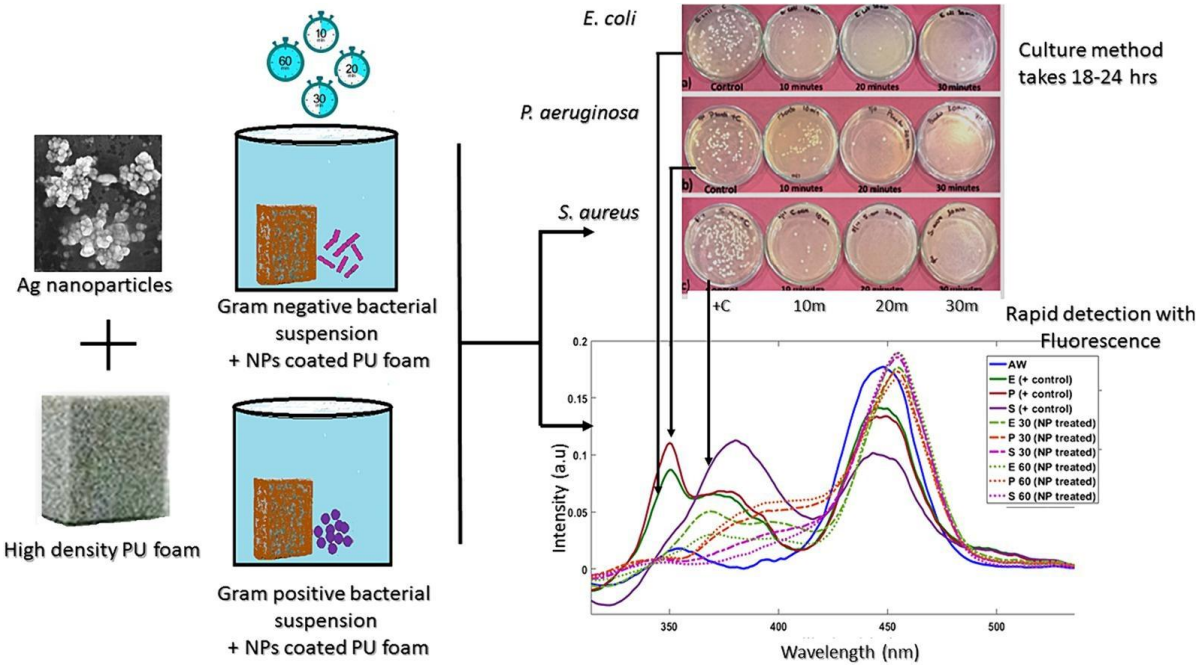
Rapid detection of bactericidal efficacy of nanoparticles coated polyurethane foam by synchronous fluorescence spectroscopy.

Ali H, Anwar S, Ali Khan R.

Spectrochim Acta A Mol Biomol Spectrosc. 2024 Jul 24;323:124877. doi: 10.1016/j.saa.2024.124877. PMID: 39096680

The ability of right-angled synchronous fluorescence spectroscopy (SFS) was explored to analyse the bacterial load in water treated with green synthesized silver nanoparticles (AgNPs) coated polyurethane foam (PUF). Gram negative (Escherichia coli, Pseudomonas aeruginosa) and Gram positive (Staphylococcus aureus) bacteria cultured in nutrient broth were diluted in autoclaved water containing NPs-coated PUF. The survival

rate of S. aureus and E. coli lowered after ten minutes as compared to P. aeruginosa; however, after thirty minutes, the percentage viability dropped and recorded as 3.4%, 0.9%, and 0.1% for E. coli, P. aeruginosa and S. aureus respectively in the treated suspensions. No spectral change was observed in the fluorescence emission from the positive control and treated bacterial suspension owing to the masking effect of the emission from nutrient broth. In parallel, SF spectra recorded for directly picked bacterial colony dissolved in water showed remarkable drop in tryptophan emission after treatment with NPs-coated PUF. The SF data changes were assisted by hierarchical cluster analysis, which also made it possible to distinguish between positive control and treated bacterial suspensions. SFS has shown to be a reliable substitute for the culture plate approach for the quick identification of bacterial contamination in water.



Green synthesis of magnetite iron oxide nanoparticles using Azadirachta indica leaf extract loaded on reduced graphene oxide and degradation of methylene blue.

Akhtar MS, Fiaz S, Aslam S, Chung S, Ditta A, Irshad MA, Al-Mohaimeed AM, Iqbal R, Al-Onazi WA, Rizwan M, Nakashima Y.

Sci Rep. 2024 Aug 6;14(1):18172. doi: 10.1038/s41598-024-69184-y.PMID: 39107555

In the current arena, new-generation functional nanomaterials are the key players for smart solutions and applications including environmental decontamination of pollutants. Among the plethora of new-generation nanomaterials, graphene-based nanomaterials and nanocomposites are in the driving seat surpassing their counterparts due to their unique physicochemical characteristics and superior surface chemistry. The purpose of the present research was to synthesize and characterize magnetite iron oxide/reduced graphene oxide nanocomposites (FeNPs/rGO) via a green approach and test its application in the degradation of methylene blue. The modified Hummer's protocol was adopted to synthesize graphene oxide (GO) through a chemical exfoliation approach using a graphitic route. Leaf extract of Azadirachta indica was used as a green reducing agent to reduce GO into reduced graphene oxide (rGO). Then, using the green deposition approach and Azadirachta indica leaf extract, a nanocomposite comprising magnetite iron

oxides and reduced graphene oxide i.e., FeNPs/rGO was synthesized. During the synthesis of functionalized FeNPs/rGO, Azadirachta indica leaf extract acted as a reducing, capping, and stabilizing agent. The final synthesized materials were characterized and analyzed using an array of techniques such as scanning electron microscopy (SEM)-energy dispersive X-ray microanalysis (EDX), Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction analysis, and UV-visible spectrophotometry. The UV-visible spectrum was used to evaluate the optical characteristics and band gap. Using the FT-IR spectrum, functional groupings were identified in the synthesized graphene-based nanomaterials and nanocomposites. The morphology and elemental analysis of nanomaterials and nanocomposites synthesized via the green deposition process were investigated using SEM-EDX. The GO, rGO, FeNPs, and FeNPs/rGO showed maximum absorption at 232, 265, 395, and 405 nm, respectively. FTIR spectrum showed different functional groups (OH, COOH, C=O), C-O-C) modifying material surfaces. Based on Debye Sherrer's equation, the mean calculated particle size of all synthesized materials was < 100 nm (GO = 60-80, rGO = 90-95, FeNPs = 70-90, Fe/GO = 40-60, and Fe/rGO = 80-85 nm). Graphene-based nanomaterials displayed rough surfaces with clustered and spherical shapes and EDX analysis confirmed the presence of both iron and oxygen in all the nanocomposites. The final nanocomposites produced via the synthetic process degraded approximately 74% of methylene blue. Based on the results, it is plausible to conclude that synthesized FeNPs/rGO nanocomposites can also be used as a potential photocatalyst degrader for other different dye pollutants due to their lower band gap.

Neem for Industrial Applications

Novel acrylamide-based baits for effective control of subterranean termites (Blattodea: Rhinotermitidae).

Abbas S, Alam A, Abbas M, Xiao F, Jiali L, Daood U, Hafeez F, Shakeel M, Ali J, Khan KA, Ghramh HA, Romano D, Ri Zhao C.

Pest Manag Sci. 2024 Jul 29. doi: 10.1002/ps.8332.PMID: 39072976

Background: Acrylamide-based bait has super water absorption making it highly attractive to subterranean termites that are lured by wood with high water content. This study investigated the control efficiency of these baits on subterranean termites. In particular, we evaluated the water-absorption capacity, attractiveness to subterranean termites, and control efficiency of these baits on subterranean termites through wooden blocks (Populus deltoides and three types of particleboards). **Results:** The results indicated a substantial water absorption capacity of acrylamide (70.6%; control: 14.8%) and a strong attraction for feeding subterranean termites (P. deltoides: 198 highest; 81 lowest subterranean termites individuals; combination of neem leaves and walnut shells: 168 highest; 36 lowest subterranean termites individuals). When acrylamide was combined with boric acid at the highest concentration, it resulted in the lowest wood consumption rates (P. deltoides: 24.1%; control: 63.8%, combination of neem leaves and walnut shells: 32.5%; control: 62.1%). **Conclusions:** In conclusion, this research supports the commercial viability of employing innovative acrylamide-based toxic baits and particleboards for subterranean termite management.

Antifungal Activity of Neem Leaf Extract With Eucalyptus citriodora Oil and Cymbopogon martini Oil Against Tinea Capitis: An In-Vitro Evaluation.

Tiple RH, Jamane SR, Khobragade DS.

Cureus. 2024 May 5;16(5):e59671. doi: 10.7759/cureus.59671. eCollection 2024 May.PMID: 38836134

Introduction Tinea capitis, often known as ringworm of the scalp, is a fungal infection that affects the scalp, eyelashes, and eyebrows. It is generally caused by dermatophytes from the genera *Trichophyton* and *Microsporum. Trichophyton tonsurans* and *Microsporum canis* are the main etiological agents responsible for most of the cases of tinea capitis globally. Tinea capitis commonly manifests as itchy, scaly patches of hair loss. Tinea capitis is the prevailing dermatophyte illness among children globally. Methods An in-vitro evaluation study was conducted to assess the antifungal properties of ethanolic extracts of neem leaves and the oils of *Eucalyptus citriodora* and *Cymbopogon martini*, both individually and in combination. The agar-well diffusion method and the M38-A2 microbroth dilution method were employed to evaluate the antifungal efficacy against pathogenic dermatophyte strains, namely *Microsporum canis* and *Trichophyton tonsurans*. The fully mature green leaves were treated with ethanol to make the neem leaf extract. Additionally, high-performance liquid chromatographic analysis was carried out to determine the contents of the terpenoids. Fluconazole, an antifungal drug, is used as a standard. Results The findings demonstrated an overall inhibition of the growth of dermatophytes at a minimal inhibitory concentration of 187.5 and 375 µg/ml for neem leaf extract and 0.625 to 2.5 µl/ml for selected herbal oils, whereas it was 0.25 µg/ml and 0.50 µg/ml for positive control against *Microsporum canis* and *Trichophyton tonsurans,* respectively. Conclusion The phytochemical investigation of the ethanolic extracts in neem leaves revealed the presence of terpenoids, which are known for their significant biological activity. The study's findings demonstrated the therapeutic capabilities of neem leaf extract in combination with the oils of *Eucalyptus citriodora* and *Cymbopogon martini* for managing the tinea capitis infection. A broader and improved antifungal spectrum was seen when neem leaf extract and oils were combined. Therefore, it can be developed into a suitable formulation for the management of tinea capitis.

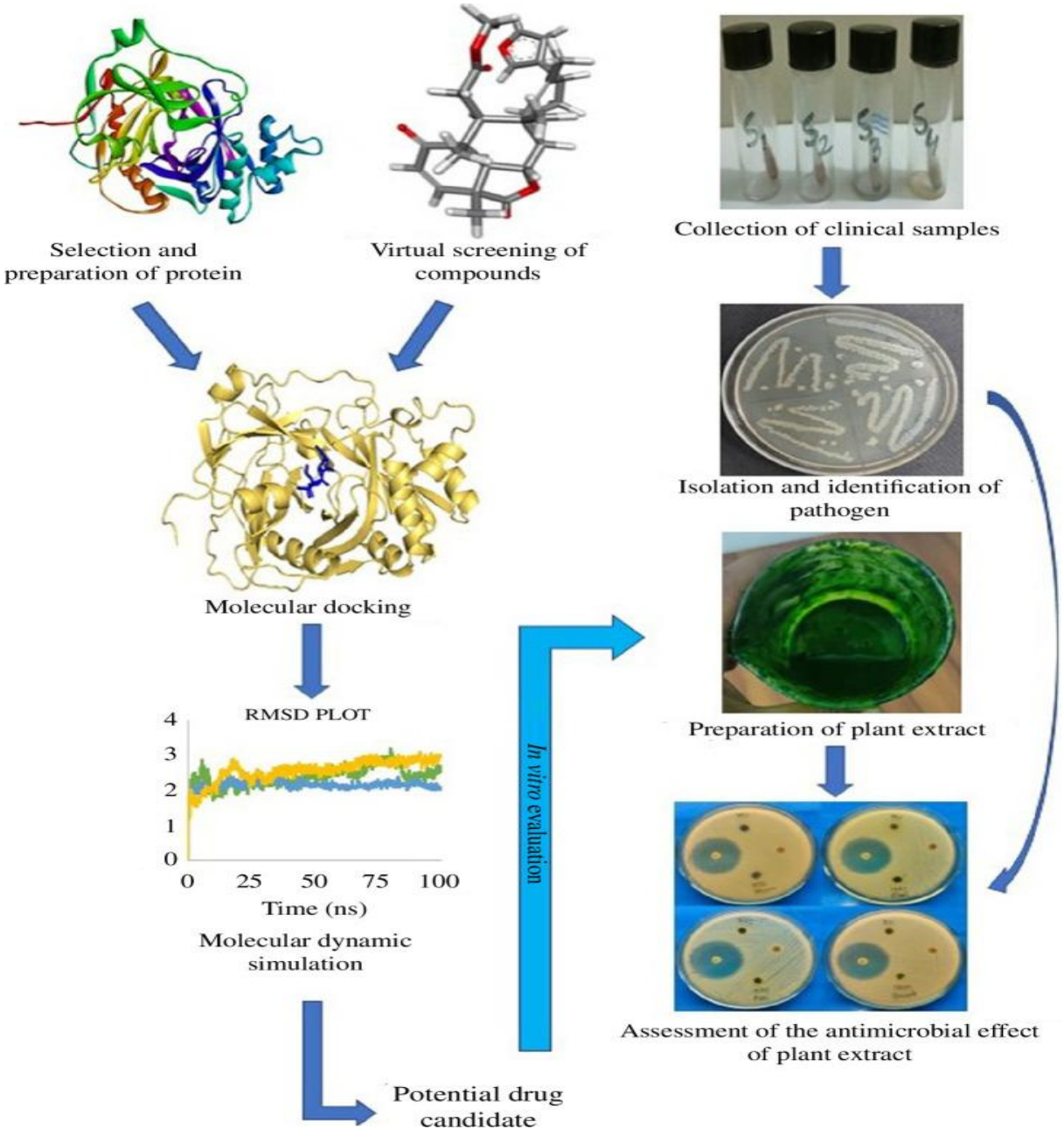
Developing phytocompound-based new drugs against multi-drug-resistant *Staphylococcus aureus*.

Shuvo MN, Halder SK, Alam N, Himel MK, Shil A.

R Soc Open Sci. 2024 Jul 24;11(7):231475. doi: 10.1098/rsos.231475. PMID: 39050719

Staphylococcus aureus, a prevalent component of the human microbiota, is associated with skin infections to life-threatening diseases, presenting challenges in treatment options and necessitating the development of effective treatments. This study integrated computational and *in vitro* approaches to identify promising phytocompounds with therapeutic potential. Staphopain B emerged as a target protein for its role in immune evasion, exhibiting stability during molecular dynamic simulation (MDS) with a root mean

square deviation value of 2.376 Å. Screening 115 phytocompounds with antibacterial properties from the PubChem database identified 12 with drug-like properties, nine of which showed superior binding affinity to Staphopain B compared to a commercial antibiotic, doxycycline (-7.8 kcal mol^{-1}). Notably, epoxyazadiradione and nimbolide displayed higher estimated free energy of binding scores (-7.91 and -7.93 kcal mol^{-1}, respectively), indicating strong protein-ligand interactions. The root mean square fluctuation values for epoxyazadiradione and nimbolide were 1.097 and 1.034 Å, respectively, which was confirmed through MDS. Crude ethanolic extracts (100% and 70%) of neem (*Azadirachta indica*) leaves demonstrated narrow inhibition against the bacteria in comparison to doxycycline in the disc-diffusion assay. This study underscores the potential of phytocompounds as therapeutic agents against *S. aureus*; however, further *in vitro* experiments and testing of the phytocompounds *in vivo* are required.



Antiviral Activity, Pharmacoinformatics, Molecular Docking, and Dynamics Studies of *Azadirachta indica* Against Nipah Virus by Targeting Envelope Glycoprotein: Emerging Strategies for Developing Antiviral Treatment.

Saha O, Siddiquee NH, Akter R, Sarker N, Bristi UP, Sultana KF, Remon SLR, Sultana A, Shishir TA, Rahaman MM, Ahmed F, Hossen F, Amin MR, Akter MS.

Bioinform Biol Insights. 2024 . doi: 10.1177/11779322241264145. PMID: 39072258

The Nipah virus (NiV) belongs to the *Henipavirus* genus is a serious public health concern causing numerous outbreaks with higher fatality rate. Unfortunately, there is no effective medication available for NiV. To investigate possible inhibitors of NiV infection, we used in silico techniques to discover treatment candidates in this work. As there are not any approved treatments for NiV infection, the NiV-enveloped attachment glycoprotein was set as target for our study, which is responsible for binding to and entering host cells. Our in silico drug design approach included molecular docking, post-docking molecular mechanism generalised born surface area (MM-GBSA), absorption, distribution, metabolism, excretion/toxicity (ADME/T), and molecular dynamics (MD) simulations. We retrieved 418 phytochemicals associated with the neem plant (*Azadirachta indica*) from the IMPPAT database, and molecular docking was used to ascertain the compounds' binding strength. The top 3 phytochemicals with binding affinities of -7.118, -7.074, and -6.894 kcal/mol for CIDs 5280343, 9064, and 5280863, respectively, were selected for additional study based on molecular docking. The post-docking MM-GBSA of those 3 compounds was -47.56, -47.3, and -43.15 kcal/mol, respectively. As evidence of their efficacy and safety, all the chosen drugs had favorable toxicological and pharmacokinetic (Pk) qualities. We also performed MD simulations to confirm the stability of the ligand-protein complex structures and determine whether the selected compounds are stable at the protein binding site. All 3 phytochemicals, Quercetin (CID: 5280343), Cianidanol (CID: 9064), and Kaempferol (CID: 5280863), appeared to have outstanding binding stability to the target protein than control ribavirin, according to the molecular docking, MM-GBSA, and MD simulation outcomes. Overall, this work offers a viable approach to developing novel medications for treating NiV infection.

Drug repositioning identifies salvinorin A and deacetylgedunin (DCG) enriched plant extracts as novel inhibitors of Mpro, RBD-ACE2 and TMPRRS2 proteins.

Shayo MJ, Samwel B, Shadrack DM, Cassel J, Salvino JM, Montaner LJ, Deogratias G, Tietjen I, Kiruri L, Hilonga S, Innocent E.

RSC Adv. 2024 Jul 4;14(29):21203-21212. doi: 10.1039/d4ra02593h. eCollection 2024 Jun 27.PMID: 38966817

The coronavirus disease 2019 (COVID-19) has spread worldwide with severe health, social, and economic repercussions. Although vaccines have significantly reduced the severity of symptoms and deaths, alternative medications derived from natural products (NPs) are vital to further decrease fatalities, especially in regions with low vaccine uptake. When paired with the latest computational developments, NPs, which have been used to cure illnesses and infections for thousands of years, constitute a renewed resource for drug discovery. In the present report, a combination of computational and *in vitro* methods reveals the repositioning of NPs and identifies salvinorin A and deacetylgedunin (DCG) as having potential anti-SARS-CoV-2 activities. Salvinorin A was found both *in silico* and *in*

vitro to inhibit both SARS-CoV-2 spike/host ACE2 protein interactions, consistent with blocking viral cell entry, and well as live virus replication. Plant extracts from *Azadirachta indica* and *Cedrela odorata*, which contain high levels of DCG, inhibited viral cell replication by targeting the main protease (Mpro) and/or inhibited viral cell entry by blocking the interaction between spike RBD-ACE2 protein at concentrations lower than salvinorin A. Our findings suggest that salvinorin A represent promising chemical starting points where further optimization may result in effective natural product-derived and potent anti-SARS-CoV-2 inhibitors to supplement vaccine efforts.

Case series of cutaneous myiasis in neglected cases of autoimmune bullous disorders.

Ramamoorthy L, Chandrashekar L.

Clin Exp Dermatol. 2024 Jul 8:llae257. doi: 10.1093/ced/llae257. PMID: 38973704

Myiasis is an infestation of the tissues and organs of living vertebrates and humans by fly larvae, usually those belonging to the Calliphoridae family. The larvae feed on the host's necrotic or living tissue. Preexisting dermatological conditions and poor hygiene have been described as predisposing factors for myiasis, and it is especially common among neglected, dependent patients. Based on our literature search, we could find only a few case reports reported on cutaneous myiasis in autoimmune bullous disorders. It is especially more common in the South Indian Tamil Nadu population due to the false belief that autoimmune blistering disorders like pemphigus and bullous pemphigoid are considered chicken pox and treated with neem and turmeric preparation with poor hygiene. Herein we report a series of eight autoimmune blistering disorders with cutaneous myiasis.

Review on application of herbal extracts in biomacromolecules-based nanofibers as wound dressings and skin tissue engineering.

Sharifi M, Bahrami SH.

Int J Biol Macromol. 2024 Jul 4:133666. doi: 10.1016/j.ijbiomac.2024.133666. PMID: 38971295

The skin, which covers an area of 2 square meters of an adult human, accounts for about 15 % of the total body weight and is the body's largest organ. It protects internal organs from external physical, chemical, and biological attacks, prevents excess water loss from the body, and plays a role in thermoregulation. The skin is constantly exposed to various damages so that wounds can be acute or chronic. Although wound healing includes hemostasis, inflammatory, proliferation, and remodeling, chronic wounds face different treatment problems due to the prolonged inflammatory phase. Herbal extracts such as Nigella Sativa, curcumin, chamomile, neem, nettle, etc., with varying properties, including antibacterial, antioxidant, anti-inflammatory, antifungal, and anticancer, are used for wound healing. Due to their instability, herbal extracts are loaded in wound dressings to facilitate skin wounds. To promote skin wounds, skin tissue engineering was developed using polymers, bioactive molecules, and biomaterials in wound dressing. Conventional wound dressings, such as bandages, gauzes, and films, can't efficiently respond to wound

healing. Adhesion to the wounds can worsen the wound conditions, increase inflammation, and cause pain while removing the scars. Ideal wound dressings have good biocompatibility, moisture retention, appropriate mechanical properties, and non-adherent and proper exudate management. Therefore, by electrospinning for wound healing applications, natural and synthesis polymers are utilized to fabricate nanofibers with high porosity, high surface area, and suitable mechanical and physical properties. This review explains the application of different herbal extracts with different chemical structures in nanofibrous webs used for wound care.

Eight months of integrated yoga, hydrotherapy and acupuncture on serum IgE levels and symptoms severity of a patient with chronic allergic rhinosinusitis: A case report

Umadevi K, Vijaya Bharathi E, Mooventhan A, Nivethitha L.

J Bodyw Mov Ther. 2024 Jul;39:541-543. doi: 10.1016/j.jbmt.2024.03.028. Epub 2024 Mar 25.PMID: 38876682

A 27-year-old man with Allergic rhino sinusitis presented to our hospital in July 2020 with complaints of continuous sneezing, coughing while rising from bed for half an hour, and the same complaints repeated in the afternoon for half an hour, as well as a continuous dry cough for half an hour in the evening. He also had complaints of itching and skin rashes, particularly in his limbs. He underwent yoga (45 minutes, 5-6 days a week) including Jalaneti (a yogic cleansing technique, i.e. nasal irrigation with warm salt water for twice a week), hydrotherapy (enema using neem leaves paste mixed with water and steam bath on first day, followed by facial steam on alternate days) and Acupuncture (one session a week) for 8 months. Results showed a reduction in immunoglobulin E (IgE) levels and symptom severity suggesting that integrated yoga, hydrotherapy, and acupuncture are effective in the management of chronic allergic rhinosinusitis. All treatments were well tolerated without adverse effects. Though the result is encouraging, further studies are required with a larger sample size.

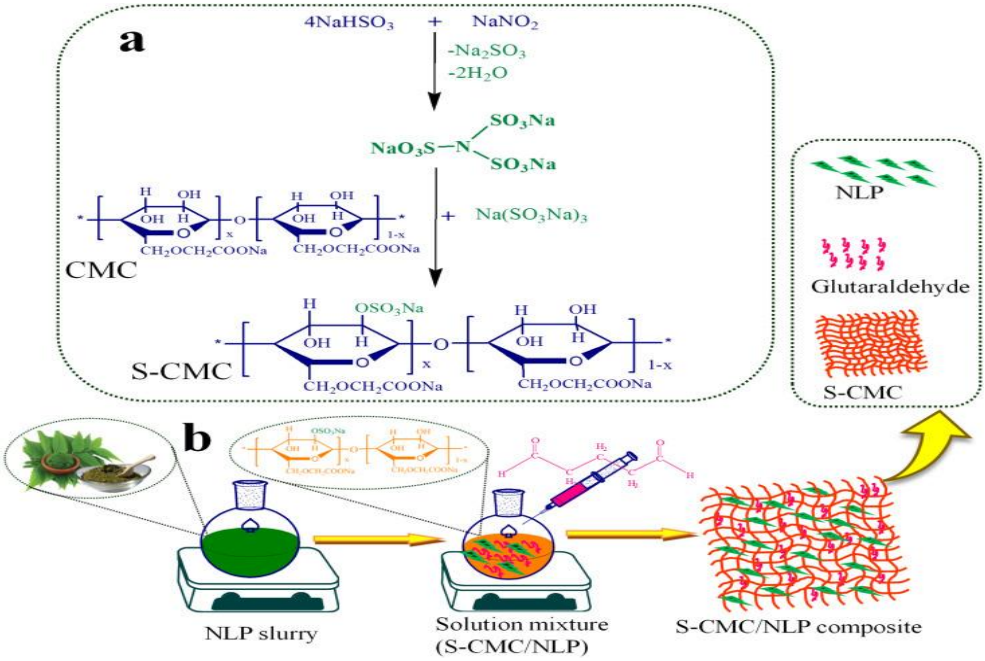
Anticoagulation activity of sulfated carboxymethyl cellulose/Azadirachta indica leaf powder-based bio-composite.

Alamry KA, Hussein MA, Khan A, Asiri AM.

RSC Adv. 2024 Jul 12;14(30):22017-22027. doi: 10.1039/d4ra02893g. eCollection 2024 Jul 5.PMID: 39006770

Polymeric bio-composites synthesized *via* a green approach using natural herbs have fascinating anticoagulant activity due to their eco-friendly and non-toxic behavior towards various physical and chemical actions. Herein, we introduce a simple and eco-friendly approach for the fabrication of a new hybrid type of bio-composite based on sulfated carboxymethyl cellulose (S-CMC) and *Azadirachta indica* leaf powder (S-CMC/NLP). First, a non-toxic sulfating agent called $N(SO_3Na)_3$ was used to modify carboxymethyl cellulose into S-CMC. With an ion exchange capacity of 0.25 meq. g^{-1}, the level of sulfation (%) of S-CMC (modified polysaccharide) was measured to be 12.01%. Three types of S-CMC/NLP bio-composites were developed by varying the concentration of NLP. FE-SEM,

EDX, and XRD were used to characterize the structural features of S-CMC/NLP bio-composites. FTIR spectroscopy indicated that the S-CMC/NLP bio-composite possesses COO^-, -OH and SO^{3-} groups, suggesting the structural similarity to heparin. In addition, the anticoagulant effect of the S-CMC/NLP bio-composite was investigated using PT and APTT assays. The APTT investigation confirmed that following the intrinsic pathway of the coagulation system, 2-NLP/S-CMC bio-composite dose-dependently (0.045-0.28 mg mL^{-1}) prolonged the time of blood coagulation compared to control (pure plasma). The S-CMC/NLP bio-composite showed its potential as a new, safe, and effective candidate for anticoagulant activity.



Comparative evaluation on surface nanohardness, surface microhardness, surface roughness, and wettability of plant-based organic nanoparticle reinforced polyetheretherketone as an implant material - An in vitro study.

Vidhyasankari N, John RR, Senthilmurugan PR, Vishnupriya V.

J Indian Prosthodont Soc. 2024 Jul 1;24(3):245-251. doi: 10.4103/jips.jips_511_23. PMID: 38946507

Aim: Synthetic inorganic materials are commonly used as reinforcing agents in polyetheretherketone (PEEK) composite, whereas natural organic plant-based reinforcing agents are negligible. Surface hardness, roughness, and wettability are indicative factors of osseointegration behavior to be used as an implant material. This study evaluated micro surface hardness (MSH), nano surface hardness (NSH), surface roughness (SR), and contact angle (CA) of PEEK-Azadirachta indica reinforced at 10 wt%, 20 wt%, and 30 wt%. **Settings and design:** This was an in vitro study. **Materials and methods:** Neem (A. indica) leaf nanoparticles were prepared and reinforced with PEEK powder at 10%, 20%, and 30% weight ratios by injection molding. Sixty specimens underwent the microhardness and CA testing using a digital microhardness tester, and CA goniometer, respectively, and later nanoindentation test to analyze the nanohardness and SR. **Statistical analysis used:** A one-way ANOVA test with a 95% confidence interval for MSH and NSH, SR, and

CA was performed on the samples. A post hoc Bonferroni test was conducted (α = 0.05) to compare the groups. **Results:** There was a significant increase in nanohardness (P = 0.000) with zero difference in microhardness (P = 0.514). The addition of 10 wt%, 20 wt%, and 30 wt% nanoparticles increased the SR value of the pure PEEK from 273.19 nm to 284.10 (3.99%), 296.91 (8.68%), and 287.54 (5.24%), respectively. In the analysis of the CA, CA 20% shows the lowest angle (63.69) with the highest for control specimens (82.39). There is an increase in the PEEK composite SR with a decrease in CA. **Conclusions:** The addition of plant-derived nanoparticles into the PEEK matrix has a significant impact on the hardness and hydrophobicity enhancing cell growth and osteoblastic differentiation during osseointegration of dental implants.

Formulation of Neem and Echinacea Gel for Oral Health Along With the Evaluation of Antimicrobial, Cytotoxic, Anti-inflammatory, and Free Radical Scavenging Activity: An In Vitro Study.

Sindhusha VB, Rajasekar A.

Cureus. 2024 Jul 1;16(7):e63631. doi: 10.7759/cureus.63631. eCollection 2024 Jul.PMID: 39092399

Background Herbs have been used in medical practice for centuries and continue to play a significant role in modern complementary and alternative medicine. Phytochemicals in these herbs possess strong antioxidant and anti-inflammatory properties, which are beneficial in targeting oral health issues, such as dental plaque, gingivitis, and oral microbial infections. As research progresses, the challenge remains to translate these natural compounds into safe, effective, and accessible treatments for a wide range of diseases. Aim The aim of this research was to formulate the neem and echinacea gel along with the evaluation of antimicrobial, anti-inflammatory, free-radical scavenging activity, and cytotoxic potential. Materials and methods The neem and echinacea gel was prepared using a concentrated powdered mixture of neem and echinacea (5 grams each) to which 100 ml of distilled water was added, and the mixture was boiled for 30 minutes at 60°C. The 10 ml concentrate was mixed with 20 ml of a carbopol and carboxymethyl cellulose (CMC) mixture and mixed thoroughly, which resulted in neem and echinacea gel. Then, the antimicrobial, anti-inflammatory, cytotoxic potential, and free-radical scavenging activity of the gel were evaluated. The data obtained were statistically analyzed with the help of a paired t-test, where a p-value of less than 0.05 was considered statistically significant. Results The antimicrobial assay showed that neem and echinacea gel at the concentration of 100 micrograms showed a greater zone of inhibition against *Staphylococcus aureus* (3.15 ± 0.26), *Streptococcus mutans* (2.48 ± 0.45), *Enterococcus faecalis* (2.89 ± 0.15), and *Candida albicans* (4.28 ± 0.87). The cytotoxic test revealed that even at an 80 µg concentration of the extract, more than 70% of the nauplii were vital, which indicated that the gel was not cytotoxic. The highest anti-inflammatory activity (78.39 ± 1.82) of the gel was seen at 50 micrograms when compared with diclofenac sodium (73.16 ± 1.80). The free radical scavenging activity showed that the 2,2-diphenyl-1-picrylhydrazyl (DPPH) absorbance of the neem and echinacea extract was highest at 50 micrograms. Conclusion The combination of neem and echinacea extract-based gel possessed high antimicrobial and anti-inflammatory activity when compared with standard drugs, such as amoxicillin and diclofenac sodium. The antioxidant activity of the gel was

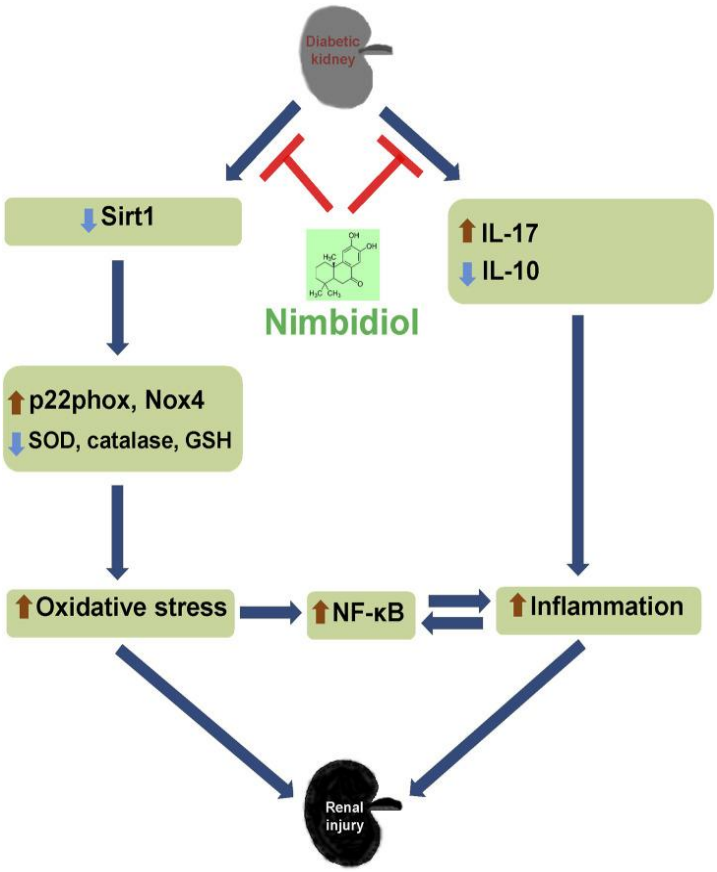
equal to butylated hydroxytoluene (BHT), and also the gel has a low cytotoxic potential even at its higher concentrations. Hence, the gel can be used as a natural remedy with minimal side effects, making it a valuable alternative to chemical agents.

Nimbidiol protects from renal injury by alleviating redox imbalance in diabetic mice.

Juin SK, Pushpakumar S, Sen U.

Front Pharmacol. 2024 May 21;15:1369408. doi: 10.3389/fphar.2024.1369408. PMID: 38835661

Introduction: Chronic hyperglycemia-induced oxidative stress plays a crucial role in the development of diabetic nephropathy (DN). Moreover, adverse extracellular matrix (ECM) accumulation elevates renal resistive index leading to progressive worsening of the pathology in DN. Nimbidiol is an alpha-glucosidase inhibitor, isolated from the medicinal plant, 'neem' (*Azadirachta indica*) and reported as a promising anti-diabetic compound. Previously, a myriad of studies demonstrated an anti-oxidative property of a broad-spectrum neem-extracts in various diseases including diabetes. Our recent study has shown that Nimbidiol protects diabetic mice from fibrotic renal dysfunction in part by mitigating adverse ECM accumulation. However, the precise mechanism remains poorly understood. **Methods:** The present study aimed to investigate whether Nimbidiol ameliorates renal injury by reducing oxidative stress in type-1 diabetes. To test the hypothesis, wild-type (C57BL/6J) and diabetic Akita (C57BL/6-*Ins2*^{Akita}/J) mice aged 10-14 weeks were used to treat with saline or Nimbidiol (400 µg kg^{-1} day^{-1}) for 8 weeks. **Results:** Diabetic mice showed elevated blood pressure, increased renal resistive index, and decreased renal vasculature compared to wild-type control. In diabetic kidney, reactive oxygen species and the expression levels of 4HNE, p22phox, Nox4, and ROMO1 were increased while GSH: GSSG, and the expression levels of SOD-1, SOD-2, and catalase were decreased. Further, eNOS, ACE2, Sirt1 and IL-10 were found to be downregulated while iNOS and IL-17 were upregulated in diabetic kidney. The changes were accompanied by elevated expression of the renal injury markers viz., lipocalin-2 and KIM-1 in diabetic kidney. Moreover, an upregulation of p-NF-κB and a downregulation of IkBα were observed in diabetic kidney compared to the control. Nimbidiol ameliorated these pathological changes in diabetic mice. **Conclusion:** Altogether, the data of our study suggest that oxidative



stress largely contributes to the diabetic renal injury, and Nimbidiol mitigates redox imbalance and thereby protects kidney in part by inhibiting NF-κB signaling pathway in type-1 diabetes.

Synthesis, Characterization, Phytochemistry, and Therapeutic Potential of Azadirachta indica Conjugated Silver Nanoparticles: A Comprehensive Study on Antidiabetic and Antioxidant Properties.

Tahir H, Rashid F, Ali S, Summer M, Afzal M.

Biol Trace Elem Res. 2024 Jul 10. doi: 10.1007/s12011-024-04293-3. Online ahead of print. PMID: 38985237

Nanotechnology has become a major topic of study, particularly in the medical and health domains. Because nanomedicine has a higher recovery rate than other conventional drugs, it has attracted more attention. Green synthesis is the most efficient and sustainable method of creating nanoparticles. The current work used ultraviolet-visible spectroscopy, Fourier-transform infrared spectroscopy, scanning electron microscopy, energy dispersive X-ray, and X-ray diffraction to thoroughly characterize the synthesized silver nanoparticles (AgNPs) from Azadirachta indica leaf extract. Characterization confirmed the synthesis of the AgNPs along with the possible linkage of the phytochemicals with the silver as well as the quantitative analysis and nature of NPs. The antioxidant activity of AgNPs and neem extract was measured by the 2,2-diphenyl-1-picrylhydrazyl assay using various concentrations (20, 40, 60, 80, and 100 µg/ml). Additionally, using diabetic mice that had been given alloxan, the in vivo antidiabetic potential of biosynthesized AgNPs was assessed. Eight groups of mice were used to assess the antidiabetic activity: one control group and seven experimental groups (untreated, extract-treated, AgNPs at low and high doses, standard drug, low dose of AgNPs + drug, and high dose of AgNPs + drug). At days 0, 7, 14, 21, and 28, blood glucose levels and body weight were measured. After 28 days, the mice were dissected, and the liver, kidney, and pancreas were examined histologically. The results depicted that the AgNPs showed higher (significant) radical scavenging activity (IC_{50} = 35.2 µg/ml) than extract (IC_{50} = 93.0 µg/ml) and ascorbic acid (IC_{50} = 64.6 µg/ml). The outcomes demonstrated that biosynthesized AgNPs had a great deal of promise as an antidiabetic agent and exhibited remarkable effects in diabetic mice given AgNPs, extract, and drug. Remarkable improvement in the body weight and blood glucose level of mice treated with high doses of AgNPs and drug was observed. The body weight and blood glucose level of diabetic mice treated with a high dose of AgNPs + standard drug showed significant improvement, going from 28.7 ± 0.2 to 35.6 ± 0.3 g and 248 ± 0.3 to 109 ± 0.1 mg/dl, respectively. Significant regeneration was also observed in the histomorphology of the kidney, liver's central vein, and islets of Langerhans after treatment with biosynthesized AgNPs. Diabetic mice given a high dose of AgNPs and drug displayed architecture of the kidney, liver, and pancreas that was nearly identical to that of the control group. According to the current research, biosynthesized AgNPs have strong antioxidant and antidiabetic potential and may eventually provide a less expensive option for the treatment of diabetes.

Therapeutic effects of OXY- Exo^{Aloe} in diabetic wound injury.

Miya MB, Ashutosh, Maulishree, Chandra Gupta P, Pathak V, Mishra R, Chaturvedi P, Kalani A.

Biochem Biophys Res Commun. 2024 Jul 14;731:150398. doi: 0.1016/j.bbrc.2024.150398. PMID: 39032360

Delayed wound healing are common complications for diabetic patients. In light of chronic hypoxia's delay in wound healing, it is hypothesized that providing a better oxygen environment at the wound site will promote diabetic wound healing. OXY-Exo^{Aloe} is an innovative and effective therapy prepared from exosome-like vesicles of aloe vera gel, ginger juice and neem fruit sap. A combination of three herbal, oxygen-delivering and medicinally valued plants was standardized to determine if the combination had the desired effect. Interestingly, when we used OXY-Exo^{Aloe} at a particular ratio on a diabetic wound, the herbal therapy speeded up wound healing by reducing swelling, and the severity of the wound. Further, our data suggests that OXY-Exo^{Aloe} promoted wound healing by increasing wound oxygenation, reducing inflammation, cytokine production, and matrix remodeling. It is also safe and effective, with no reported side effects.

Nimbolide protects against diabetic cardiomyopathy by regulating endoplasmic reticulum stress and mitochondrial function via the Akt/mTOR pathway.

Zhang H, Zhao X, Wei W, Shen C.

Tissue Cell. 2024 Jul 15;90:102478. doi: 10.1016/j.tice.2024.102478. PMID: 39053131

Nimbolide has been demonstrated to possess protective properties against gestational diabetes mellitus and diabetic retinopathy. However, the role and molecular mechanism of nimbolide in diabetic cardiomyopathy (DCM) remain unknown. Diabetes was induced in rats via a single injection of streptozotocin (STZ) and then the diabetic rats were administered nimbolide (5 mg/kg and 20 mg/kg) or dimethyl sulfoxide daily for 12 weeks. H9c2 cardiomyocytes were exposed to high glucose (25 mM glucose) to mimic DCM in vitro. The protective effects of nimbolide against DCM were evaluated in vivo and in vitro. The potential molecular mechanism of nimbolide in DCM was further explored. We found that nimbolide dose-dependently decreased blood glucose and improved body weight of diabetic rats. Additionally, nimbolide dose-dependently improved cardiac function, alleviated myocardial injury/fibrosis, and inhibited endoplasmic reticulum (ER) stress and apoptosis in diabetic rats. Moreover, nimbolide dose-dependently improved mitochondrial function and activated the Akt/mTOR signaling. We consistently demonstrated the cardioprotective effects of nimbolide in an in vitro model of DCM. The involvement of ER stress and mitochondrial pathways were further confirmed by using inhibitors of ER stress and mitochondrial division. By applying a specific Akt inhibitor SC66, the cardioprotective effects of nimbolide were partially blocked. Our study indicated that nimbolide alleviated DCM by activating Akt/mTOR pathway. Nimbolide may be a novel therapeutic agent for DCM treatment.

Biosynthesis of zinc oxide nanoparticles via neem extract and their anticancer and antibacterial activities.

El-Beltagi HS, Ragab M, Osman A, El-Masry RA, Alwutayd KM, Althagafi H, Alqahtani LS, Alazragi RS, Alhajri AS, El-Saber MM.

PeerJ. 2024 Jun 25;12:e17588. doi: 10.7717/peerj.17588. eCollection 2024.PMID: 38948224

In the present study, zinc oxide nanoparticles (ZnO-NPs) were synthesized using neem leaf aqueous extracts and characterized using transmission electron microscopy (TEM), ultraviolet visible spectroscopy (UV-Vis), and dynamic light scattering (DLS). Then compare its efficacy as anticancer and antibacterial agents with chemically synthesized ZnO-NPs and the neem leaf extract used for the green synthesis of ZnO-NPs. The TEM, UV-vis, and particle size confirmed that the developed ZnO-NPs are nanoscale. The chemically and greenly synthesized ZnO-NPs showed their optical absorbance at 328 nm and 380 nm, respectively, and were observed as spherical particles with a size of about 85 nm and 62.5 nm, respectively. HPLC and GC-MS were utilized to identify the bioactive components in the neem leaf aqueous extract employed for the eco-friendly production of ZnO-NPs. The HPLC analysis revealed that the aqueous extract of neem leaf contains 19 phenolic component fractions. The GC-MS analysis revealed the existence of 21 bioactive compounds. The antiproliferative effect of green ZnO-NPs was observed at different concentrations (31.25 µg/mL-1000 µg/mL) on Hct 116 and A 549 cancer cells, with an IC50 value of 111 µg/mL for A 549 and 118 µg/mL for Hct 116. On the other hand, the antibacterial activity against gram-positive and gram-negative bacteria was estimated. The antibacterial result showed that the MIC of green synthesized ZnO-NPs against gram-positive and gram-negative bacteria were 5, and 1 µg/mL. Hence, they could be utilized as effective antibacterial and antiproliferative agents.

Nimbolide: A Potential Phytochemical Agent in Multimodal Pancreatic Cancer Therapies.

Jogi M, Asnani H, Singh S, Kumar P.

Mini Rev Med Chem. 2024 Jun 13. doi: 10.2174/0113895575293138240527061556. Online ahead of print. PMID: 38874049

A significant contributor to cancer-related death, pancreatic cancer (PC) has a terrible prognosis in general that has not altered over many years. Currently, it is extremely difficult to prevent disease or discover it early enough to initiate treatment. The major challenge in PC is acquired chemo-radio resistance, which makes it very difficult to manage. PC is a challenging malignancy to treat, and several major impediments significantly impact the effectiveness of its treatment. These obstacles primarily include chemoresistance, drug toxicity, and limited drug bioavailability. Phytochemicals can be used as an alternative to chemotherapeutic drugs, or they can augment the anticancer properties of the chemotherapeutic agents. Nimbolide (NL) is a prominent limonoid compound found in Azadirachta indica, and has garnered substantial attention as a phytochemical with anticancer potential. It has powerful antiproliferative effects on a variety of cancer cell lines and is effective as a chemotherapeutic in preclinical studies. The primary modes of action of NL include suppression of metastasis and angiogenesis,

activation of apoptosis, anti-proliferation, and control of enzymes that metabolize carcinogens. Despite numerous pharmacodynamic (PD) investigations, NL is still in the early stages of the drug development process because no comprehensive pharmacokinetic (PK) studies or long-term toxicity studies. Preclinical PK and toxicological assessments should be conducted to establish an appropriate dosage range, ensuring the safety of NL for its application in initial human clinical trials. This review endeavors to provide a comprehensive summary of the current developmental stage of NL along with nanoparticles as a principal candidate for therapeutic purposes in PC.

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

Sijisha KS, Anusha R, Priya S.

Fundam Clin Pharmacol. 2024 Aug;38(4):758-766. doi: 10.1111/fcp.13000. Epub 2024 Mar 14.PMID: 38482560

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 epoxyazadiradione (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 IC_{50} 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.

Anticoccidial potentials of Azadirachta indica ethosomal nanovesicle in broiler chicks.

Algammal AA, Mohamed MA, Abd Eldaim M, Eisa AMA, El-Shenawy AA, Bazh EK, Ammar NI, Hamad R.

Vet Parasitol. 2024 Jul 25;331:110270. doi: 10.1016/j.vetpar.2024.110270. PMID: 39079237

This study evaluated the efficacy of Azadirachta indica ethosomal nanovesicle against Eimeria tenella infection in broiler chicks. Azadirachta indica ethanolic extract was screened phtochemically and analyzed active components of the extracts using high-performance liquid chromatography (HPLC). Azadirachta indica ethosomal nanovesicle was synthesized and characterized by zeta potential and scanning electron microscope. Broiler chicks were allocated into seven groups. Control group. The second group administered nanosized ethosomal vesicles (1 mL/kg b.wt.). The third group administered Azadirachta indica nanovesicles (30 mg/kg b.wt.) from 10th day of age. Fourth group was infected with E. tenella at a dose of 1 mL containing 40000 oocyst/ chick at 14th day of age. The fifth group administered Azadirachta indica nanovesicle (30 mg/kg b.wt.) from 10th day of age and infected with E. tenella as fourth group. The sixth group infected with E. tenella as the fourth group and treated with Azadirachta indica nanovesicle (30 mg/kg b.wt. for 4 days after clinical signs appearance. The seventh group infected with E. tenella as the fourth group and treated with diclazuril group (1 mL/4 L of water) for 2 successive days. Coccidiosis significantly decreased body weight, feed intake, reduced glutathione (GSH) level while increased feed conversion ratio, oocyst count, malonaldehyde (MDA) and nitric oxide (NO) serum levels, protein expression of interleukin-1 beta (IL-1β), interleukin 6 (IL-6), BAX and Caspase 3, in cecal tissue and induced cecal tissue injury. However, administration of coccidiosis chicks Azadirachta indica nanovesicle enhanced body weight, and serum GSH. While decreased feed intake, feed conversion ratio, oocyst count, MDA, and NO serum levels, and protein expression of IL-1β, IL-6, BAX, and caspase 3 in cecal tissues and ameliorated cecal tissue damage. This study indicated that, A. indica ethosomal nanovesicle had potent anticoccidial properties.