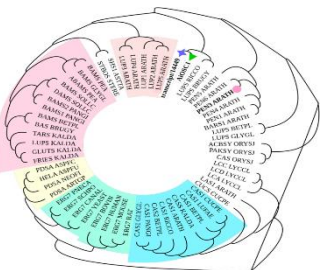
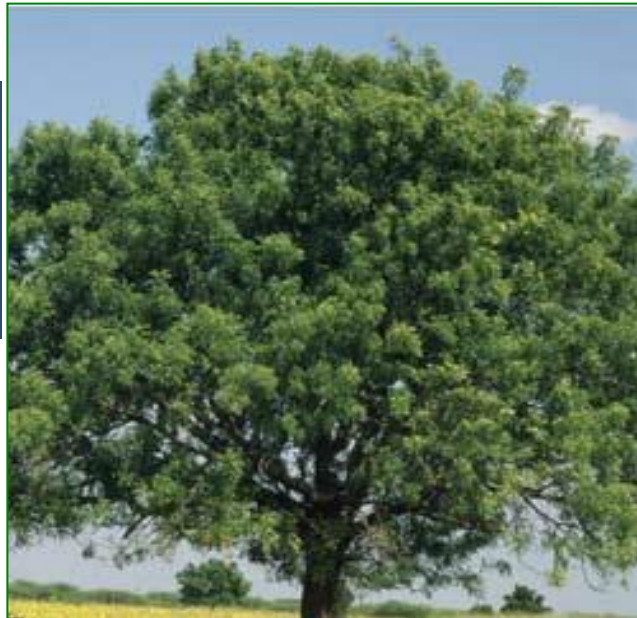
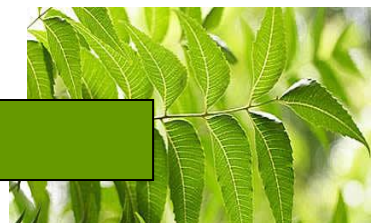


Neem Research Newsletter

Volume 1, Issue 2, 2021



WORLD NEEM ORGANISATION (WNO)



From
The Editor's Desk.....

At the outset, I wish all neem enthusiasts worldwide, a very Happy, Productive, and Peaceful New Year. It gives me great pleasure to present the second issue of the Neem Newsletter on behalf of the World Neem Organisation (WNO). This issue provides abstracts of research papers published from July 1 to December 31 2021 on the impact of neem in diverse areas such as agriculture, environment, human health, and industry besides basic sciences. Illustrations are provided wherever available as well as PMIDs for those readers who wish to delve more deeply. Considering the voluminous data that is being generated on neem, it is proposed to bring out quarterly issues of the newsletter from 2022. I would appreciate if you bring to my notice any work on neem that has not found a place in this newsletter so that it can be included in the next one. Feedback/suggestions are most welcome.

S. Nagini

Core Founding Member, WNO
Chief Scientific Coordinator &

Regional Director, South India



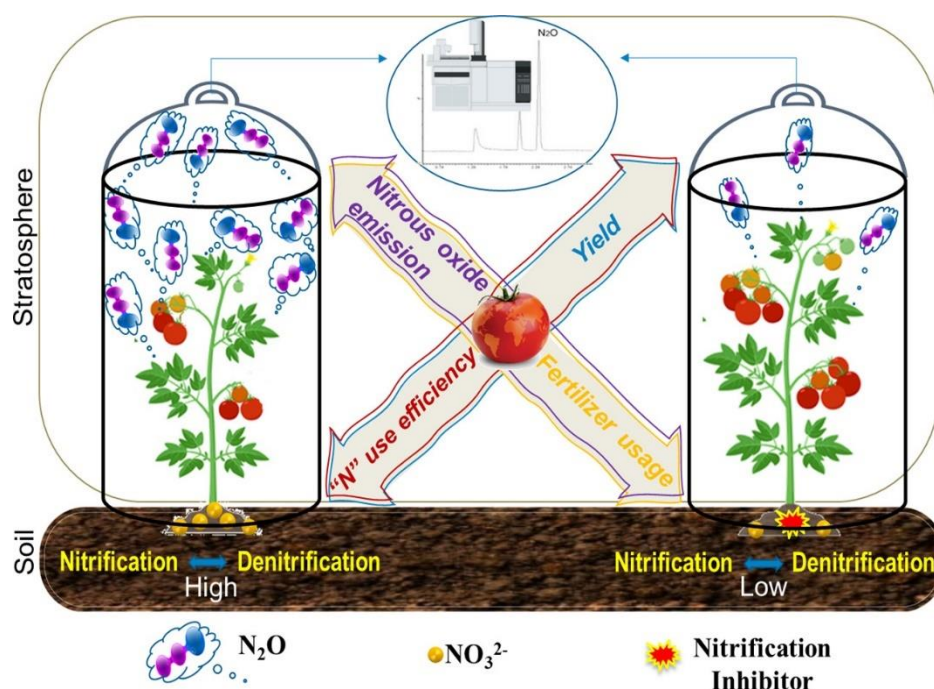
Neem in Agriculture & Aquaculture

Mitigation of nitrous oxide emission through fertigation and 'N' inhibitors- A sustainable climatic crop cultivation in tomato.

Davamani V, Poornima R, Arulmani S, Parameswari E, John JE, Deepasri M.

Sci Total Environ. 2021 Dec 16:152419. PMID: 34923005

The impacts of nitrous oxide (N_2O) released from the fertilized agro-ecosystems are of increasing concern. Governing fertilizer requirements and utilizing nitrification inhibitors (NI) are effective methodologies to increase nitrogen retention and reduce N_2O emissions from soil. Therefore, the effect of potassium thiosulfate (KTS) and **neem-coated urea (NCU)** on N_2O efflux under irrigated tomato cultivation was assessed. Soil Test Crop Response (STCR) based recommendation of NPK with normal Urea and KTS at 1% of applied N ($183:160:125 \text{ kg ha}^{-1}$) (STCR-U-KTS) recorded the least N_2O emission and high efficiency in suppressing the nitrate reductase activity. STCR-NCU was on par with STCR-U-KTS, reporting a higher reduction of N_2O (21.1, 31.2, and 34.4% during the basal application, 1st, and 2nd top dressing, respectively) compared to the blanket recommendation of nutrients. Similarly, STCR-U + KTS recorded the highest reduction (26.2, 25.6, and 30.9% during the basal application, 1st, and 2nd top dressing, respectively) after fertilizer application. Besides, the yield of tomatoes is increased in the STCR-NCU (14.08%) and STCR-U-KTS (12.48%) with good quality fruit along (AA, Lycopene, and TSS contents) with low N_2O emissions. The DeNitrification-DeComposition (DNDC) model further revealed that the simulated data and assessed findings were in good accord, proving the model's reliability and use as a tool for predicting the efficiency of fertilizer application.



Mycotoxins in *Zea mays*, their quantification and HPLC analysis of physico-biological detoxification

Murad M, Ahmad KS, Iram S, Hanif NQ, Gul MM, Elnaggar AY, El-Bahy ZM.
Nat Prod Res. 2021 Dec 21:1-5.

Present research involves the isolation, extraction and identification of mycotoxins from ten corn samples collected from the northern province of Pakistan. Average concentration of aflatoxin B1 and B2 by HP-TLC found in all corn samples was 27.87 and 1.35 µg/kg, respectively. Following HP-TLC, detoxification of the identified and isolated mycotoxin was performed, which was analyzed by HPLC. Screening of mycoflora exhibited *Aspergillus niger* and *Fusarium* as the most dominant fungal strains. Aflatoxin B1 was physically detoxified under UV-Lamp and direct sunlight displaying detoxification percentage of 48% and 99%, respectively. Biological detoxification involved the use of botanicals such as neem leaves, garlic and ginger powder, which portrayed an approximate detoxification of 70% from corn samples. Current research concludes that the tested physical and biological methods can be easily adopted at field and storage rooms after the harvesting of crops to avoid fungal contamination and subsequent food spoilage.

Efficacy of bio-rational pesticides for the management of *Leucinodes orbonalis* Guenee in Rupandehi, Nepal.

Khanal D, Pandey R, Dhakal R, Neupane N, Shrestha A, Nepali Joseph M, Paudel A, Pandey M.

Heliyon. 2021 Oct 30;7(11):e08286. PMID: 34778578

The field experiment was conducted from March to June of 2017 in field conditions at the Institute of Agriculture and Animal Science (IAAS), Paklihawa Campus, Rupandehi, Nepal to evaluate the efficacy of botanicals, microbial, and chemical insecticide against *Leucinodes orbonalis* Guenee. We assessed seven treatments including control in randomized complete block design with four replications and two sprays. The treatments evaluated for the management of *L. orbonalis* were i) Jholmal, 250 ml/l of water ii) *Beauveria bassiana* (Daman), 4 g/l water iii) Abamectin 5 % (Biotrine), 0.5 ml/l of water iv) *Bacillus thuringiensis var. kurstaki* (Mahastra), 4 g/l of water v) Emamectin benzoate (Cobra), 0.5 g/l of water vi) Azadirachtin 1500 ppm (Neem Kavach), 5 ml/l of water vii) Control (pure water application). All the treatments applied were found to be superior to the control. The results revealed that the lowest percentage of infested fruit i.e. 57.97% and 34.52% were found at 14 days after the first and second spray of Emamectin benzoate treatment respectively, as well as it was found to be significant over control in both sprays. The marketable yield of plot treated with Emamectin benzoate in eggplant was found to be the highest i.e. 7.19 t/ha and 7.13 t/ha which was followed by Neem Kavach with the yield of 6.69 t/ha and 7.06 t/ha and that of control plots was 2.98 t/ha and 2.56 t/ha after first and second spray respectively. Further, our study concluded both marketable yield and Benefit-Cost (BC) ratio of brinjal fruit were the highest under the treatment of Emamectin benzoate followed by Jholmal and Neem Kavach. From this experiment, we concluded that Emamectin benzoate was the most effective treatment for the management of *L. orbonalis* while Jholmal and Neem Kavach proved to be the best alternative.

A biocide delivery system composed of nanosilica loaded with neem oil is effective in reducing plant toxicity of this biocide.

Goetten de Lima G, Wilke Sivek T, Matos M, Lundgren Thá E, de Oliveira KMG, Rodrigues de Souza I, de Moraes de Lima TA, Cestari MM, Esteves Magalhães WL, Hansel FA, Moraes Leme D.

Environ Pollut. 2022 Feb 1;294:118660. PMID: 34896221

One possible way to reduce the environmental impacts of pesticides is by nanostructuring biocides in nanocarriers because this promotes high and localized biocidal activity and can avoid toxicity to non-target organisms. Neem oil (NO) is a natural pesticide with toxicity concerns to plants, fish, and other organisms. Thus, loading NO in a safe nanocarrier can contribute to minimizing its toxicity. For this study, we have characterized the integrity of a nanosilica-neem oil-based biocide delivery system (SiO₂NP#NO BDS) and evaluated its effectiveness in reducing NO toxicity by the *Allium cepa* test. NO, mainly consisted of unsaturated fatty acids, was well binded to the SiO₂NP with BTCA crosslinker. Overall, this material presented all of its pores filled with the NO with fatty acid groups at both the surface and bulk level of the nanoparticle. The thermal stability of NO was enhanced after synthesis, and the NO was released as zero-order model with a total of 20 days without burst release. The SiO₂NP#NO BDS was effective in reducing the individual toxicity of NO to the plant system. NO in single form inhibited the seed germination of *A. cepa* (EC₅₀ of 0.38 g L⁻¹), and the effect was no longer observed at the BDS condition. Contrarily to the literature, the tested NO did not present cyto- and geno-toxic effects in *A. cepa*, which may relate to the concentration level and composition.

Chronic exposure to a common biopesticide is detrimental to individuals and colonies of the paper wasp *Polistes versicolor*

Teixeira GVM, De Souza AR, Barbosa WF, Bernardes RC, Lima MAP.

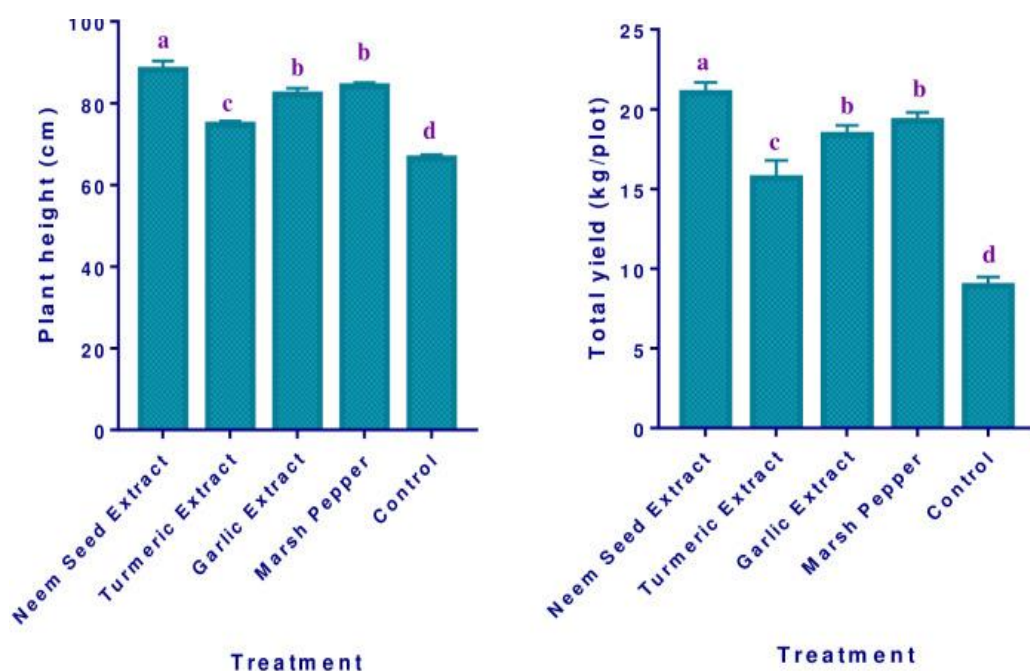
Sci Total Environ. 2021 Dec 3;810:152108.

Risk assessments of agrochemicals on non-target insects are biased in studies with surrogate groups, such as pollinators. In social insects, such investigations are generally restricted to lethal tests with adults maintained individually, simulating a non-realistic scenario. Here, we performed a holistic approach to resemble a chronic field exposure of *Polistes versicolor* (Hymenoptera: Vespidae) to a common biopesticide. These wasps are predators that perform biological control in the agroecosystems. Wasps were chronically subjected to the ingestion of different concentrations of azadirachtin. The neonicotinoid imidacloprid was used as a positive control. For the first time, we demonstrated that the biopesticide azadirachtin is detrimental for individual and colony survival and impairs colony reproduction of a social wasp maintained in the laboratory. Our data also indicated that neonicotinoid imidacloprid is harmful to wasps and their colonies. Therefore, the concomitant use of azadirachtin and paper wasps in integrated pest management strategies should be carefully evaluated, because the constant use of this pesticide can be detrimental for social wasps, possibly reducing biological control.

The impact of different plant extracts on population suppression of *Helicoverpa armigera* (Hub.) and tomato (*Lycopersicon esculentum* Mill) yield under field conditions.

Ali S, Li Y, Haq IU, Abbas W, Shabbir MZ, Khan MM, Mamay M, Niaz Y, Farooq T, Skalicky M, Zuan ATK, Nasif O, Ansari MJ. *PLoS One*. 2021 Dec 1;16(12):e0260470. PMID: 34852006

Helicoverpa armigera (Hub.) is a destructive pest of the tomato (*Lycopersicon esculentum* Mill) crop in Pakistan. Although insecticides are the primary management strategy used to control *H. armigera*, most of them are not effective due to considerable toxic residual effects on the fruits. Nonetheless, *H. armigera* is rapidly evolving resistance against the available pesticides for its management. This situation calls upon the need of alternative management options against the pest. Different plant extracts have been suggested as a viable, environment-friendly option for plant protection with minimal side effects. Furthermore, the plant extracts could also manage the insect species evolving resistance against pesticides. This study evaluated the efficacy of different plant extracts (i.e., Neem seed, turmeric, garlic and marsh pepper) against *H. armigera*. Furthermore, the impact of the plant extracts on growth and yield of tomato crop was also tested under field conditions. The results revealed that all plant extracts resulted in higher mortality of *H. armigera* compared to control. Similarly, the highest plant height was observed for the plants treated with the plant extracts compared to untreated plants. Moreover, the highest tomato yield was observed in plants treated with plant extracts, especially with neem seed (21.013 kg/plot) followed by pepper extract (19.25 kg/plot), and garlic extract 18.4 kg/plot) compared to the untreated plants (8.9 kg/plot). It is concluded that plant extracts can be used as eco-friendly approaches for improving tomato yield and resistance management of *H. armigera*.



Insecticidal capacity of polyphenolic seed compounds from neem (*Azadirachta indica*) on *Spodoptera frugiperda* (J. E. Smith) larvae.

Hernandez-Trejo A, Rodríguez-Herrera R, Sáenz-Galindo A, López-Badillo CM, Flores-Gallegos AC, Ascacio-Valdez JA, Estrada-Drouaillet B, Osorio-Hernández E.

J Environ Sci Health B. 2021 Nov 16:1-8. PMID: 34783634

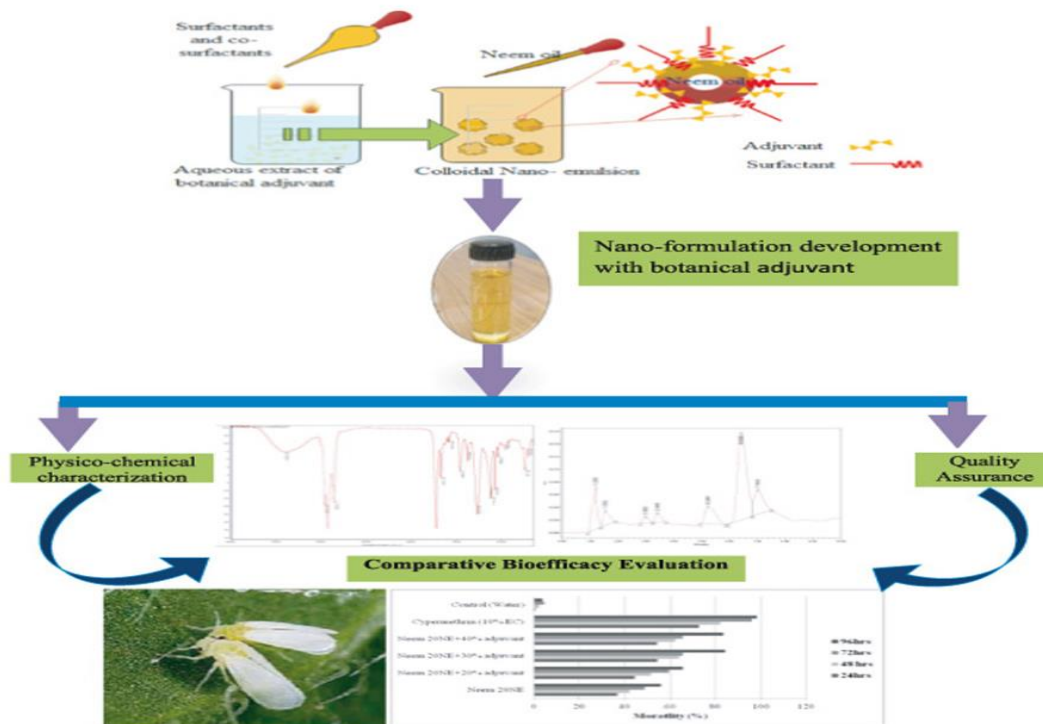
The objective of this study was to evaluate the insecticidal activity of the polyphenolic compounds found in neem on *S. frugiperda* larvae. Three neem extracts (1:12 (m/v) with 70% ethanol, 1:12 (m/v) with 0% ethanol (only water), and 1:4 (m/v) with 0% ethanol) were employed. Subsequently, the extraction of phytochemical compounds of each extract was performed using ultrasound and microwave technologies simultaneously. The compound characterization was performed by HPLC-mass. In addition, the insecticidal evaluation of the neem extract was performed against *S. frugiperda* of the second-stage larvae. The extracts were applied by spraying the larvae according to each bioassay. Results showed that the extract obtained with a 1:12 (m/v) relationship and 70% ethanol was effective for the control of *S. frugiperda* larvae. In this extract, the predominant organic compound families were: methoxyflavones, flavonols, hydroxycoumarins, anthocyanins, methoxycinnamic acid, and alkylflavones. Phytochemical compounds obtained from neem seeds with environmentally friendly solvents and alternative technologies (ultrasound and microwave) have potent insecticidal activity against *S. frugiperda* larvae.

Bioengineering of neem nano-formulation with adjuvant for better adhesion over applied surface to give long term insect control.

Iqbal N, Hazra DK, Purkait A, Agrawal A, Kumar J. *Colloids Surf B Biointerfaces.* 2022 Jan;209(Pt 2):112176. PMID: 34785423

Although safe and eco-friendly botanical pesticides have been intensively promoted to combat pest attacks in agriculture, but their stability and efficacies remain an issue for their wide acceptability as sustained and effective approaches. The purpose of this work was to develop stable neem oil based nano-emulsion (NE) formulation with enhanced activity employing suitable bio-inspired adjuvant. So, Neem NEs (with and without) natural adjuvants (*Cymbopogon citratus* and *Prosopis juliflora*) in different concentrations were prepared and quality parameters dictating kinetic stability, acidity/alkalinity, viscosity, droplet size, zeta potential, surface tension, stability and compatibility were monitored using Viscometer, Zetasizer, Surface Tensiometer, High Performance Liquid Chromatography (HPLC) and Fourier Transform Infrared Spectroscopy (FTIR). Nano-emulsion biosynthesis optimization studies suggested that slightly acidic (5.9-6.5) NE is kinetically stable with no phase separation; creaming or crystallization may be due to botanical adjuvant (lemongrass oil). Findings proved that *Prosopis juliflora*, acted as bio-polymeric adjuvant to stabilize NE by increasing Brownian motion and weakening the attractive forces with smaller droplets (25-50 nm), low zeta potential (-30 mV) and poly-dispersive index (<0.3). Botanical adjuvant (30%) based NE with optimum viscosity (98.8cPs) can give long term storage stability and improved adhesiveness and wetting with reduced surface tension and contact angle. FT-IR analysis assured azadirachtin's stability and compatibility with adjuvant. With negligible degradation (1.42%) and higher half-life ($t_{1/2}$) of 492.95 days, natural adjuvant based NE is substantially stable formulation, may be due to presence of glycosidic and phenolics compounds. Neem 20NE (with 30% adjuvant)

exhibited remarkable insecticidal activity (91.24%) against whitefly (*Bemisia tabaci* G.) in brinjal (*Solanum melongena*) as evidenced by in-vivo assay. Results thus obtained suggest, bio-pesticide formulation may be used as safer alternative to chemical pesticides to minimize pesticide residues and presence of natural adjuvant may improve the stability and efficacy of biopesticides for safe crop protection in organic agriculture and Integrated Pest Management.



Potential of Essential Oils from Anise, Dill and Fennel Seeds for the Gypsy Moth Control.

Kostić I, Lazarević J, Šešlija Jovanović D, Kostić M, Marković T, Milanović S.

Plants (Basel). 2021 Oct 15;10(10):2194. PMID: 34686003

The gypsy moth (*Lymantria dispar* L. (Lepidoptera: Erebidæ)) is a serious pest of hardwood forests. In the search for an environmentally safe means of its control, we assessed the impact of different concentrations of essential oils (EOs) from the seeds of three Apiaceae plants (anise *Pimpinella anisum*, dill *Anethum graveolens*, and fennel *Foeniculum vulgare*) on behavior, mortality, molting and nutritional physiology of gypsy moth larvae (GML). EOs efficacy was compared with commercial insecticide NeemAzal®-T/S (neem). The main compounds in the Eos were trans-anethole in anise; carvone, limonene, and α -phellandrene in dill; and trans-anethole and fenchone in fennel seed. At 1% EOs concentration, anise and fennel were better antifeedants and all three EOs were more toxic than neem. Neem was superior in delaying 2nd to 3rd larval molting. In the 4th instar, 0.5%, anise and fennel EOs decreased relative consumption rate more than neem, whereas all three EOs were more effective in reducing growth rate, approximate digestibility and efficiency of conversion of food into body mass leading to higher metabolic costs to GML. Decrease in consumption and metabolic parameters compared to control GML confirmed that adverse effects of the EOs stem from both pre- and post-ingestive mechanisms. The results indicate the potential of three EOs to be used for gypsy moth control.

Biochar and slow-releasing nitrogen fertilizers improved growth, nitrogen use, yield, and fiber quality of cotton under arid climatic conditions.

Manzoor S, Habib-Ur-Rahman M, Haider G, Ghafoor I, Ahmad S, Afzal M, Nawaz F, Iqbal R, Yasin M, Tanveer-UI-Haq, Danish S, Ghaffar A.

Environ Sci Pollut Res Int. 2021 Oct 1. PMID: 34595718

The efficiency of nitrogenous fertilizers in South Asia is on a declining trajectory due to increased losses. Biochar (BC) and slow-releasing nitrogen fertilizers (SRNF) have been found to improve nitrogen use efficiency (NUE) in certain cases. However, field-scale studies to explore the potential of BC and SRNF in south Asian arid climate are lacking. Here we conducted a field experiment in the arid environment to demonstrate the response of BC and SRNF on cotton growth and yield quality. The treatments were comprised of two factors, (A) nitrogen sources, (i) simple urea, (ii) neem-coated urea, (iii) sulfur-coated urea, (iv) bacterial coated urea, and cotton stalks biochar impregnated with simple urea, and (B) nitrogen application rates, $N_1=160 \text{ kg ha}^{-1}$, $N_2 = 120 \text{ kg ha}^{-1}$, and $N_3 = 80 \text{ kg ha}^{-1}$. Different SRNF differentially affected cotton growth, morphological and physiological attributes, and seed cotton yield (SCY). The bacterial coated urea at the highest rate of N application (160 kg ha^{-1}) resulted in a higher net leaf photosynthetic rate ($32.8 \mu\text{mol m}^{-2} \text{ s}^{-1}$), leaf transpiration rate (8.10 mmol s^{-1}), and stomatal conductance ($0.502 \text{ mol m}^{-2} \text{ s}^{-1}$), while leaf area index (LAI), crop growth rate (CGR), and seed cotton yield (4513 kg ha^{-1}) were increased by bacterial coated urea at 120 kg ha^{-1} than simple urea. However, low rate N application (80 kg ha^{-1}) of bacterial coated urea showed higher nitrogen use efficiency ($39.6 \text{ kg SCY kg}^{-1} \text{ N}$). The fiber quality (fiber length, fiber strength, ginning outturn, fiber index, and seed index) was also increased with the high N application rates than N_2 and N_3 application. To summarize, the bacterial coated urea with recommended N (160 kg ha^{-1}) and 75% of recommended N application (120 kg ha^{-1}) may be recommended for farmers in the arid climatic conditions of Punjab to enhance the seed cotton yield, thereby reducing nitrogen losses.

Conservation agricultural practices for minimizing ammonia volatilization and maximizing wheat productivity.

Bhaskar KA, Al-Hashimi A, Meena M, Meena VS, Langyan S, Shrivastava M, Sayyed RZ, El-Enshasy HA, Almunqedhi BMA, Singh R.

Environ Sci Pollut Res Int. 2021 Sep 10. PMID: 34508308

A large amount of ammonia volatilization from the agricultural system causes environmental problems and increases production costs. Conservation agriculture has emerged as an alternate and sustainable crop production system. Therefore, in the present study, ammonia losses from different agricultural practices were evaluated for the wheat crop under different tillage practices. The results showed that the cumulative emission of ammonia flux from the wheat field varied from 6.23 to 24.00 kg ha^{-1} ($P \leq 0.05$) in conservation tillage (CA) and 7.03 to 26.58 kg ha^{-1} ($P \leq 0.05$) in conventional tillage (CT) among different treatments. Application of basal 80% nitrogen resulted in the highest ammonia flux in conventional and conservation tillage practices. The ammonia volatilization followed the following trend: urea super granules with band placement > neem-coated urea with band placement > neem-coated urea with broadcast before irrigation > neem-coated urea with broadcast after irrigation > slow-release N fertilizer (urea stabilized with DCD and N(n-butyl)thiophosphoric

triamide) with band placement. The conservation agricultural practices involving conservation tillage appear to be a sustainable approach for minimizing ammonia volatilization and improving wheat productivity.

Pest categorisation of *Xanthomonas citri* pv. *viticola*.

EFSA Panel on Plant Health (PLH), Bragard C, Di Serio F, Gonthier P, Jaques Miret JA, Justesen AF, MacLeod A, Magnusson CS, Milonas P, Navas-Cortes JA, Parnell S, Potting R, Thulke HH, Van der Werf W, Civera AV, Yuen J, Zappalà L, Migheli Q, Stefani E, Vloutoglou I, Czwieneczek E, Maiorano A, Streissl F, Reignault PL.

EFSA J. 2021 Dec 16;19(12):e06929. Dec. PMID: 34963789

The EFSA Plant Health Panel performed a pest categorisation of *Xanthomonas citri* pv. *viticola* (Nayudu) Dye, a Gram-negative bacterium belonging to the Xanthomonadaceae family. The pathogen is a well-defined taxonomic unit and is the causal agent of the leaf spot and bacterial canker of *Vitis vinifera*. This bacterium is present in India and Brazil, where it affects table grape cultivation; the same pathogen is able to cause a disease on *Azadirachta indica* and on some weed species. Reports indicate that the bacterium is present in Thailand as well. The pathogen has never been reported from the EU territory and it is not included in EU Commission Implementing Regulation 2019/2072. The pathogen can be detected on its host plants using direct isolation, serological or PCR-based methods. Its identification is achieved using biochemical and nutritional assays, together with a multilocus sequence analysis based on seven housekeeping genes. The main pathway for the entry of the pathogen into the EU territory is plant propagation material. In the EU, there is large availability of host plants, with grapevine being one of the most important crops in Europe and more specifically in its Mediterranean areas. Since *X. citri* pv. *viticola* is only reported in tropical and subtropical areas (BSh and Aw climatic zones according to the Köppen-Geiger classification), there is uncertainty whether the climatic conditions in the EU territory are suitable for its establishment. Nevertheless, due to the great importance of grapevine for the EU agriculture, any disease outbreak may have a high-economic impact. Phytosanitary measures are available to prevent the introduction of the pathogen into the EU. *X. citri* pv. *viticola* satisfies the criteria that are within the remit of EFSA to assess for this species to be regarded as a potential Union quarantine pest.

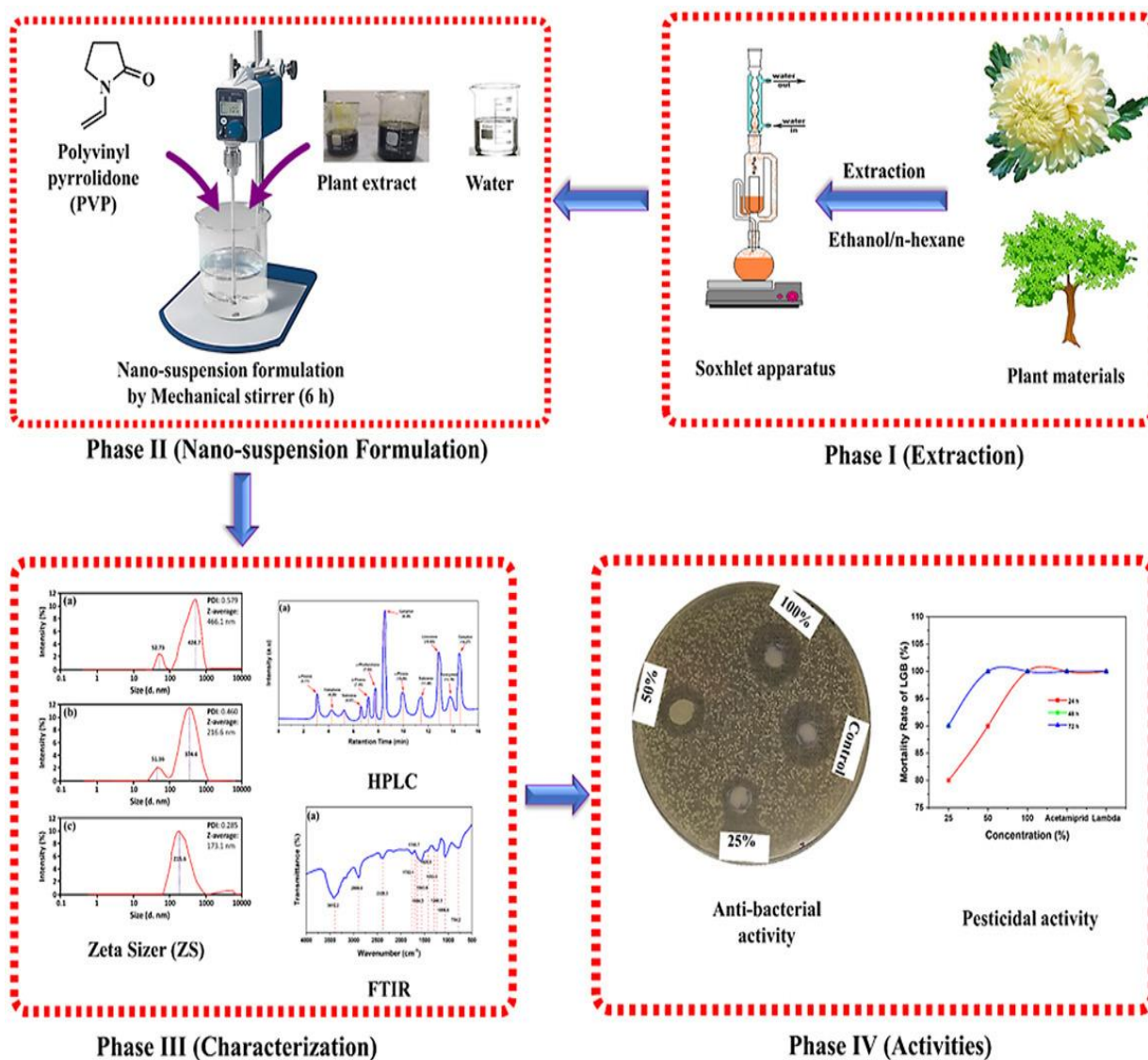
Evaluation and optimization of nanosuspensions of *Chrysanthemum coronarium* and *Azadirachta indica* using Response Surface Methodology for pest management.

Hazafa A, Jahan N, Zia MA, Rahman KU, Sagheer M, Naeem M.

Chemosphere. 2021 Dec 24:133411. PMID: 34958785

The rapidly emerging field of nanotechnology is considered an important achievement in the agriculture sector to increase the pest mortality rate and improve crop production. The present study aims to evaluate the novel pesticidal and anti-microbial activities of *Chrysanthemum coronarium* and *Azadirachta indica* in the nano-suspensions form. The anti-solvent precipitation method was used to formulate nano-suspensions proposed by Response Surface Methodology (RSM). Physicochemical nature of plant extract and nano-suspensions was characterized through analysis of Zeta-sizer, FT-IR, and HPLC.

Characterization results revealed a minimum particle size of 121.1 and 170.1 nm for *Chrysanthemum coronarium* and *Azadirachta indica*, respectively. The pesticidal activity of nano-suspension was performed against red flour beetle (RFB) and lesser grain borer (LGB) pests, which showed the maximum mortality rate of 100% with 100% concentration of plant extracts and nano-suspensions of *Chrysanthemum coronarium* and *Azadirachta indica* against both insects. While combination of these both plants revealed the maximum 100% mortality with a 50% concentration of nano-suspensions (mixing ratio 1:1) after 72 h. The antibacterial activity showed the maximum zone inhibition of 9.96 ± 0.17 and 14.17 ± 0.50 mm against *Staphylococcus aureus* and *E. coli* with nano-suspension of *Chrysanthemum coronarium*, and 12.09 ± 0.11 and 14.10 ± 0.49 mm with nano-suspension of *Azadirachta indica*, respectively. It is concluded that individual nano-suspensions showed better pesticidal as well as antimicrobial activities than combinations. However, the constructed nanosuspension can be applied to control plant pests and diseases simultaneously.



Insecticidal Triterpenes in Meliaceae: Plant Species, Molecules and Activities: Part I (*Aphanamixis-Chukrasia*).

Lin M, Yang S, Huang J, Zhou L.

Int J Mol Sci. 2021 Dec 9;22(24):13262. PMID: 34948062

Plant-originated triterpenes are important insecticidal molecules. The research on insecticidal activity of molecules from Meliaceae plants has always received attention due to the molecules from this family showing a variety of insecticidal activities with diverse mechanisms of action. In this paper, we discuss 102 triterpenoid molecules with insecticidal activity of plants of eight genera (*Aglaia*, *Aphanamixis*, *Azadirachta*, *Cabralea*, *Carapa*, *Cedrela*, *Chisocheton*, and *Chukrasia*) in Meliaceae. In total, 19 insecticidal plant species are presented. Among these species, *Azadirachta indica* A. Juss is the most well-known insecticidal plant and azadirachtin is the active molecule most widely recognized and highly effective botanical insecticide. However, it is noteworthy that six species from *Cedrela* were reported to show insecticidal activity and deserve future study. In this paper, a total of 102 insecticidal molecules are summarized, including 96 nortriterpenes, 4 tetracyclic triterpenes, and 2 pentacyclic triterpenes. Results showed antifeedant activity, growth inhibition activity, poisonous activity, or other activities. Among them, 43 molecules from 15 plant species showed antifeedant activity against 16 insect species, 49 molecules from 14 plant species exhibited poisonous activity on 10 insect species, and 19 molecules from 11 plant species possessed growth regulatory activity on 12 insect species. Among these molecules, azadirachtins were found to be the most successful botanical insecticides. Still, other molecules possessed more than one type of obvious activity, including 7-deacetylgedunin, salannin, gedunin, azadirone, salannol, azadiradione, and methyl angolensate. Most of these molecules are only in the primary stage of study activity; their mechanism of action and structure-activity relationship warrant further study.

The impact of insecticides and plant extracts on the suppression of insect vector (*Bemisia tabaci*) of Mungbean yellow mosaic virus (MYMV)

Younas M, Zou H, Laraib T, Rajpoot NA, Khan NA, Zaidi AA, Ayaz Kachelo G, Akhtar MW, Hayat S, Al-Sadi AM, Sayed S, Kesba H, Ansari MJ, Zuan ATK, Li Y, Arif M.

PLoS One. 2021 Sep 16;16(9):e0256449. PMID: 34529693

Mungbean yellow mosaic virus (MYMV) is an important constraint in successful production of mungbean (*Vigna radiata* L.) in many countries, including Pakistan. The MYMV spreads by insect vector whitefly (*Bemisia tabaci* Gennadius). The use of resistant cultivars is the most effective management tactics for MYMV. Twenty mungbean varieties/lines were screened against insect vector of MYMV under field condition in the current study. Resistance levels for varieties/lines were assessed through visual scoring of typical disease symptoms. Furthermore, the impacts of two insecticides 'Imidacloprid' and 'Thiamethoxam' and two plant extracts, i.e., neem (*Azadirachta indica*), and Eucalyptus (*Eucalyptus camaldulensis*) were tested on the suppression of whitefly. Field screening indicated that none of the tested varieties/lines proved immune/highly resistant, while significant variations were recorded among varieties/lines for resistance level. All varieties/lines were systemically infected with MYMV. The varieties 'AARI-2006' and

'Mung-14043' were considered as resistant to MYMV based on visual symptoms and the lowest vector population. These varieties were followed by 'NM-2006' and 'NL-31', which proved as moderately resistant to MYMV. All remaining varieties/lines were grouped as moderately to highly susceptible to MYMV based on visual symptoms' scoring. These results revealed that existing mungbean germplasm do not possess high resistance level MYMV. However, the lines showing higher resistance in the current study must be exploited in breeding programs for the development of resistant mungbean varieties/lines against MYMV. Imidacloprid proved as the most effective insecticide at all concentrations to manage whitefly population. Therefore, use of the varieties with higher resistance level and spraying Imidacloprid could lower the incidence of MYMV.

Antiparasitic potentiality of ethanol and methanol extracts of *Azadirachta indica* leaf for eggs and copepodid stage of *Argulus japonicus*: in vitro study.

Kumari P, Kumar S, Deo AD, Rajendran KV, Raman RP.

J Parasit Dis. 2021 Sep;45(3):769-777. PMID: 34475659

In the present study, eggs and copepodid stages of *Argulus japonicus* were treated with ethanol and methanol extract of *Azadirachta indica* (neem) leaf and its antiparasitic efficacy (AE %) was determined. The experiments were performed in triplicate along with the positive (2% DMSO) and negative (without DMSO and extract) control groups. The reduced cumulative hatching percentage of eggs by 13% (in ethanolic) and 17% (in methanolic) extract of neem leaf at 1.5 g L⁻¹ was obtained during 15-day exposure compared to the control group showing 70-85% eggs hatching. The AE of 100% for ethanolic and 91.66% for methanolic extract against the copepodid stage was found at 1.25 and 1.5 g L⁻¹ respectively in 6 h. The histological analysis of the eggs showed the undifferentiated decaying mass of cells with extensively damaged eggs when treated with ethanolic extract of neem leaf. Further, severe degeneration in the branchial region, digestive tract and eye cells was observed in the copepodids treated with ethanol extract than the methanol extract. The terpenoids a potential antiparasitic compound of ethanolic extract produced more AE than the methanolic extract. Thus, the ethanolic extract of neem leaf can be potentially utilized as a natural parasiticide to disrupt the egg and other life phases of *A. japonicus*.

Neem- Bioactive Constituents

Dataset on analytical characterization of bioactive components from *Azadirachta indica*, *Canna indica*, *Magnifera indica* and *Moringa oleifera* leaf extracts and their applications in nanoparticles biosynthesis.

Bolade OP, Williams AB, Benson NU.

Data Brief. 2021 Sep 21;38:107407. PMID: 34621933

This paper presents data on the bioactive phytoconstituents in *Azadirachta indica*, *Canna indica*, *Magnifera indica*, and *Moringa oleifera* analyzed using quantitative and qualitative phytochemical screening methods, Fourier Transform Infrared Spectroscopy and Gas Chromatography-Mass Spectrometry (GC-MS). Extracts were prepared in water, ethanol (EtOH) and EtOH:water mix. Identification of bioactive components was based on their spectral data and retention times compared with National Institute of Standards and Technology (NIST) mass spectral library. The most prominent absorption bands indicated are O-H stretching vibration, C-H stretch of polyols, aromatic C=C stretching vibration, O-H stretch of polyols, C-H stretching vibration and C-OH polyols. The GC-MS characterization for *A. indica* showed the presence of phenols, organic acids and carbohydrates with cannabidiol as the most abundant. Crude extracts of *M. oleifera* showed six phenolic compounds with 4-hydroxy-bezoic acid and cannabidiol present prominently. Six phenolic phytoconstituents were identified in *M. indica* extracts with 1,2,3-benzenetriol as the major polyphenolic compound. Biogenic iron oxide nanoparticles were synthesized and the formation was confirmed using a UV spectrometer (UV-3000 ORI, Germany) between 200 and 800 nm spectral range. X-ray diffraction (XRD) characterization of the biosynthesized iron oxide nanoparticles was carried out using Empyrean, Malvern PanAnalytical.

Extraction of total antioxidants from *Azadirachta indica* (neem) using three phase partitioning and its process intensification using ultrasound.

Shewale SP, Panadare D, Rathod VK.

Prep Biochem Biotechnol. 2021 Sep 16:1-6. PMID: 34528862

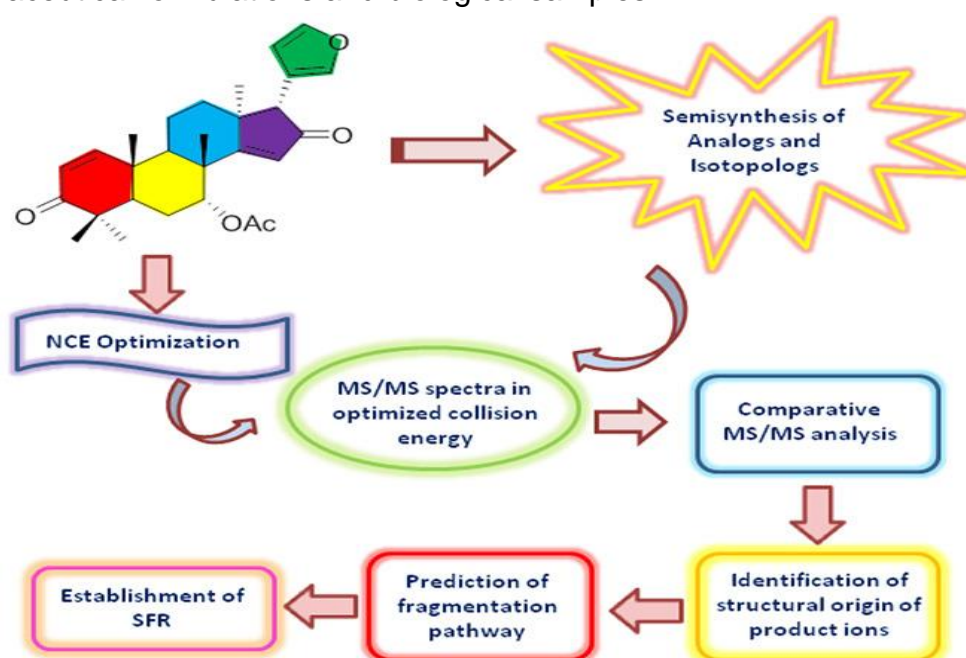
The majority of the naturally occurring antioxidants are obtained from plant sources. The antioxidant activity is mostly exhibited by polyphenols present in the plant cells. *Azadirachta Indica* (Neem) leaves are renowned for their medicinal applications due to their anti-inflammatory, antimalarial, antifungal, antibacterial, antiviral, antioxidant, and anticarcinogenic properties. This work aims to optimize the extraction of *Azadirachta Indica* (Neem) leaf antioxidants using three-phase partitioning (TPP). The optimized conditions are operating time 15 minutes, slurry ratio 1:30 (g/mL), salt concentration 30% (w/v), aqueous to solvent ratio 1:1.5 (v/v), and stirring speed 400 rpm that infer 74.66% extraction yield. Additionally, ultrasonic pretreatment was also employed to increase the extraction yield up to 86.61%. Sonication pretreatment for 4 min operated at 30 W power, and 75% duty cycle was observed to offer maximum antioxidant extraction about 3.3 mg/g.

Accurate Identification of Bioactive Meliaceae Limonoids by UHPLC-MS/MS Based Structure-Fragment Relationships (SFRs).

Mulani FA, Nandikol SS, Haldar S, Thulasiram HV.

ACS Omega. 2021 Oct 1;6(40):26454-26476. PMID: 34661002

Limonoids are bioactive plant specialized metabolites found in the Meliaceae family. The basic limonoids, i.e., azadiradione, epoxyazadiradione, and gedunin have been exploited for various bioactivities and therefore are the potential drug leads for tomorrow. However, their low abundance, structural similarity, and lack of adequate mass fragmentation data have hampered their accurate identification and quantification from various sources. In the present study, basic limonoids such as azadirone, azadiradione, epoxyazadiradione, and gedunin isolated from Neem were utilized for the synthesis of their derivatives and isotopologs. A total of 30 one compounds were used in this study among which five were isolated, two were biotransformed, and 24 were synthesized. Among the synthesized compounds nine are novel compounds including six deuterated analogs/isotopologs which are (1,3-²H)-1,2-dihydro-3 β -hydroxyazadiradione (**9**), (1,3,16-²H)-1,2-dihydro-3 β -16 β -dihydroxyazadiradione (**10**), 3 β -hydroxyazadiradione (**11**), 3 β -16 β -dihydroxyazadiradione (**12**), (3-²H)-3 β -hydroxyazadiradione (**13**), (3,16-²H)-3 β -16 β -dihydroxyazadiradione (**14**), (1,3,7-²H)-1,2-dihydro-3 β -hydroxy-7-deacetylazadiradione (**15**), 1,2,20,21,22,23-hexahydroazadiradione (**17**), and (1,3-²H)-1,2-dihydro-3 β -hydroxygedunin (**29**). These limonoids along with their semisynthesized derivatives were subjected to ultra high performance liquid chromatography mass spectrometry (UHPLC-MS/MS) and the fragmentation pathway was established based on structure-fragment relationships (SFRs), utilizing high resolution MS/MS data. We have developed a most reliable and easily reproducible protocol describing in depth analysis of SFRs based on the structural modifications and synthesis of isotopologs. Also, the MS/MS fragment library of these basic limonoids generated in this study acts as a fingerprint for accurate identification and quantification of limonoids by MS/MS analysis in various plant tissue extracts, phytopharmaceutical formulations and biological samples.



Removal of agricultural wastewater pollutants by integrating two waste materials, fish scales and neem leaves, as novel potential adsorbent.

Preetham V, Vengala J.

Water Sci Technol. 2021 Nov;84(10-11):2980-2996. PMID: 34850708

Only 2.5% of the world's water is fresh, despite the fact that water covers approximately 70% of the planet. This water is used for several recreational purposes and gets polluted by wastewater disposal directly into freshwater bodies. Effluents dispersed into water bodies could be from various sources like industries, households, and agricultural activities. These effluents comprise heavy metals and chemical wastes directly released into water bodies without treatment and could include major contaminants like nitrates, nitrites, ammonia and phosphates. The present study mainly focuses on removal of four significant pollutants from agriculture wastes, i.e., nitrates, nitrites, ammonia, and phosphates. These pollutants are removed using adsorbents via a process known as adsorption. Adsorbents used in the study are fish scales and neem leaves. Several studies have been carried out to measure the efficiency of adsorbents in the removal of contaminants. These studies include equilibrium studies, kinetic studies and isotherm studies. Based on a complete analysis and results obtained, 95% to 99% of contaminants can be removed effectively with an adsorbent dosage of 0.4g (0.2 g of fish scale and 0.2 g of neem leaves powder), optimum pH of 6 and at 303K constant temperature. The dosage variance stems from changing the dosages of two adsorbents in three ways, i.e., by taking both adsorbents in equal dosages, and increasing the dosage of one adsorbent compared to the other and vice versa. The contact time varied from 0 to 140min and the Initial concentration of pollutants has also been varied from 30 to 70 mg/L. In addition to the above variations, thermodynamic studies were also done, and based on the negative values of ΔG and positive value of ΔH and ΔS , it is evident that the reaction of novel adsorbent (combination of fish scales and neem leaves) is spontaneous and endothermic.

Thermal and Flame Retardant Behavior of Neem and Banyan Fibers When Reinforced with a Bran Particulate Epoxy Hybrid Composite.

Raja T, Mohanavel V, Sathish T, Djearamane S, Velmurugan P, Karthick A, Nasif O, Alfarraj S, Shing Wong L, Sureshkumar S, Ravichandran M.

Polymers (Basel). 2021 Nov 9;13(22):3859. PMID: 34833158

Awareness of environmental concerns influences researchers to develop an alternative method of developing natural fiber composite materials, to reduce the consumption of synthetic fibers. This research attempted testing the neem (*Azadirachta indica*) fiber and the banyan (*Ficus benghalensis*) fiber at different weight fractions, under flame retardant and thermal testing, in the interest of manufacturing efficient products and parts in real-time applications. The hybrid composite consists of 25% fiber reinforcement, 70% matrix material, and 5% bran filler. Their thermal properties-short-term heat deflection, temperature, thermal conductivity, and thermal expansion-were used to quantify the effect of potential epoxy composites. Although natural composite materials are widely utilized, their uses are limited since many of them are combustible. As a result, there has been a lot of focus on making them flame resistant. The thermal analysis revealed the sample B

was given 26% more short-term heat resistance when the presence of banyan fiber loading is maximum. The maximum heat deflection temperature occurred in sample A (104.5 °C) and sample B (99.2 °C), which shows a 36% greater thermal expansion compared with chopped neem fiber loading. In sample F, an increased chopped neem fiber weight fraction gave a 40% higher thermal conductivity, when compared to increasing the bidirectional banyan mat of this hybrid composite. The maximum flame retardant capacity occurred in samples A and B, with endurance up to 12.9 and 11.8 min during the flame test of the hybrid composites.



Removal of hexavalent chromium by biochar derived from *Azadirachta indica* leaves: Batch and column studies.

Thangagiri B, Sakthivel A, Jeyasubramanian K, Seenivasan S, Dhaveethu Raja J, Yun K.

Chemosphere. 2022 Jan;286(Pt 1):131598. PMID: 34325269

This report details the preparation, characterization, and applications of an inexpensive adsorbent obtained from *Azadirachta indica* leaves (Neem biochar (NBC)) and used to remove Cr(VI) from the synthetic waste water. The obtained NBC was characterized by XRD, FTIR, FESEM, EDX and Zeta potential measurements. Adsorption experiments conducted at various pH levels confirmed that 58.54 mg g⁻¹ of Cr(VI) was removed by NBC at pH 2. Experiments conducted at various temperatures revealed that the Cr(VI) adsorption on NBC fits the Langmuir-type adsorption isotherm. A fixed-bed column study was conducted to obtain breakthrough curve for the adsorption process, which confirmed that the NBC usage rate was 4.63 g/L. Cr(VI)NBC was reactivated by NaOH treatment, and the reactivated NBC was used as a sorbent to remove fresh Cr(VI) from the synthetic waste water repeatedly. A cost analysis was also performed for the Cr(VI) removal confirmed that the process was less expensive.

Potential biodegradable face mask to counter environmental impact of Covid-19

Pandit P, Maity S, Singha K, Annu, Uzun M, Shekh M, Ahmed S.

Clean Eng Technol. 2021 Oct;4:100218. PMID: 34322678

On the eve of the outbreak of the COVID-19 pandemic, there is a tremendous increase in the production of facemasks across the world. The primary raw materials for the manufacturing of the facemasks are non-biodegradable synthetic polymers derived from petrochemicals. Disposal of these synthetic facemasks increases waste-load in the environment causing severe ecological issues for flora and fauna. The synthesis processes of the polymers from the petrochemical by-products were also not eco-friendly, which releases huge greenhouse and harmful gases. Therefore, many research organizations and entrepreneurs realize the need for biodegradable facemasks to render similar performance as the existing non-biodegradable masks. The conventional textile

fabrics made of natural fibers like cotton, flax, hemp, etc., can also be used to prepare facemasks with multiple layers in use for general protection. Such natural textile masks can be made anti-microbial by applying various herbal anti-microbial extracts like turmeric, neem, basil, aloe vera, etc. As porosity is the exclusive feature of the masks for arresting tiny viruses, the filter of the masks should have a pore size in the nanometre scale, and that can be achieved in nanomembrane manufactured by electrospinning technology. This article reviews the various scopes of electrospinning technology for the preparation of nanomembrane biomasks. Besides protecting us from the virus, the biomasks can be useful for skin healing, skincare, auto-fragrance, and organized cooling which are also discussed in this review article.



Air pollution tolerance, anticipated performance, and metal accumulation capacity of common plant species for green belt development.

Mondal S, Singh G.

Environ Sci Pollut Res Int. 2021 Nov 29. PMID: 34843046

Green vegetation enrichment is a cost-effective technique for reducing atmospheric pollution. Fifteen common tropical plant species were assessed for identifying their air pollution tolerance, anticipated performance, and metal accumulation capacity at Jharia Coalfield and Reference (JCF) site using Air Pollution Tolerance Index (APTI), Anticipated Performance Index (API), and Metal Accumulation Index (MAI). Metal accumulation efficiencies were observed to be highest for *Ficus benghalensis* L. (12.67mg/kg) and *Ficus religiosa* L. (10.71 mg/kg). The values of APTI were found to be highest at JCF for *F. benghalensis* (APTI: 25.21 ± 0.95), *F. religiosa* (APTI: 23.02 ± 0.21), *Alstonia scholaris* (L.) R. Br. (APTI: 18.50 ± 0.43), *Mangifera indica* L. (APTI: 16.88 ± 0.65), *Azadirachta indica* A. Juss. (APTI: 15.87 ± 0.21), and *Moringa oleifera* Lam. (APTI: 16.32 ± 0.66). *F. benghalensis* and *F. religiosa* were found to be excellent performers to mitigate air pollution at JCF as per their API score. Values of MAI, APTI, and API were observed to be lowest at reference sites for all the studied plant species due to absence of any air

polluting sources. The findings revealed that air pollution played a significant impact in influencing the biochemical and physiological parameters of plants in a contaminated coal mining area. The species with the maximum MAI and APTI values might be employed in developing a green belt to minimize the levels of pollutants into the atmosphere.

Urban tree carbon density and CO₂ equivalent of National Zoological Park, Delhi

Snehlata, Rajlaxmi A, Kumar M.

Environ Monit Assess. 2021 Nov 25;193(12):841. PMID: 34822017

In a highly urbanized city like Delhi, the urban forest plays a vital role in climate change mitigation by capturing and storing carbon dioxide (CO₂) from the atmosphere. Urban vegetation helps in increasing carbon sink and CO₂ equivalent (CO₂eq) and also provides other aesthetic and psychological environmental benefits. To understand how urban trees are vital for carbon sink, the present study aimed to quantify the carbon density and CO₂eq in trees at National Zoological Park (NZP), New Delhi, a tropical semi-arid region of India. For this, we estimated tree biomass or dry matter content of 25 species with the help of allometric equations which are available in published literature and applicable for the tropical region. It was observed that the highest diameter at breast height (DBH) was contributed by *Ficus* sp. while the maximum density among adult tree species found in *Albizia procera*. The total mean dry matter content, C density, and CO₂eq of NZP were 92.10 Mg ha⁻¹, 43.61 Mg-C ha⁻¹, and 168.83 Mg ha⁻¹, respectively. The highest biomass, C density, and CO₂eq obtained in the species of *Ficus benghalensis* followed by *Ficus racemosa* and *Azadirachta indica*. The data indicates that the trees having the capacity to store carbon are essential for the maintenance of a sustainable environment. Thus, the study suggests that there is a substantial scope to increase the carbon density and CO₂eq in urban city through adopting various management strategies viz. afforestation and reforestation program on degraded and abandoned land to maintain a clean and sustainable environment.

Utilizing treated wastewater in tree plantation in Indian desert: part I - species suitability, plant growth and biomass production.

Singh G, Nagora PR, Haksar P, Chauhan AR.

Int J Phytoremediation. 2021 Oct 25:1-11. PMID: 3469494

Treated wastewater can partly meet the requirements of water for irrigating tree crops in dry areas to better utilize, produce biomass and reduce land degradation. Seedlings of *Acacia nilotica*, *Azadirachta indica*, *Eucalyptus camaldulensis*, *Prosopis cineraria*, *P. juliflora*, *Tamarix aphylla*, *Salvadora persica*, *S. oleoides* and *Tecomella undulata* were planted and irrigated with bore-well (BW) and treated wastewater (WW) at ½ET (Evaporation-transpiration) and ¾ET. Plants irrigated at BW/2 attained less height and collar diameter, and showed low growth increments and dry biomass. These variables increased by 1.2-2.0-fold at WW3/4 irrigation. Plants produced 1.4-fold higher biomass with WW over BW, whereas it was 1.5-fold higher at ¾ET over ½ET. Responses of species to BW/WW irrigation differed in biomass allocation to roots and other parts as a mechanism to uptake water and nutrients. Conclusively, *A. nilotica*, *A. indica*, *P. juliflora* and *T. aphylla* had stronger preference to increased irrigation level, whereas *E. camaldulensis*, *S. persica*, *S. oleoides* and *T. undulata* had preferred nutrients added

through treated wastewater. *A. nilotica*, *E. camaldulensis*, *P. juliflora* and *A. indica* were best species in growth and biomass production and wastewater utilization. These can be replicated in urban afforestation to enhance bio-product and reduce degradation in environmental quality.

Hazardous emissions and concentrations of toxic metalloids and trace elements in charcoals from six commonly used tropical timbers for carbonization.

Glalah M, Antwi-Boasiako C.

Environ Sci Pollut Res Int. 2021 Sep 10. PMID: 34508316

Carbonized wood is a biofuel from cellulose pyrolysis with frequent smoke and life-threatening carcinogenic emissions. Carbon monoxide (CO), particulate matter (PM_{2.5}), metalloids and trace elements from charcoals from six commonly used tropical timbers for carbonization in Donkorkrom (Ghana) were assessed. During combustion, *Anogeissus leiocarpa* charcoal emitted the least CO (4.28 ± 1.08 ppm) and PM_{2.5} (3.83 ± 1.57 µg/m³), while particulate matter was greatest for *Erythrophleum ivorense* (28.05 ± 3.08 ppm) and *Azadirachta indica* (27.67 ± 4.17 µg/m³) charcoals. *Erythrophleum ivorense* charcoal produced much lead (16.90 ± 0.33 ppm), arsenic (1.97 ± 0.10 ppm) and mercury (0.58 ± 0.003 ppm) but the least chromium (0.11 ± 0.01 ppm) and zinc (2.85 ± 0.05 ppm). Nickel was greatest for *A. indica* charcoal (0.71 ± 0.01 ppm) and least for *Vitellaria paradoxa* (0.07 ± 0.004 ppm). Trace elements ranged from 342.01 ± 2.54 ppm (*A. indica*) to 978.47 ± 1.80 ppm (*V. paradoxa*) for potassium and $1.74 \pm 0.02\%$ (*V. paradoxa*) to $2.24 \pm 0.10\%$ (*A. indica*) for sulphur. Besides *A. leiocarpa* charcoal, which ranked safest during combustion, the high PM_{2.5} and CO emissions make the other biofuels hazardous indoors. Kitchens need air filters to absorb these emissions together with the use of improved cook stoves. These carcinogenic metalloids would necessitate that their ashes be properly discarded without human contact. Yet, the charcoals would be much suitable as soil amendment bio-char for plant growth quality improvement.

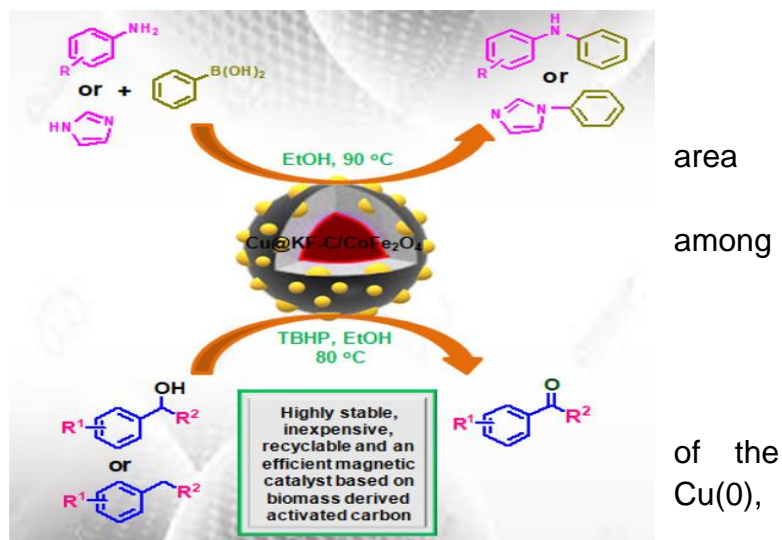
Biomass-Derived Activated Carbon-Supported Copper Catalyst: An Efficient Heterogeneous Magnetic Catalyst for Base-Free Chan-Lam Coupling and Oxidations.

Sharma S, Kaur M, Sharma C, Choudhary A, Paul S.

ACS Omega. 2021 Jul 20;6(30):19529-19545. PMID: 34368539

Development of heterogeneous catalysts from biomass-derived activated carbon is a challenging task. Biomass-derived activated carbon possesses a large specific surface area, highly porous structure, and good thermal/chemical stability. Magnetic copper catalysts based on biomass-derived activated carbon exhibited good catalytic activity in base-free Chan-Lam coupling and oxidations. Herein, biomass-derived activated carbon was prepared by the carbonization of neem dead leaves (abundant waste biomass) followed by chemical activation with KOH. Such a porous carbon material was used as a low cost and highly efficient support material for the preparation of inexpensive and environmentally benign magnetic catalysts [Cu@KF-C/MFe₂O₄, M = Co, Cu, Ni, and Zn]. In addition, KF modification was done to impart basic character to the catalyst that can perform C-N coupling under base-free conditions. Initially, Brunauer-Emmett-Teller (BET)

analysis of the synthesized catalysts was carried out, which indicated that Cu@KF-C/CoFe₂O₄ possess more surface area as well as pore volume, and so accounting for the highest activity among the other synthesized catalysts. Further, X-ray photoelectron spectroscopy (XPS) analysis was performed, which inferred that Cu@KF-C/CoFe₂O₄ contains most copper in reduced form, i.e., which is the active species



responsible for better catalytic activity toward Chan-Lam coupling reactions as well as oxidation of alcohols and hydrocarbons. The physiochemical properties of the most active catalyst, Cu@KF-C/CoFe₂O₄, was examined by BET, XPS, Fourier transform infrared Spectroscopy (FTIR), thermogravimetric analysis (TGA), field emission gun scanning electron microscopy (FEG-SEM), high-resolution transmission electron microscopy (HR-TEM), energy dispersive X-ray (EDX) mapping, energy dispersive X-ray (EDX), inductively coupled plasma atomic emission spectroscopy (ICP-AES), powder X-ray diffraction (XRD), and vibrating sample magnetometry (VSM). Moreover, Cu@KF-C/CoFe₂O₄ shows excellent stability as well as reusability and could be easily separated with the help of an external magnet.

Isolation, biochemical characterization, and development of a biodegradable antimicrobial film from *Cirrhinus mrigala* scale collagen

Kulkarni P, Maniyar M, Nalawade M, Bhagwat P, Pillai S.

Environ Sci Pollut Res Int. 2021 Oct 26. PMID: 34704223

Collagen is a promising candidate for food and pharmaceutical applications due to its excellent biocompatibility, low antigenicity, and controlled biodegradability; however, its heavy price restricts its utilization. Fish scales generated during the processing are generally regarded as waste material and an environmental pollutant, though they are a promising source of collagen. In the present study, *Cirrhinus mrigala* scales were demineralized and extracted for acid-soluble collagen (ASC) using acetic acid, with a collagen yield of 2.7%. UV-Vis spectra, SDS-PAGE, FTIR analyses, and amino acid composition confirmed the type I nature of the collagen extracted. The denaturation temperature of the collagen was found to be 30.09 °C using differential scanning calorimetry (DSC). The collagen was highly soluble at acidic pH and lower NaCl concentrations while its solubility was lowered in alkaline conditions and NaCl concentrations above 0.5 M. The collagen exhibited good emulsifying potential with an emulsion activity index (EAI) and emulsion stability index (ESI) of 21.49 ± 0.22 m² g⁻¹ and 15.67 ± 0.13 min, respectively. Owing to the good physicochemical characteristics of the extracted collagen, collagen-chitosan-neem extract (CCN) films were prepared subsequently which showed good antimicrobial activity against *Bacillus subtilis* NCIM 2635, *Staphylococcus aureus* NCIM 2654, *Escherichia coli* NCIM 2832, and

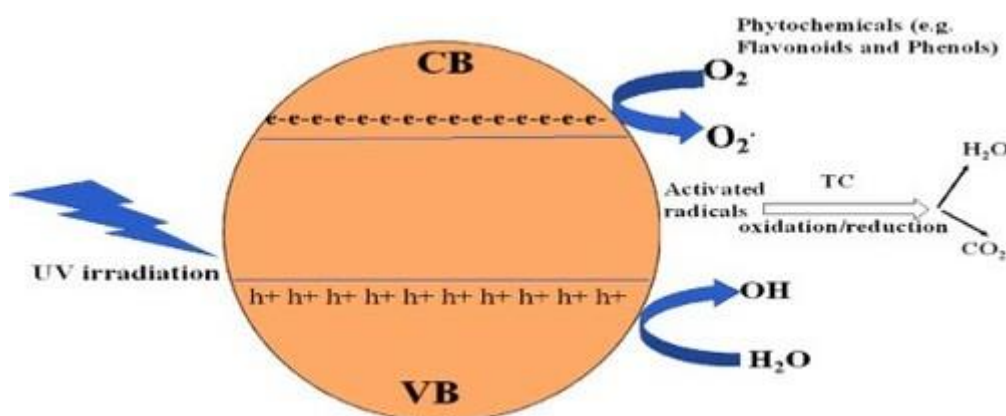
Pseudomonas aeruginosa NCIM 5032, suggesting the potential of collagen in the development of antimicrobial films. These results demonstrate that the collagen from fish waste could be valorized and used effectively along with chitosan and neem extract for the synthesis of novel biodegradable films with antimicrobial efficacy.

Biogenic fabrication and enhanced photocatalytic degradation of tetracycline by bio structured ZnO nanoparticles.

Abdullahi Ari H, Adewole AO, Ugya AY, Asipita OH, Musa MA, Feng W.

Environ Technol. 2021 Dec 2:1-16. PMID: 34736374

Zinc oxide nanoparticles (ZnO NPs) were synthesized using Zinc Nitrate as precursor salt, and plant leaves extracts from *Azadirachta indica* (Common name: Neem), *Cymbopogon citratus* (Common name: Lemongrass), and *Mangifera indica* (Common name: Mango), as both chelating and reducing agents for the synthesis of ZnO NPs by a simple cost-effective and eco-friendly green method. The biosynthesized ZnO NPs were well characterized by various methods. XRD pattern revealed a hexagonal wurtzite phase of ZnO, with no other impurity peaks present revealing XRD crystalline sizes of 13.94-16.37 nm calculated using Scherrer equation. The XPS confirmed the presence of Zn, O, and C, and the carbon peaks are almost in agreement with peaks observed by FT-IR. TEM showed the different ZnO with spherical shapes and some aggregations. BET surface area gave 24.98, 21.62, and 22.72 m²/g, respectively for ZnO-AI, ZnO-Cyc, and ZnO-MI, while BJH pore volume and average pore diameter were estimated to be 0.217 cc/g, 0.209 cc/g, 0.211 cc/g, and 2.132 nm, 2.025 nm, and 2.100 nm respectively for ZnO-AI, ZnO-Cyc, and ZnO-MI. Furthermore, the bio-synthesized ZnO NPs were evaluated for their catalytic and photocatalytic performance in the degradation of aqueous tetracycline (TC). The biosynthesized ZnO NPs exhibit good photodegradation efficiency for TC in varying degrees with ZnO-AI > ZnO-MI > ZnO-Cyc. Optimum operational parameters for TC degradation using the ZnO-AI were established, and maximum degradation efficiency of 84.8% was obtained. In addition, the catalyst can also be regenerated and reused up to three cycles, with the third cycle still achieving greater than 80% TC degradation.

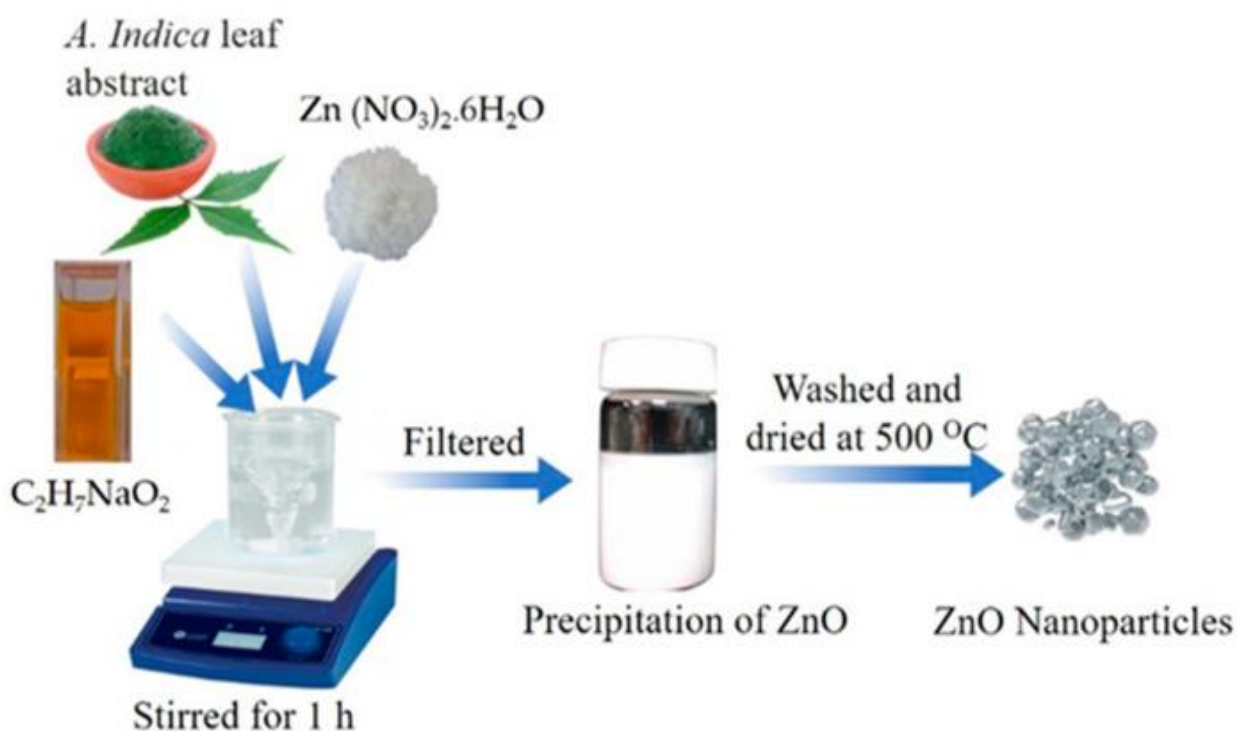


Study on the Synthesis of ZnO Nanoparticles Using *Azadirachta indica* Extracts for the Fabrication of a Gas Sensor.

Acharya TR, Lamichhane P, Wahab R, Chaudhary DK, Shrestha B, Joshi LP, Kaushik NK, Choi EH.

Molecules. 2021 Dec 19;26(24):7685. PMID: 34946767

This paper compared the effects of *A. indica* plant proteins over chemical methods in the morphology of zinc oxide nanoparticles (ZnO NPs) prepared by a co-precipitation method, and ethanol sensing performance of prepared thin films deposited over a fluorene-doped tin oxide (FTO) bind glass substrate using spray pyrolysis technique. The average crystallite sizes and diameters of the grain-sized cluster ZnO NPs were 25 and (701.79 ± 176.21) nm for an undoped sample and 20 and (489.99 ± 112.96) nm for *A. indica* dye-doped sample. The fourier transform infrared spectroscopy (FTIR) analysis confirmed the formation of the Zn-O bond at 450 cm⁻¹, and also showed the presence of plant proteins due to *A. indica* dye extracts. ZnO NPs films exhibited good response (up to 51 and 72% for without and with *A. indica* dye-doped extracts, respectively) toward ethanol vapors with quick response-recovery characteristics at a temperature of 250 °C for undoped and 225 °C for *A. indica* dye-doped ZnO thin films. The interaction of *A. indica* dye extracts helps to decrease the operating temperature and increased the response and recovery rates of the sensor, which may be due to an increase in the specific surface area, resulting in adsorption of more oxygen and hence high response results.



[Construction of yeast cell factories for production of azadirachtin precursor tirucalla-7,24-dien-3 β -ol].

Liu JR, Su XY, Liu JL, Wang CX. *Zhongguo Zhong Yao Za Zhi*. 2021 Oct;46(19):4959-4968. PMID: 34738390 [Article in Chinese].

Azadirachtin, as a botanical insecticide, is a highly oxidized limonoid triterpenoid existing in the seeds of *Azadirachta indica*. However, due to the low content in the seeds, the production of azadirachtin by seed extraction has low yield. Chemical synthesis of azadirachtin is characterized by complex process and low yield. Synthetic biology provides an alternative for the supply of azadirachtin. In this study, two oxidosqualene cyclases AiOSC1 and MaOSC1 respectively derived from *A. indica* and *Melia azedarach* were identified in yeast. A yeast strain producing tirucalla-7,24-dien-3 β -ol was constructed by integration of AiOSC1, Arabidopsis thaliana-derived squalene synthase gene (AtAQS2), and *Saccharomyces cerevisiae*-derived truncated 3-hydroxy-3-methyl-glutaryl coenzyme A reductase gene (PgtHMGR) into the delta site of yeast. Then, the function of MaCYP71BQ5 was successfully verified in yeast after this gene was introduced into the constructed yeast strain. This study not only laid a foundation for the biosynthesis of tirucalla-7,24-dien-3 β -ol, but also provided a chassis cell for the functional identification of cytochrome oxidases (CYP450 s) in azadirachtin biosynthesis pathway.

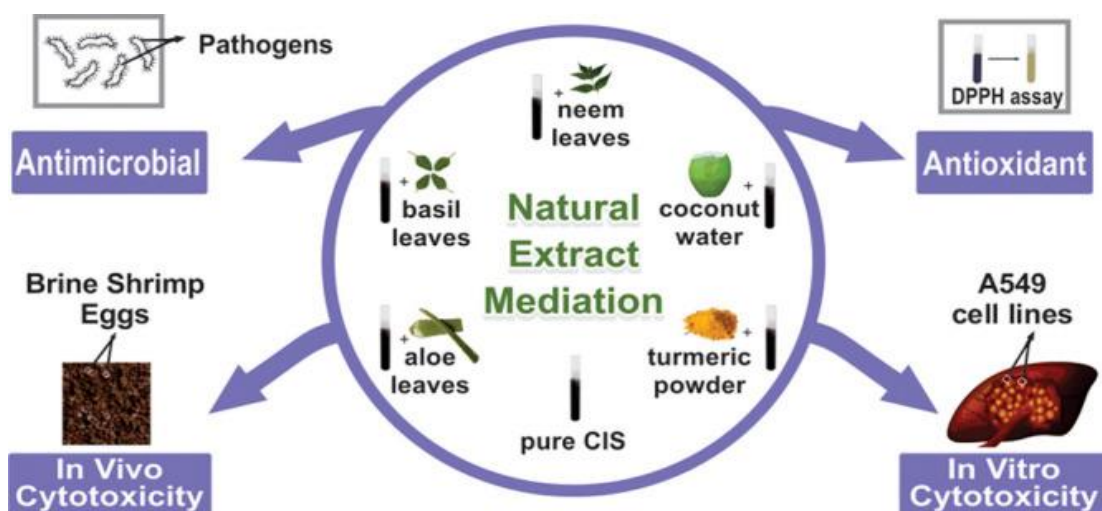
Biocompatible CuInS₂ Nanoparticles as Potential Antimicrobial, Antioxidant, and Cytotoxic Agents

Giri RK, Chaki S, Khimani AJ, Vaidya YH, Thakor P, Thakkar AB, Pandya SJ, Deshpande MP.

ACS Omega. 2021 Sep 29;6(40):26533-26544. PMID: 34661008

A simple hydrothermal route is employed to synthesize pure copper indium disulfide (CIS) and CIS nanoparticles (NPs) mediated by various natural plant extracts. The plant extracts used to mediate are *Azadirachta indica* (neem), *Ocimum sanctum* (basil), *Cocos nucifera* (coconut), *Aloe vera* (aloe), and *Curcuma longa* (turmeric). The tetragonal unit cell structure of as-synthesized NPs is confirmed by X-ray diffraction. The analysis by energy-dispersive X-rays shows that all the samples are near-stoichiometric. The morphologies of the NPs are confirmed by high-resolution scanning and transmission modes of electron microscopy. The thermal stability of the synthesized NPs is determined by thermogravimetric analysis. The optical energy band gap is determined from the absorption spectra using Tauc's equation. The antimicrobial activity analysis and the estimation of the minimum inhibitory concentration (MIC) value of the samples are performed for *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Enterobacter aerogenes*, and *Staphylococcus aureus* pathogens. It shows that the aloe-mediated CIS NPs possess a broad inhibitory spectrum. The best inhibitory effect is observed against *S. aureus*, whereas the least effect was exhibited against *P. vulgaris*. The least MIC value is found for aloe-mediated CIS NPs (0.300 mg/mL) against *S. aureus*, *P. aeruginosa*, and *E. aerogenes*, along with basil-mediated NPs against *E. coli*. The antioxidant activity study

showed that the IC₅₀ value to inhibit the scavenging activity is maximum for the control (vitamin C) and minimum for pure CIS NPs. The in vivo cytotoxicity study using brine shrimp eggs shows that the pure CIS NPs are more lethal to brine shrimp than the natural extract-mediated CIS NPs. The in vitro cytotoxicity study using the human lung carcinoma cell line (A549) shows that the IC₅₀ value of turmeric extract-mediated CIS NPs is minimum (15.62 ± 1.58 µg/mL). This observation reveals that turmeric extract-mediated CIS NPs are the most potent in terms of cytotoxicity toward the A549 cell line.



Antimalarial Effects

Phytomedicine in Disease Management: In-Silico Analysis of the Binding Affinity of Artesunate and Azadirachtin for Malaria Treatment

Okoh MP, Singla RK, Madu C, Soremekun O, Adejoh J, Alli LA, Shen B.

Front Pharmacol. 2021 Nov 30;12:751032. PMID: 34916935

In the rural communities of sub-Saharan African (sSA) countries, malaria is being managed using phytocompounds. Artesunate is reported to inhibit Gephyrin E, a central, multi-domain scaffolding protein of inhibitory post-synapses. Neem plant and its metabolites like azadirachtin are being indicated for management of malaria by traditional healers. The present study was aimed to cheminformatically analyse the binding potential of artesunate and azadirachtin with various reactive moieties of Gephyrin E, to reduce malaria scourge. With molecular dynamics (MD), binding free energy estimation and binding affinity of artesunate and azadirachtin to Gephyrin E was done. GRIP docking was done to study the interactions of these test ligands with Gephyrin E (6FGC). MD simulation gave insights to structural changes upon binding of artesunate and azadirachtin in the ligand-binding pocket of Gephyrin E. Root mean square deviation (RMSD) and root mean square fluctuation (RMSF) were calculated. From the estimation, azadirachtin had a total binding energy of -36.97 kcal/mol; artesunate had a binding energy of -35.73 kcal/mol. The GRIP docking results provided a clearer evidence that artesunate has comparatively better binding affinity to Gephyrin E than azadirachtin, and the critical binding sites (in activity order) were cavity 3, 2, 8, and 6 for artesunate while for azadirachtin, it was cavity 6, 3, 8, and 2. The GRIP docking provided detailed interactions at the atomic levels, providing evidence; both compounds have chances to overcome the drug resistance problem, albeit higher for artesunate. Our findings added another piece of evidence that azadirachtin may be effective as an anti-malarial agent. The results herein may provide impetus for more studies into bioactive components of plant origin towards the effective management of malaria disease phenotype.

Preclinical Trial of Traditional Plant Remedies for the Treatment of Complications of Gestational Malaria

Amadi PU, Agomuo EN, Ukaga CN, Njoku UC, Amadi JA, Nwaekpe CG.

Medicines (Basel). 2021 Dec 17;8(12):79. PMID: 34940291

Background: Most pregnant women living in high malaria endemic regions of Nigeria use herbal remedies for the management of malaria-in-pregnancy, rather than the commonly prescribed drugs. Remedies common to this area involve a suspension of *A. indica* (AI) leaves and in some cases, a suspension containing a mixture of AI and *D.edulis* (PS). **Aim:** This study examined the therapeutic efficacies of AI, PS, or a combination of AI and PS in a pregnant rat model for exoerythrocytic stages of *Plasmodium falciparum* parasite. **Method:** A predetermined sample size of 30 dams was used (for a power level and confidence interval of 95%), and divided equally into six

groups made up of non-malarious dams, untreated malarious dams, and malarious dams either treated exclusively with 1 mL of 3000 mg/kg b.w AI, 1000 mg/kg b.w PS, AI + PS (50% v/v), or 25 mg/kg b.w CQ. **Result:** No maternal mortality was recorded. AI significantly improved maternal weight gain from 32.4 to 82.2 g and placental weight from 0.44 to 0.53 g. In the curative test, AI and AI + PS significantly reduced the average percentage parasitemia (APP) in the pregnant rats from >80% to <20%. No significant difference in the APP was found between the pregnant rats treated with any of CQ or AI during the suppressive test. Results for the prophylactic test of the study groups showed that the APP was significantly reduced from 24.69% to 3.90% when treated with AI and 3.67% when combined with PS. AI + PS reduced diastolic blood pressure from 89.0 to 81.0 mm/Hg and compared with that of the non malarious dams. AI or AI + PS significantly increased the platelet counts ($10^3 \mu\text{L}$) from 214.1 to 364.5 and 351.2, respectively. AI and AI + PS improved birth weight from 2.5 to 3.9 g and crown rump length from 2.6 to 4.1 cm. For biomarkers of preeclampsia, combining AI and PS led to the reversal of the altered levels of creatine kinase, lactate dehydrogenase, cardiac troponin, soluble Fms-Like Tyrosine Kinase-1, and placental growth factor. **Conclusions:** This study validates the use of *A. indica* for the treatment of gestational malaria due to its antiplasmodial and related therapeutic effects and in combination with pear seeds for the management of malaria-in-pregnancy-induced preeclampsia.

Insecticidal effect of ethnobotanical plant extracts against *Anopheles arabiensis* under laboratory conditions

Ejeta D, Asme A, Asefa A.

Malar J. 2021 Dec 14;20(1):466. PMID: 34906139

Background: The emergence and spread of resistant strains of malaria vectors to chemical insecticides are becoming major problems for malaria vector management. Natural plant products have a vital role to play in the current challenge of malaria control. The current study was conducted to evaluate insecticidal effect of ethnobotanical plant extracts against the primary malaria vector, *Anopheles arabiensis* in northwestern Ethiopia. **Methods:** Primarily, ethnobotanical plants used for *Anopheles* mosquito control were surveyed in Dangur district, northwestern Ethiopia. Insecticide-susceptible strains of *Anopheles arabiensis* mosquito were reared in the insectary of the Tropical and Infectious Diseases Research Centre, Assosa University. After surveying plants used for mosquito control in local people, four frequently used plants were identified for extraction. The larvicidal and adulticidal potential of frequently used plant extracts against susceptible strains of the laboratory colony were evaluated. **Results:** A total of 15 plants were identified as ethnobotanical plants that help local people with mosquito control. *Azadirachta indica*, *Ocimum lamiifolium*, *Ocimum americanum*, *Moringa olifeira* leaf, and *Moringa olifeira* seed species of local plants were found to be frequently used to kill and/or repel mosquitoes in the study district. All the plant extracts were found to have potential larvicidal activity against fourth instar larvae of *An. arabiensis* and only ethanol and methanol extract of *Azadirachta indica* and *Ocimum lamiifolium* were found to have potential adulticidal effect against adult of *An. arabiensis*. The highest larvicidal activity was observed in ethanol extract of *Azadirachta indica* with 95% larval mortality and lowest Lethal Concentration 50 (LC 50) of 40.73parts per million (ppm) and LC90 of 186.66 ppm.

The highest adulticidal activity was observed in methanol extract of *Azadirachta indica* with 75% adult mortality at 300 ppm and lowest LC50 of 106.65 ppm and LC90 of 1,293 ppm. The lowest larvicidal and adulticidal activity was observed in methanol extracts of *Ocimum lamiifolium* with 63.35% larval mortality and leaf extract of *Moringa olifeira* with 50% adult mortality at 300 ppm, respectively. **Conclusion:** Ethanol extract of *Azadirachta indica* exerted a remarkable larvicidal effect against *An. arabiensis* and thus it can be used for botanical mosquito insecticide development. Since the current finding is based on susceptible strain of *An. arabiensis*, further work on wild mosquitoes is recommended.

Antiplasmodial, antimalarial activities and toxicity of African medicinal plants: a systematic review of literature.

Tajbakhsh E, Kwenti TE, Kheyri P, Nezaratizade S, Lindsay DS, Khamesipour F.

Malar J. 2021 Aug 25;20(1):349. PMID: 34433465

Background: Malaria still constitutes a major public health menace, especially in tropical and subtropical countries. Close to half a million people mainly children in Africa, die every year from the disease. With the rising resistance to frontline drugs (artemisinin-based combinations), there is a need to accelerate the discovery and development of newer anti-malarial drugs. A systematic review was conducted to identify the African medicinal plants with significant antiplasmodial and/or anti-malarial activity, toxicity, as well as assessing the variation in their activity between study designs (in vitro and in vivo). **Methods:** Key health-related databases including Google Scholar, PubMed, PubMed Central, and Science Direct were searched for relevant literature on the antiplasmodial and anti-malarial activities of African medicinal plants. **Results:** In total, 200 research articles were identified, a majority of which were studies conducted in Nigeria. The selected research articles constituted 722 independent experiments evaluating 502 plant species. Of the 722 studies, 81.9%, 12.4%, and 5.5% were in vitro, in vivo, and combined in vitro and in vivo, respectively. The most frequently investigated plant species were *Azadirachta indica*, *Zanthoxylum chalybeum*, *Picrilia nitida*, and *Nauclea latifolia* meanwhile Fabaceae, Euphorbiaceae, Annonaceae, Rubiaceae, Rutaceae, Meliaceae, and Lamiaceae were the most frequently investigated plant families. Overall, 248 (34.3%), 241 (33.4%), and 233 (32.3%) of the studies reported very good, good, and moderate activity, respectively. *Alchornea cordifolia*, *Flueggea virosa*, *Cryptolepis sanguinolenta*, *Zanthoxylum chalybeum*, and *Maytenus senegalensis* gave consistently very good activity across the different studies. In all, only 31 (4.3%) of studies involved pure compounds and these had significantly ($p = 0.044$) higher antiplasmodial activity relative to crude extracts. Out of the 198 plant species tested for toxicity, 52 (26.3%) demonstrated some degree of toxicity, with toxicity most frequently reported with *Azadirachta indica* and *Vernonia amygdalina*. These species were equally the most frequently inactive plants reported. The leaves were the most frequently reported toxic part of plants used. Furthermore, toxicity was observed to decrease with increasing antiplasmodial activity. **Conclusions:** Although there are many indigenous plants with considerable antiplasmodial and anti-malarial activity, the progress in the development of new anti-malarial drugs from African medicinal plants is still slothful, with only one clinical trial with *Cochlospermum planchonii* (Bixaceae) conducted to date. There is, therefore, the need to scale up anti-malarial drug discovery in the African region.

Suppressive, curative, and prophylactic potentials of an antimalarial polyherbal mixture and its individual components in Plasmodium berghei-Infected mice.

Alaribe SC, Oladipupo AR, Uche GC, Onumba MU, Ota D, Awodele O, Oyibo WA. *J Ethnopharmacol.* 2021 Sep 15;277:114105. PMID: 33961995

Ethnopharmacological relevance: Malaria remains one of the most prevalent infectious diseases in tropical regions of the world, particularly in sub-Saharan Africa, where it remains epidemiologically holoendemic. The absence of effective vaccines and Plasmodium resistance to antimalarial drugs have been the major challenges to malaria control measures. An alternative strategy could be the application of validated and standardized herbal formulations. **Aim of the study:** To evaluate the antimalarial activity of a polyherbal mixture (APM) and compare it to those of its individual constituent plants. **Methods:** APM consisted of stem barks of *Mangifera indica* (MI), *Azadirachta indica* (AI), *Nauclea latifolia* (and roots, NL) and roots of *Morinda lucida* (ML). Dihydroartemisinin-piperaquine (DHP) and pyronaridine-artesunate (PA) served as positive controls. Antimalarial activity was evaluated using suppressive, curative and prophylactic assays in mice infected with *Plasmodium berghei*. **Results:** All the herbal mixtures, individually and in combination, showed significant ($p < 0.05$) antiplasmodial activities in the various assays. They produced considerable parasite suppression ($>50\%$), substantial clearance ($>70\%$), and notable prophylaxis ($>60\%$, except for NL: 35%). APM (95.4-98.7%) and AI (92%), respectively, elicited greater and comparable suppression relative to DHP (88%) and PA (87.3%). However, all the herbal decoctions, individually (72-93.6%) and in combination (82.5-91%), showed lower parasite clearance than DHP (100%) and PA (99.5%). Meanwhile, APM showed relatively greater suppression and prophylaxis than its constituent plants, suggesting that the combination produced synergistic or additive effects. **Conclusion:** These findings could substantiate the use of these plants, singly or in combination, as traditional remedies for malaria. Further studies are recommended to evaluate their clinical usefulness.

Antibacterial Effects

In vitro antibacterial activity of nimbolide against *Helicobacter pylori*

Wylie MR, Windham IH, Blum FC, Wu H, Merrell DS.

J Ethnopharmacol. 2022 Mar 1;285:114828. PMID: 34763046

Ethnopharmacological relevance: Nimbolide is one of hundreds of phytochemicals that have been identified within the neem tree (*Azadirachta indica* A. Juss). As an evergreen tree native to the Indian subcontinent, components of the neem tree have been used for millennia in traditional medicine to treat dental, gastrointestinal, urinary tract, and blood-related ailments, ulcers, headaches, heartburn, and diabetes. In modern times, natural oils and extracts from the neem tree have been found to have activities against a variety of microorganisms, including human pathogens. **Aim of the study:** *Helicobacter pylori*, a prevalent gastric pathogen, shows increasing levels of antibiotic resistance. Thus, there is an increasing demand for novel therapeutics to treat chronic infections. The in vitro activity

of neem oil extract against *H. pylori* was previously characterized and found to be bactericidal. Given the numerous phytochemicals found in neem oil extract, the present study was designed to define and characterize specific compounds showing bactericidal activity against *H. pylori*. **Materials and methods:** Azadirachtin, gedunin, and nimbolide, which are all common in neem extracts, were tested for antimicrobial activity; the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were determined for nine strains of *H. pylori*. The specific properties of nimbolide were further characterized against *H. pylori* strain G27. Bactericidal kinetics, reversibility, effectiveness at low pH, and activity under bacteriostatic conditions were examined. The hemolytic activity of nimbolide was also measured. Finally, neem oil extract and nimbolide effectiveness against *H. pylori* biofilms were examined in comparison to common antibiotics used to treat *H. pylori* infection. **Results:** Nimbolide, but not azadirachtin or gedunin, was effective against *H. pylori*; MICs and MBCs against the nine tested strains ranged between 1.25-5 µg/mL and 2.5-10 µg/mL, respectively. Additionally, neem oil extract and nimbolide were both effective against *H. pylori* biofilms. Nimbolide exhibited no significant hemolytic activity at biologically relevant concentrations. The bactericidal activity of nimbolide was time- and dose-dependent, independent of active *H. pylori* growth, and synergistic with low pH. Furthermore, nimbolide-mediated *H. pylori* cell death was irreversible after exposure to high nimbolide concentrations (80 µg/mL, after 2 h of exposure time and 40 µg/mL after 8 h of exposure). **Conclusions:** Nimbolide has significant bactericidal activity against *H. pylori*, killing both free living bacterial cells as well as cells within a biofilm. Furthermore, the lack of hemolytic activity, synergistic activity at low pH and bactericidal properties even against bacteria in a state of growth arrest are all ideal pharmacological and biologically relevant properties for a potential new agent. This study underscores the potential of neem oil extract or nimbolide to be used as a future treatment for *H. pylori* infection.

Analysis of Plant Origin Antibiotics against Oral Bacterial Infections Using In Vitro and In Silico Techniques and Characterization of Active Constituents.

Rafey A, Amin A, Kamran M, Haroon U, Farooq K, Foubert K, Pieters L.

Antibiotics (Basel). 2021 Dec 8;10(12):1504. PMID: 34943716

The pervasiveness of oral bacterial infections in diabetic patients is a serious health concern that may produce severe complications. We investigated 26 Ayurvedic medicinal plants traditionally used for treatment of the oral bacterial infections with the aim to look for new promising drug leads that can be further employed for herbal formulation design. The plants were grouped into three categories based on traditional usage. All plant extracts were examined for antibacterial, antibiofilm and anti-quorum-sensing properties. The plants with significant activities including *Juglans regia*, *Syzygium aromaticum*, *Eruca sativa*, *Myristica fragrans*, *Punica granatum* and *Azadirachta indica* were further analyzed using HPLC-DAD-QToF and GC-MS. In silico and in vitro activity was evaluated for selected constituents. Finally, it could be concluded that eugenol and 2-phenylethylisothiocyanate are major contributors towards inhibition of bacterial biofilms and quorum sensing.

Evaluation of the Antidiarrheal and Antioxidant Effects of Some Chewing Sticks Commonly Used for Oral Hygiene in Ghana.

Essuman EK, Boakye AA, Tetey CO, Hunkpe G, Kortei NK, Kwansa-Bentum H, Waikhom SD, Aninagyei E.

Evid Based Complement Alternat Med. 2021 Oct 5;2021:7270250. PMID: 34650615

Microbial etiology of diarrhea is a significant cause of death, especially in children in developing countries. The presence of microbes that are resistant to current treatment options for diarrhea suggests the need to find newer antimicrobial agents for treatment. Therefore, this study focused on investigating the antimicrobial effect of some Ghanaian chewing sticks commonly used for oral hygiene, *Azadirachta indica*, *Garcinia afzelii*, and *Garcinia kola*, against selected diarrhea-causing organisms. From the stem and bark of each plant, 70% methanolic extract was experimented on *Salmonella* and *Shigella* species, namely, *Shigella sonnei*, *Shigella flexneri*, *Salmonella typhimurium enterica*, *Salmonella typhi* attenuated, and *Klebsiella oxytoca* for microbial susceptibility using the agar well diffusion method. Additionally, the antioxidant profile of the methanolic extracts were investigated using 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical, 2,2'-azino-bis (3-ethylbenzthiazoline-6-sulphonic) acid (ABTS) scavenging activities, and ferric-reducing antioxidant potential (FRAP) assays, while the total polyphenolic content was determined using the Folin-Ciocalteu reagent. *G. afzelii* and *A. indica* stem demonstrated the highest antimicrobial effect, inhibiting the growth of all test organisms. Additionally, the extracts demonstrated high antioxidant potential and were found to possess significant amounts of phenolic compounds. Therefore, methanolic extracts of *G. afzelii* and *A. indica* stem are promising candidates for the identification of safe novel compounds to mitigate diarrheal diseases.

Acute gastroenteritis and the usage pattern of antibiotics and traditional herbal medications for its management in a Nigerian community

Adeyemi OO, Alabi AS, Adeyemi OA, Talabi OT, Abidakun OM, Joel IY, Stonehouse NJ

PLoS One. 2021 Oct 4;16(10):e0257837. PMID: 34607333

Acute gastroenteritis (AGE) is the highest cause of mortality worldwide in children under the age of 5 years, with the highest mortalities occurring in low-to-middle income countries. Treatment can involve use of unregulated herbal medication and antibiotics. A cross sectional study was carried out to investigate the use of antibiotics and traditional herbal medications in the management of AGE among Yòrùbá-speaking communities in Kwara State, Nigeria. Our findings suggest habitual use of antibiotics (54.6%) and herbal medication (42.5%) in the management of AGE with high levels of self-prescription of antibiotics (21.7%) and herbal medications (36.2%) within the community. Ethanolic extracts of selected herbal plants reported (i.e. *Aristolochia ringens*, *Azadirachta indica*, *Chromolaena odorata*, *Etanda Africana*, *Ficus capensis*, *Ficus vogelii*, *Mangifera indica*, *Momordica charantia*, *Ocimum gratissimum*, *Senna alata*, *Sorghum bicolor* and *Vernonia amygdalina*) were investigated for antibacterial properties, using bacteria known to be causative agents of AGE. Our findings showed that, with exception of *Ficus vogelii*, which enhanced bacterial growth, the plant extracts reported all showed some antibacterial activity. We further discuss our findings within a regulatory context, with the aim to guide the use of traditional and herbal medication in low-to medium income countries (LMICs) and reduce the potential risks associated with the development of antimicrobial resistance.

Antiviral effects

Antiviral Potential of Selected Medicinal Herbs and Their Isolated Natural Products

Perera WPRT, Liyanage JA, Dissanayake KGC, Gunathilaka H, Weerakoon WMTDN, Wanigasekara DN, Fernando WSK, Rajapaksha RMH, Liyanage RP, Perera BT.

Biomed Res Int. 2021 Dec 8;2021:7872406. PMID: 34926691

Viruses are responsible for a variety of human pathogenesis. Owing to the enhancement of the world population, global travel, and rapid urbanization, and infectious outbreaks, a critical threat has been generated to public health, as preventive vaccines and antiviral therapy are not available. Herbal medicines and refined natural products have resources for the development of novel antiviral drugs. These natural agents have shed light on preventive vaccine development and antiviral therapies. This review intends to discuss the antiviral activities of plant extracts and some isolated plant natural products based on mainly preclinical (in vitro and in vivo) studies. Twenty medicinal herbs were selected for the discussion, and those are commonly recognized antiviral medicinal plants in Ayurveda (*Zingiber officinale*, *Caesalpinia bonducella*, *Allium sativum*, *Glycyrrhiza glabra*, *Ferula assafoetida*, *Gymnema sylvestre*, *Gossypium herbaceum*, *Phyllanthus niruri*, *Trachyspermum ammi*, *Withania somnifera*, *Andrographis paniculata*, *Centella asiatica*, *Curcuma longa*, *Woodfordia fruticosa*, *Phyllanthus emblica*, *Terminalia chebula*, *Tamarindus indica*, *Terminalia arjuna*, *Azadirachta indica*, and *Ficus religiosa*). However, many viruses remain without successful immunization and only a few antiviral drugs have been approved for clinical use. Hence, the development of novel antiviral drugs is much significant and natural products are excellent sources for such drug developments. In this review, we summarize the antiviral actions of selected plant extracts and some isolated natural products of the medicinal herbs.

Mechanistic insights into the Japanese encephalitis virus RNA dependent RNA polymerase protein inhibition by bioflavonoids from *Azadirachta indica*.

Dwivedi VD, Singh A, El-Kafraway SA, Alandijany TA, Faizo AA, Bajrai LH, Kamal MA, Azhar EI.

Sci Rep. 2021 Sep 13;11(1):18125. PMID: 34518560

Japanese encephalitis (JE) virus is a flavivirus causing encephalitis causing neurological damage. RNA-dependent-RNA-polymerase (RdRp) is responsible for genome replication making it excellent anti-viral target. In this study, the crystal structure of JE RdRp (jRdRp) and bioflavonoids reported in *Azadirachta indica* were retrieved from specific databases. Structure-based virtual screening was employed using MTiOpenScreen server and top four compounds selected with the most negative docking scores. Conformations were redocked using AutoDock Vina; these complexes showed mechanistic interactions with Arg⁴⁷⁴, Gly⁶⁰⁵, Asp⁶⁶⁸, and Trp⁸⁰⁰ residues in the active site of jRdRp, i.e., guanosine-5'-triphosphate. Furthermore, 100 ns classical molecular dynamics simulation and binding free energy calculation showed stability of docked bioflavonoids in the active jRdRp pocket and significant contribution of van-der-Waals interactions for docked complex stability during simulation. Therefore, this study predicted the anti-viral activity of Gedunin, Nimbolide, Ohchinin acetate, and Kulactone against jRdRp and can be considered for further antiviral drug development.

Exploring Phytochemicals of Traditional Medicinal Plants Exhibiting Inhibitory Activity Against Main Protease, Spike Glycoprotein, RNA-dependent RNA Polymerase and Non-Structural Proteins of SARS-CoV-2 Through Virtual Screening
Nallusamy S, Mannu J, Ravikumar C, Angamuthu K, Nathan B, Nachimuthu K, Ramasamy G, Muthurajan R, Subbarayalu M, Neelakandan K.

Front Pharmacol. 2021 Jul 8;12:667704. PMID: 34305589

Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) being a causative agent for global pandemic disease nCOVID'19, has acquired much scientific attention for the development of effective vaccines and drugs. Several attempts have been made to explore repurposing existing drugs known for their anti-viral activities, and test the traditional herbal medicines known for their health benefiting and immune-boosting activity against SARS-CoV-2. In this study, efforts were made to examine the potential of 605 phytochemicals from 37 plant species (of which 14 plants were endemic to India) and 139 antiviral molecules (Pubchem and Drug bank) in inhibiting SARS-CoV-2 multiple protein targets through a virtual screening approach. Results of our experiments revealed that SARS-CoV-2 M^{Pro} shared significant dissimilarities against SARS-CoV M^{Pro} and MERS-CoV M^{Pro} indicating the need for discovering novel drugs. This study has screened the phytochemical cyanin (*Zingiber officinale*) which may exhibit broad-spectrum inhibitory activity against main proteases of SARS-CoV-2, SARS-CoV and MERS-CoV with binding energies of (-) 8.3 kcal/mol (-) 8.2 kcal/mol and (-) 7.7 kcal/mol respectively. Amentoflavone, agathisflavone, catechin-7-o-gallate and chlorogenic acid were shown to exhibit multi-target inhibitory activity. Further, *Mangifera indica*, *Anacardium occidentale*, *Vitex negundo*, *Solanum nigrum*, *Pedaliium murex*, *Terminalia chebula*, *Azadirachta indica*, *Cissus quadrangularis*, *Clerodendrum serratum* and *Ocimum basilicum* were reported as potential sources of phytochemicals for combating nCOVID'19. More interestingly, this study has highlighted the anti-viral properties of the traditional herbal formulation "Kabasura kudineer" recommended by AYUSH, a unit of Government of India. Short listed phytochemicals could be used as leads for future drug design and development. Genomic analysis of identified herbal plants will help in unraveling molecular complexity of therapeutic and anti-viral properties which proffer lot of chance in the pharmaceutical field for researchers to scout new drugs in drug discovery.

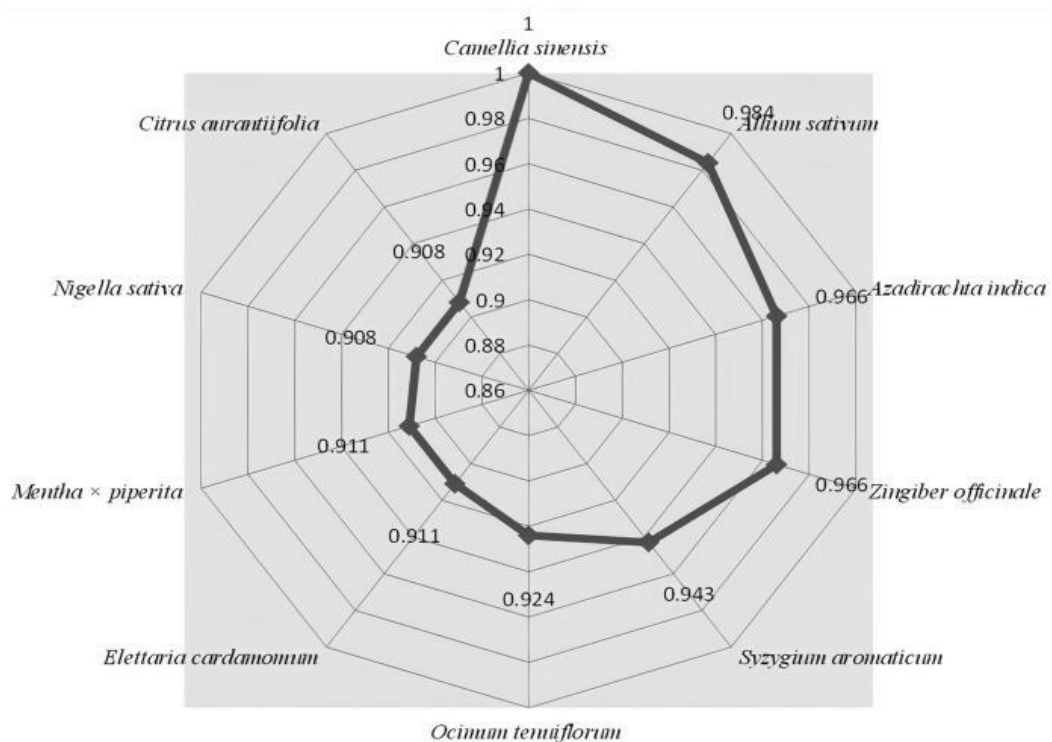
Previously published ethno-pharmacological reports reveal the potentiality of plants and plant-derived products used as traditional home remedies by Bangladeshi COVID-19 patients to combat SARS-CoV-2

Rafiqul Islam ATM, Ferdousi J, Shahinozzaman M.

Saudi J Biol Sci. 2021 Nov;28(11):6653-6673. PMID: 34305428

Several plants have traditionally been used since antiquity to treat various gastroenteritis and respiratory symptoms similar to COVID-19 outcomes. The common symptoms of COVID-19 include fever or chills, cold, cough, flu, headache, diarrhoea, tiredness/fatigue, sore throat, loss of taste or smell, asthma, shortness of breath, or difficulty breathing, etc. This study aims to find out the plants and plant-derived products which are being used by the COVID-19 infected patients in Bangladesh and how those plants are being used for

the management of COVID-19 symptoms. In this study, online and partially in-person survey interviews were carried out among Bangladeshi respondents. We selected Bangladeshi COVID-19 patients who were detected Coronavirus positive (+) by RT-PCR nucleic acid test and later recovered. Furthermore, identified plant species from the surveys were thoroughly investigated for safety and efficacy based on the previous ethnomedicinal usage reports. Based on the published data, they were also reviewed for their significant potentialities as antiviral, anti-inflammatory, and immunomodulatory agents. We explored comprehensive information about a total of 26 plant species, belonging to 23 genera and 17 different botanical families, used in COVID-19 treatment as home remedies by the respondents. Most of the plants and plant-derived products were collected directly from the local marketplace. According to our survey results, greatly top 5 cited plant species measured as per the highest RFC value are *Camellia sinensis* (1.0) > *Allium sativum* (0.984) > *Azadirachta indica* (0.966) > *Zingiber officinale* (0.966) > *Syzygium aromaticum* (0.943). Previously published ethnomedicinal usage reports, antiviral, anti-inflammatory, and immunomodulatory activity of the concerned plant species also support our results. Thus, the survey and review analysis simultaneously reveals that these reported plants and plant-derived products might be promising candidates for the treatment of COVID-19. Moreover, this study clarifies the reported plants for their safety during COVID-19 management and thereby supporting them to include in any future pre-clinical and clinical investigation for developing herbal COVID-19 therapeutics.



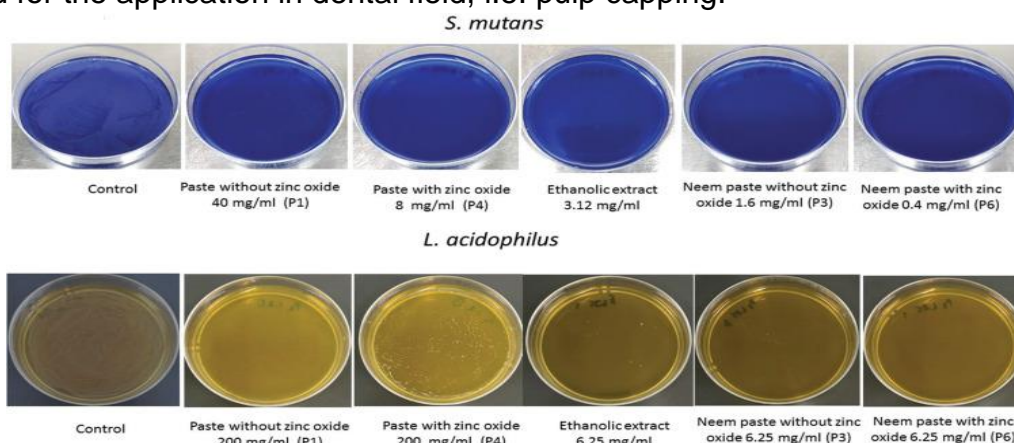
Oro dental Protection

The inhibitory effect of a novel neem paste against cariogenic bacteria

Tasanarong T, Patntirapong S, Aupaphong V.J

Clin Exp Dent. 2021 Nov 1;13(11):e1083-e1088. PMID: 34824693

Background: Dental caries is a major oral health problem, which associates with cariogenic bacteria. *Streptococcus mutans* and *Lactobacillus acidophilus* are facultative anaerobic bacteria that are found in tooth decay. Accordingly, neem leaf extract was developed due to its great anti-microbial property against many bacteria. The aim of this study was to determine anti-cariogenic properties of neem leaf extract in a novel paste preparation. **Material and methods:** The neem extract was derived from maceration of dry neem leaves in ethanol for 48 h. The ethanolic extract was subjected to chemical identification using GC-MS. Neem pastes were prepared from ethanolic extract mixed with polyethylene glycol paste with or without zinc oxide. *S. mutans* and *L. acidophilus* test were initiated at bacterial concentration of 10⁸ CFU/ml. The antibacterial activity was then performed by disc diffusion method following by minimum bactericidal concentration (MBC) technique. **Results:** GC-MS result displayed 35 compounds. Compounds found in the extract were n-Hexadecanoic acid (31.18%), Hentriacontane (18%), Phytol (16.79%). Disc diffusion showed that ethanolic extract and neem pastes inhibited growth of both bacteria. For MBC, neem paste with zinc oxide at concentration of neem 0.4 mg/ml was the most effective concentration on inhibiting *S. mutans* growth. Neem pastes and ethanolic extract at concentration of neem 6.25 mg/ml inhibited *L. acidophilus* growth. **Conclusions:** The ethanolic neem leaf extract and novel neem pastes had antimicrobial effect on both *S. mutans* and *L. acidophilus*. By this property, neem paste could be developed for the application in dental field, i.e. pulp capping.



Synergistic antibacterial activity of herbal extracts with antibiotics on bacteria responsible for periodontitis

Abullais Saquib S, Abdullah AlQahtani N, Ahmad I, Arora S, Mohammed Asif S, Ahmed Javali M, Nisar N.

J Infect Dev Ctries. 2021 Nov 30;15(11):1685-1693. PMID: 34898497

Introduction: Development of bacterial resistance and antimicrobial side-effect has shifted the focus of research toward Ethnopharmacology. A biologically active compound derived from the plants may increase the effectiveness of antibiotic when used in combination. The present study aims to determine the synergistic antibacterial effect of ethanolic extracts of *Punica granatum* (pericarp), *Commiphora molmol*, *Azadirachta indica*

(bark) in combination with amoxicillin, metronidazole, tetracycline, and azithromycin on periodontopathic bacteria: *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola* and *Aggregatibacter actinomycetemcomitans*. **Methodology:** Periodontopathic bacterial strains were isolated from the plaque sample that was collected from periodontitis patients and grown under favorable conditions. Susceptibility of bacteria to the antibiotics and extracts was determined by disc diffusion method by measuring the diameter of the inhibition zones. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of plant extracts were evaluated against each bacterium. Synergistic effect of plant extract in combination with antibiotics was tested against each bacterium by measuring the diameter of zone of inhibition (ZOI). **Results:** Findings revealed that all plant extracts exhibited an inhibitory effects on the proliferation and growth of periodontopathic bacteria. The maximum antibacterial effect was exhibited by *C. molmol* on *P. gingivalis* (ZOI = 20 ± 0.55 mm, MIC = 0.53 ± 0.24 mg/mL and MBC = 5.21 ± 1.81 mg/mL) ($p < 0.05$), meanwhile, no antibacterial activity was exhibited by *P. granatum* on *T. forsythia*. Synergistic antibacterial effect was recorded when plant extracts were used in combination with antibiotics. The best synergism was exhibited by *P. granatum* with amoxicillin against *A. actinomycetemcomitans* (24 ± 1.00 mm) ($p < 0.05$). **Conclusions:** The synergistic test showed significant antibacterial activity when plant extracts were combined with antibiotics against all the experimented bacteria.

Efficacy of medicinal plant extracts as dental and periodontal antibiofilm agents: A systematic review of randomized clinical trials.

Furquim Dos Santos Cardoso V, Amaral Roppa RH, Antunes C, Silva Moraes AN, Santi L, Konrath EL.

J Ethnopharmacol. 2021 Dec 5;281:114541. PMID: 34416298

Ethnopharmacological relevance: The presence of biofilm in oral cavity is associated with dental plaque and related diseases, including gingivitis, periodontitis and inflammatory responses. Some medicinal plants traditionally used for biofilm-associated pathologies such as *Camellia sinensis* (L.) Kuntze, *Punica granatum* L. and *Lippia sidoides* Cham. are currently incorporated into dosage forms as antiplaque agents. **Aims:** To present the current application of medicinal plant extracts associated in drug dosages to control microbial biofilms, with emphasis on those present in the oral cavity, especially to treat dental plaque. **Materials and methods:** A PRISMA-compliant systematic search was conducted using the PubMed, Web of Science and Scopus databases. After the abstract and full-text analysis, the Cochrane Collaboration's tools for clinical studies was applied to assess the methodological quality of randomized clinical trials. **Results:** Of 964 potentially eligible studies, 47 studies met the inclusion criteria and were included in the systematic review. *Camellia sinensis* was the most commonly used species (8 studies), with positive results in reducing both the PI and GI in the form of mouthwash, toothpaste and gel. The *Melaleuca alternifolia* oil (5 studies) demonstrated low reduction in PI but important effects on GI scores. *Azadirachta indica* (4 studies) extracts presented efficacy similar to CHX to improve the periodontal parameters, including PI and GI. *Ricinus communis* oil (3 studies), despite reducing microbiological counts and GI, did not prove to be better than the hypochlorite solution, used as an alternative treatment for dentures. The main bioactive compounds described for the plant species are polyphenols, essential oils and alkaloids, most of them with identified antibiofilm activities. **Conclusions:** These active species could lead to future development of safer and newer treatments for oral biofilm-associated infections. However, more studies are needed to further understand the clinical relevance of their application.

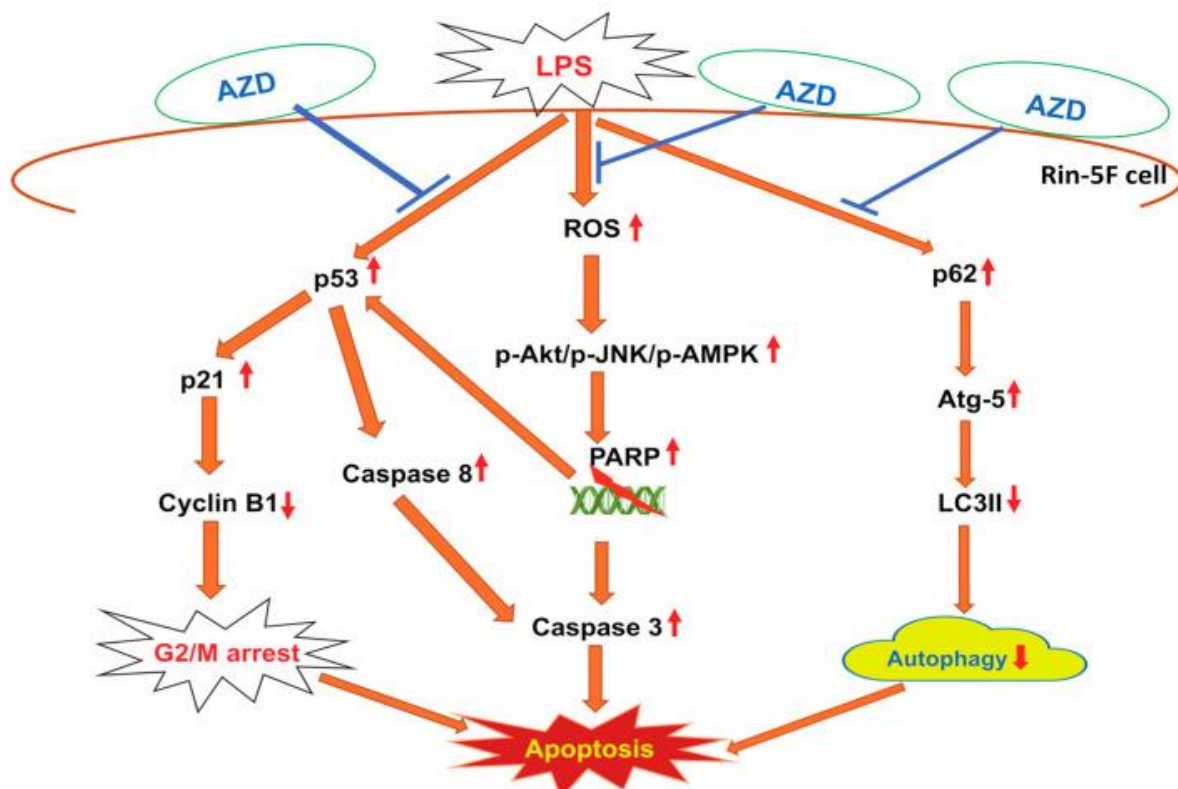
Anti-Inflammatory Effects

Azadirachtin Attenuates Lipopolysaccharide-Induced ROS Production, DNA Damage, and Apoptosis by Regulating JNK/Akt and AMPK/mTOR-Dependent Pathways in Rin-5F Pancreatic Beta Cells

John A, Raza H.

Biomedicines, 2021 Dec 18;9(12):1943. PMID: 34944759

Pancreatic inflammation and the resulting cellular responses have been implicated in pancreatitis, diabetes, and pancreatic cancer. Inflammatory responses due to the bacterial endotoxin, lipopolysaccharide (LPS), have been demonstrated to alter cellular metabolism, autophagy, apoptosis, and cell proliferation in different cell populations, and hence increases the risks for organ toxicity including cancer. The exact molecular mechanism is however not clear. In the present study, we investigated the role and mechanism of an antioxidant, azadirachtin (AZD), a limonoid extracted from the neem tree (*Azadirachta indica*), against LPS-induced oxidative stress in the pancreatic β -cell line, Rin-5F. We demonstrated that cells treated with LPS (1 μ g/mL for 24 h) showed increased reactive oxygen species (ROS) production, DNA damage, cell cycle arrest, and apoptosis. Our results also showed that LPS induced alterations in the AMP-activated protein kinase (AMPK)/mammalian target of rapamycin (mTOR) pathways, suppressing autophagy and augmenting apoptosis. Treatment with Azadirachtin (25 μ M for 24 h), on the other hand, rendered some degree of protection to the pancreatic cells from apoptosis by inducing the autophagy signals required for cell survival. These results may have significance in elucidating the mechanisms of pancreatic β -cell survival and death by balancing the molecular communication between autophagy and apoptosis under inflammatory and pathological conditions.



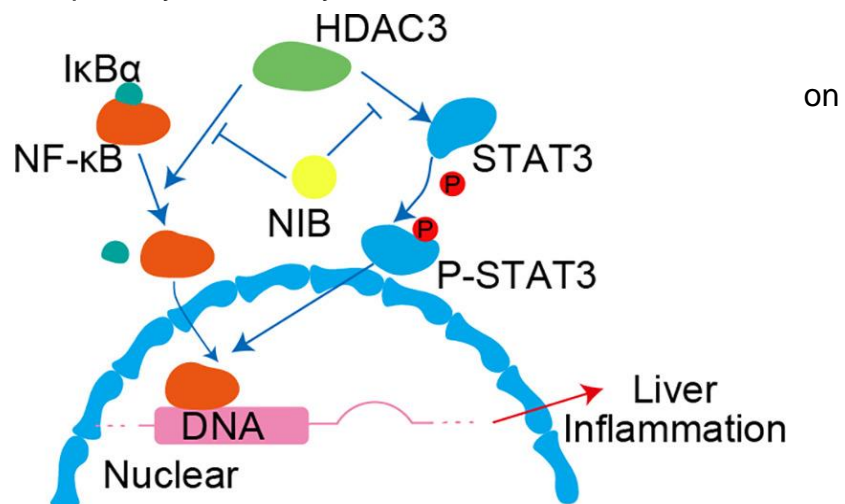
Nimbolide attenuated the inflammation in the liver of autoimmune hepatitis mice through regulation of HDAC3

Xia D, Chen D, Cai T, Zhu L, Lin Y, Yu S, Zhu K, Wang X, Xu L, Chen Y.

Toxicol Appl Pharmacol. 2022 Jan 1;434:115795. PMID: 34780724

A chronic liver disease named autoimmune hepatitis (AIH) will carry elevated levels of inflammatory cytokines, but there is currently no effective treatment to cure it. Histone deacetylase 3 (HDAC3) takes an important position in regulating the expression of inflammatory genes. Nimbolide (NIB) is a limonoid extracted from the neem tree (*Azadirachta indica*) that has been found to be effective against many diseases, including cancer, scleroderma, and acute respiratory distress syndrome.

Here, we investigated the protective effect of nimbolide in AIH liver. Mice and AML12 cells were employed to establish AIH model with liver antigen S100 and cell injury model of LPS, and then treated with different concentrations of nimbolide. After the successful establishment of the animal model and cell model,



inflammatory cytokines of IL-1 β , IL-6 and TNF- α as well as cellular signaling related to inflammation such as STAT3, I κ B- α and NF- κ B were examined. We observed for the first time about nimbolide can effectively inhibit inflammation in AIH mice's liver and AML12 cells by inhibiting HDAC3 expression. HDAC3 knocked down by siRNA in cells can also effectively alleviate the inflammation in AML12 cells, further confirming that HDAC3 plays an important role in the inflammation of liver cells. These results suggest nimbolide could be a potential new treatment for autoimmune hepatitis, and HDAC3 may become a new target for autoimmune hepatitis.

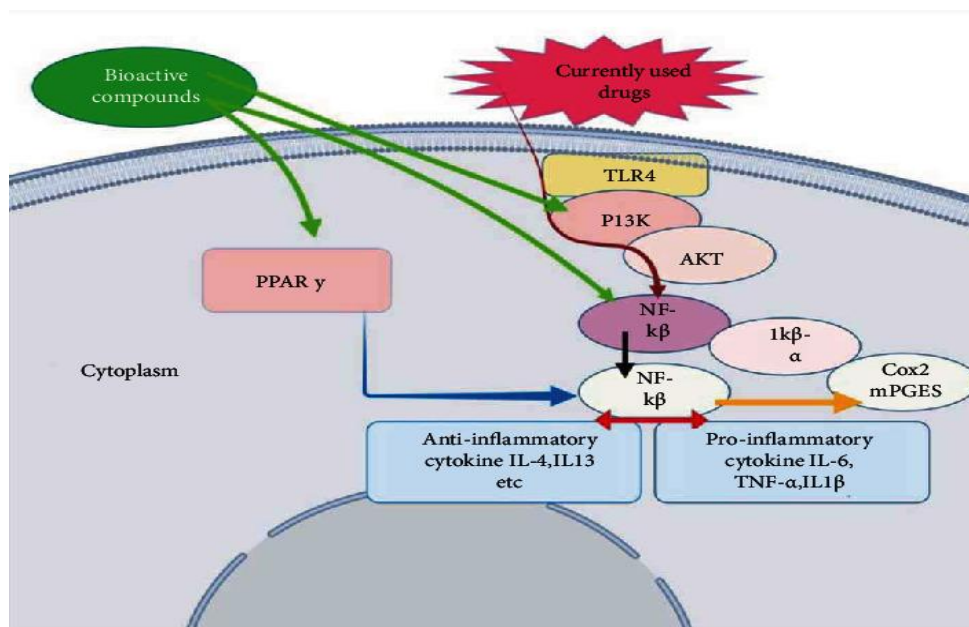
Pharmacologic Activities of Plant-Derived Natural Products on Respiratory Diseases and Inflammations

Timalsina D, Pokhrel KP, Bhusal D.

Biomed Res Int. 2021 Oct 4;2021:1636816. PMID: 34646882

Respiratory inflammation is caused by an air-mediated disease induced by polluted air, smoke, bacteria, and viruses. The COVID-19 pandemic is also a kind of respiratory disease, induced by a virus causing a serious effect on the lungs, bronchioles, and pharynxes that results in oxygen deficiency. Extensive research has been conducted to find out the potent natural products that help to prevent, treat, and manage respiratory diseases. Traditionally, wider floras were reported to be used, such as *Morus alba*, *Artemisia indica*, *Azadirachta indica*, *Calotropis gigantea*, but only some of the potent compounds from some of the plants have been scientifically validated. Plant-derived natural products such as colchicine, zingerone, forsythiaside A, mangiferin, glycyrrhizin, curcumin, and many other compounds

are found to have a promising effect on treating and managing respiratory inflammation. In this review, current clinically approved drugs along with the efficacy and side effects have been studied. The study also focuses on the traditional uses of medicinal plants on reducing respiratory complications and their bioactive phytoconstituents. The pharmacological evidence of lowering respiratory complications by plant-derived natural products has been critically studied with detailed mechanism and action. However, the scientific validation of such compounds requires clinical study and evidence on animal and human models to replace modern commercial medicine.



Systematic review of Ethiopian medicinal plants used for their anti-inflammatory and wound healing activities

Nigussie D, Makonnen E, Tufa TB, Brewster M, Legesse BA, Fekadu A, Davey G.
J Ethnopharmacol. 2021 Aug 10;276:114179. PMID: 33989738

Ethnopharmacological relevance: Plant materials are used worldwide as complementary and alternative therapeutics for the treatment of various illnesses. In Ethiopia, folk medicines are utilized across a wide range of cultures and settings. Ethiopia has numerous plant species of which around 12% are endemic, making it a rich source of medicinal plants that are potentially important for human wellbeing. **Aim of the study:** The aim of this study was to assess Ethiopian medicinal plants with anti-inflammatory or wound healing activities, in an attempt to compile the information required for further investigation of their potential role in the management of lymphoedema. **Methods:** A systematic review protocol was developed according to the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) statement. The protocol for this review was registered on PROSPERO with registration number CRD42019127471. This review considers all controlled in vivo and in vitro anti-inflammatory and wound healing studies evaluating the efficacy and safety of Ethiopian medicinal plants. The search strategy included all articles containing descriptors such as Ethiopia, medicinal plants, herbal products, care, management, lymphoedema, lymphedema, swelling, podoconiosis, elephantiasis, wound, wound healing, inflammation, an anti-inflammatory that were published until June 28, 2019. Outcomes were measured as the percentage of

inflammatory and pro-inflammatory cell inhibition, as the percentage of carrageenan-induced oedema (anti-inflammation) inhibition, and the percentage of cell migration and proliferation (wound healing). For quality assessment of individual animal studies, the Risk of Bias tool for animal intervention studies (SYRCLE's RoB tool) criteria were used. For quality assessment of individual in vitro studies, the OECD guidelines and the WHO Good Laboratory Practice (GLP) handbook were used. **Results:** A total of 46 articles on anti-inflammatory and 17 articles on wound healing properties were reviewed. For the in vivo studies, Swiss albino mice and Wistar rats were used, and the concentration of plant extracts or fractions administered to the lab animals varied considerably. Acetone extract of *Vernonia amygdalina* showed the fastest anti-inflammatory activity at lower concentrations in carrageenan-induced paw oedema. **Conclusion:** *Lawsonia inermis*, *Azadirachta indica*, *Achyranthes aspera*, and *Cuminum cyminum* are the most studied plant species in terms of anti-inflammatory activity, while *Lawsonia inermis* and *Azadirachta indica* are the most studied ones for wound healing. The most common in vivo techniques used for the anti-inflammatory and the wound healing assays were carrageenan-induced paw oedema, and excision and incision wound models, respectively.

Skin Diseases

Clinical study to assess efficacy and safety of Purifying Neem Face Wash in prevention and reduction of acne in healthy adults

[Rajaiah Yogesh H, Gajjar T, Patel N, Kumawat R.J](#)

Cosmet Dermatol. 2021 Sep 30. PMID: 34590784

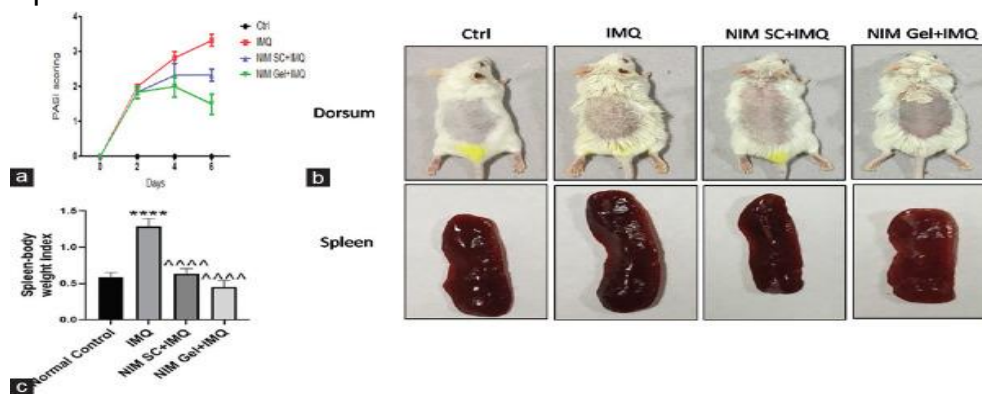
Background: Acne vulgaris is a chronic, inflammatory skin condition of pilosebaceous units. The standard treatment involves topical and oral antibiotics, retinoids, benzoyl peroxide, and other synthetic compounds, mostly associated with adverse effects. Hence, herbal skincare products are considered nowadays. **Aim:** To evaluate the safety and efficacy of Purifying Neem Face Wash (PNFW), an herbal skincare product in the prevention and/or reduction of mild-to-moderate acne. **Methods:** An open-label, single-center, single-arm, four-week clinical study was conducted with subjects having either mild-to-moderate acne or oily skin and non-existent acne. The performance of PNFW in the reduction and/or prevention of acne was detected by counting cutaneous inflammatory and non-inflammatory acne lesions in each of the four visits. Sebum level and skin hydration of both cheeks were measured via sebumeter and corneometer, respectively. Self-assessment questionnaires were used to assess the subjects' responses toward PNFW. **Results:** Out of 120 study subjects, 79% and 72% showed either reduction or no new appearance of inflammatory and non-inflammatory acne lesions, respectively, from baseline to Visits 3 and 4. Skin sebum level and skin hydration showed a statistically significant decrease ($p < 0.001$) and increase ($p < 0.001$), respectively, in Visits 3 and 4. Self-assessment surveys showed the satisfaction of the subjects about the product in terms of condition improvement, ease in use, and fragrance. **Conclusion:** The present study indicated the beneficial effect of the herbal ingredients (neem and turmeric) of Himalaya's PNFW in the prevention and reduction of mild-to-moderate acne with no side effects.

Natural product topical therapy in mitigating imiquimod-induced psoriasis-like skin inflammation-underscoring the anti-psoriatic potential of Nimbolide

More NB, Sharma N, Pulivendala G, Bale S, Godugu C.

Indian J Pharmacol. 2021 Jul-Aug;53(4):278-285.PMID: 34414905

Background: Psoriasis is a chronic inflammatory dermatological disorder having complex pathophysiology with autoimmune and genetic factors being the major players. Despite the availability of a gamut of therapeutic strategies, systemic toxicity, poor efficacy, and treatment tolerance due to genetic variability among patients remain the major challenges. This calls for effective intervention with the superior pharmacological profile. Nimbolide (NIM), a major limonoid is an active chemical constituent found in the leaves of the Indian Neem tree, *Azadirachta indica*. It has gained immense limelight in the past decades for the treatment of various diseases owing to its anti-proliferative, anti-inflammatory, and anti-cancer potentials. **Objective:** The present study was centered around evaluating the anti-psoriatic effect of NIM in the experimental model of Imiquimod (IMQ)-induced psoriasis-like inflammation model. **Materials and methods:** Application of IMQ topically on the dorsum of Balb/c mice from day 0-6 prompted psoriasis-like inflammatory symptoms. Treatment groups included topical administration of NIM incorporated carbopol gel formulation and NIM free drug given through subcutaneous route. Protein expression studies such as immunohistochemistry, Western blotting, and ELISA were employed. **Results:** It was clearly observed from our results that NIM significantly ameliorated the expression of inflammatory and proliferation mediators. Further, NIM in the treatment groups significantly improved classic Psoriasis Area Severity Index scoring when compared to IMQ administered group. **Conclusion:** It is noteworthy that NIM showed a predominant therapeutic effect as compared to other treatment group. To recapitulate, NIM has shown promising activity as an anti-psoriatic agent by remarkably ameliorating inflammation and associated proliferation.



Clinical interventions for tungiasis (sand flea disease): a systematic review

Abrha S, Heukelbach J, Peterson GM, Christenson JK, Carroll S, Kosari S, Bartholomeus A, Feldmeier H, Thomas J.

Lancet Infect Dis. 2021 Aug;21(8):e234-e245. PMID: 34237261

Tungiasis (sand flea disease) is an epidermal parasitic skin disease occurring in resource-limited communities. There is no standard treatment for tungiasis, and available treatment options are scarce. To our knowledge, this is the first systematic review aimed to assess randomised controlled trials (RCTs) investigating interventions for tungiasis. We systematically searched databases including MEDLINE (EBSCOhost), CENTRAL,

CINAHL, PubMed, Web of Science, SciELO, LILACS and Embase (Scopus) for RCTs in any language, from inception of the databases until June 12, 2021. RCTs exploring preventive and therapeutic interventions for tungiasis were eligible. We used the revised Cochrane Collaboration's risk of bias tool to assess the risk of bias and Jadad scale to quantify the methodological quality of the RCTs. Of the 1839 identified records, only eight RCTs involving 808 participants were included, and several methodological deficiencies were identified in most of the trials. Trial interventions included: oral drugs niridazole and ivermectin and topical interventions of ivermectin lotion, metrifonate lotion, thiabendazole lotion, thiabendazole ointment, dimeticones (NYDA), and a neem seed and coconut oil-based mixture for treatment and coconut oil-based lotion (Zanzarin) for prevention. The coconut oil-based lotion for prevention and dimeticones for treatment of tungiasis have displayed the most promise. Most of the RCTs included in this study had low methodological quality. There is a clear unmet need for high-quality RCTs examining safe and effective prevention and treatment alternatives of tungiasis in endemic settings.

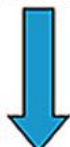
Efficacy of herbal anti-microbial soap in Tinea corporis: A randomized controlled study **R TK, Bhat MDA, Zaman R, Najjar FA.**

J Ethnopharmacol. 2021 Dec 27;114934. PMID: 34968662

Ethnopharmacological relevance: Curcuma longa L., Azadirachta indica A Juss. Cassia tora L. has been used in Unani medicine for various skin ailments. Several researches have been conducted on these plants which have shown anti-microbial, anti-bacterial, anti-fungal, antiviral, anti-oxidant, wound healing, anti-inflammatory, and immune modulation activities. Skin diseases and the use of these drugs are mentioned in classical Unani literature like The Canon of medicine, Continens Liber, Hippocratic treatments, The Complete Book of the Medical Art etc. AIM: The aim of the study was to formulate anti-microbial soap and to evaluate its clinical efficacy of in the management of Tinea corporis. **Materials and methods:** The anti-microbial soap was prepared by hydroalcoholic extracts of Curcuma longa L., Azadirachta indica A Juss. and Cassia tora L. The prepared soap was evaluated for various physicochemical parameters, microbiological evaluation, stability study, skin irritation, In-vitro anti-microbial activity, GCMS analysis, and a clinical trial was carried out to evaluate its efficacy. A Single Blind Randomized Placebo Controlled trail on 30 patients aged between 18 and 60 years of either gender was carried out. The participants were randomly allocated to receive either anti-microbial soap or Placebo soap for 4 weeks. Subjective parameters including erythema, pruritis and desquamation were assessed weekly while as objective parameter including Photograph of lesion, Total Symptom Score (TSS) and KOH mount was assessed at baseline and at the end of the trial. **Results:** The improvement in subjective parameters was found significant in test group. Erythema, scaling, and desquamation was completely relieved by 70%, 80% and 25% patients respectively in test group while as none of the patients got complete relief in control group. There was statistically significant reduction in average TSS 8.65 ± 0.6708 to 3.05 ± 1.35 $p < 0.001$. KOH mount turned negative in 80% patients in test group while as only 20% turned negative in control group. **Conclusion:** It is concluded that Unani drugs can be utilized in better way by modifying into a convenient dosage form. Anti-microbial soap was formulated by adding minimal additives to achieve effectiveness, with cost effective benefits and less or no side effects. Anti-microbial soap was effective in management of management of Tinea corporis. Moreover, further studies on large sample size are required to fine-tune these observations.



Tinea



AMS group (n= 20)

placebo group (n= 10)



Wash affected area twice a day

(4 weeks)



Decrease in infection



Wash affected area twice a day

(4 Weeks)



AMS →

Anti-inflammatory

Anti-septic

Anti fungal activities

Contraceptive Effects

Azadirachta indica A. Juss (neem) as a contraceptive: An evidence-based review on its pharmacological efficiency.

Patil SM, Shirahatti PS, V B CK, Ramu R, M N NP.

Phytomedicine. 2021 Jul 15;88:153596. PMID: 34092456

Background: *Azadirachta indica* A. Juss. is an Indian medicinal plant with innumerable pharmacological properties. Studies have proven that the phytochemicals from neem possess remarkable contraceptive abilities with limited knowledge on its mechanism of action. **Purpose:** The present review aims to summarize the efficiency of *A. indica* treatment as a contraceptive. **Methods:** The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines were used. Published scientific articles on antifertility, antispermatogenic, antiovulation, hormone altering, contraceptive, and abortifacient activities of *A. indica* were collected from reputed Journals from 1980 to 2020 using electronic databases. Specific keywords search was completed to collect numerous articles with unique experiment design and significant results. This was followed by the selection of the requisite articles based on the criteria designed by the authors. Data extraction was based on the common research elements included in the articles. **Results:** A total of 27 studies were considered for reviewing, which included key pharmacological investigations. In the beginning, authors evaluated a number of publications on the contraceptive properties of *A. indica*, in which it was revealed that most of the publications were made between 2005 and 2009. All the collected articles were categorised and reviewed as antifertility, antispermatogenic, antiovulation, hormone altering, contraceptive, and abortifacient. Authors also assessed studies based on the plant parts used for pharmacological evaluations including leaves, seeds, stem-bark, and flowers. The article was primarily divided into different sections based on the previous works of authors on phytochemistry and pharmacological review articles. **Conclusion:** Although *A. indica* is not reported with the complete alleviation of reproductive system in both male and female animal models, studies have proven its efficacy as a contraceptive. Extracts and phytochemicals from neem neither reduced the libido nor retarded the growth of secondary sexual characters, thus indicating only a temporary and reversible contraceptive activity. However, there is a dearth for clinical studies to prove the efficacy of *A. indica* as a herbal contraceptive.



Antidiabetic Effects

Therapeutic role of *Azadirachta indica* leaves ethanolic extract against diabetic nephropathy in rats neonatally induced by streptozotocin

EI-Beltagy AEBM, Saleh AMB, Attaallah A, Gahnem RA.

Ultrastruct Pathol. 2021 Nov 2;45(6):391-406. PMID: 34720017

Diabetic nephropathy (DN) is manifested by chronic loss of renal function due to damage of glomeruli and renal tubules. Therefore, this study is mainly designed to evaluate the therapeutic role of *Azadirachta indica* (neem) leaves extract as a novel approach for treatment of DN in rats neonatally induced by streptozotocin (STZ). For this study, 40 offspring were selected after parturition and categorized into four groups (n = 10). Group 1: control group, group 2: neem leaves extract supplemented group, group 3: diabetic group that injected with a single dose of STZ and group 4: diabetic group treated with neem extract. The results revealed deleterious histological and ultrastructural changes in the renal tissues of diabetic rats. Such changes included atrophied glomeruli, dilated renal cortical tubules and scattered hemorrhage spots, thickening of glomerular basement membrane, expansion of mesangial matrix and pyknotic podocyte. Additionally, the proximal convoluted tubule and distal tubule showed cytoplasmic vacuolation, vacuolated mitochondria, scattered lipid droplets, lost microvilli and disrupted basal lamina and basal infoldings. Moreover, significant decreased levels of serum antioxidants (SOD&CAT) and significant increased levels of serum MDA, urea and creatinine were noticed in diabetic rats. Neem leaves extract successfully alleviated the histological and ultrastructural as well as biochemical changes induced by diabetes.

Aqueous *Azadirachta indica* (Neem) Extract Attenuates Insulin Resistance to Improve Glycemic Control and Endothelial Function in Subjects with Metabolic Syndrome

Pingali U, Vuppalanchi B, Nutalapati C, Gundagani S.

J Med Food. 2021 Nov;24(11):1135-1144. PMID: 34582720

Neem (*Azadirachta indica*) exhibits multiple therapeutic benefits in preclinical studies, but clinical studies are lacking. This clinical study investigated the efficacy and safety of an aqueous *A. indica* leaf and twig extract (NEEM) on metabolic parameters in subjects with metabolic syndrome (MetS). Subjects were randomized to receive (1) placebo or (2) 125 mg, (3) 250 mg, or (4) 500 mg of NEEM twice daily (n = 20/group) for 12 weeks. Fasting blood sugar (FBS) and insulin, postprandial blood sugar (PPBS), insulin resistance (IR), hemoglobin A1c (HbA1c), endothelial function, circulating markers of inflammation and oxidative stress, lipid profiles, and platelet aggregation were measured at weeks 0, 4, 8, and 12. NEEM supplementation dose dependently improved the trajectories for FBS, PPBS, IR, and HbA1c over time, as well as endothelial function and most markers of inflammation and oxidative stress. Therefore, NEEM may be considered a promising therapeutic to attenuate the hyperglycemia and associated cardiometabolic derangements in people with MetS. Clinical trial registration no.: CTRI/2019/03/018034 [registered on: March 12, 2019].

Azadirachta indica A. Juss (neem) against diabetes mellitus: a critical review on its phytochemistry, pharmacology, and toxicology

Patil SM, Shirahatti PS, Ramu R.

J Pharm Pharmacol. 2021 Sep 25. PMID: 34562010

Objective: We aim to provide a critical review focused on the various pharmacological activities of *Azadirachta indica* A. Juss related to diabetes management. We also emphasise on phytochemistry and toxicology of *A. indica*, which could provide a comprehensive approach for plant-based drug development in future. **Key findings:** From 2784 identified studies, only 83 were considered after double screening based on the inclusion criteria. Further, 63 pharmacological investigations were considered for review. Resultant studies deliberated on using different extracts and phytochemicals of *A. indica* on blood glucose level, lipid profile, oxidative stress, carbohydrate digestion enzymes, diabetic complications, glucose tolerance, and uptake of glucose. **Summary:** In the end, one can know the efficacy of *A. indica* as a potent antidiabetic herbal medicine. However, based on gaps in research, recommendations have been provided to evaluate *A. indica* in a systematic manner to develop plant-based drugs, nutraceuticals, and to evaluate their clinical efficiency and safety against diabetes mellitus.

Evaluation on Antidiabetic Properties of Medicinal Plants from Myanmar

Zhang D, Arunachalam K, Wang Y, Zhang Y, Yang J, Hein PP, Mon AM, Li J, Inta A, Yang X.

Scientific World Journal. 2021 Aug 26;2021:1424675. PMID: 34504407

Objectives: To explore the effective and safe medicines for treating diabetes. **Methods:** Hydroalcoholic extracts of 130 medicinal plants belonging to 66 families were evaluated using porcine pancreatic lipase (PPL) inhibition and glucose uptake methods together with a literature review. **Results:** The extracts of 22 species showed the PPL inhibition activity; 18 extracts of 15 species stimulated glucose uptake in 3T3-L1 adipocytes. Among them, *Mansonia gagei* J.R. Drumm., *Mesua ferrea* L., and *Centella asiatica* (L.) Urb. exhibited both activities. The extracts of *Caladium lindenii* (André) Madison rhizomes and *Azadirachta indica* A. Juss. leaves presented the utmost lipase inhibitory activity with IC_{50} of 6.86 ± 0.25 and $11.46 \pm 0.06 \mu\text{g/mL}$, respectively. The extracts of *Coptis teeta* Wall. rhizomes and *Croton tiglium* L. seeds stimulated the maximum glucose uptake. Ten species are reported to have antidiabetic activity for the first time. Flavonoids and triterpenoids are the dominant antidiabetic compounds in selected medicinal plants from Myanmar. **Conclusions:** *P. zeylanica*, *L. cubeba*, *H. crenulate*, *M. gagei*, *C. teeta*, and *M. ferrea* are worthy to advance further study according to their strong antidiabetic activities and limited research on effects in *in vivo* animal studies, unclear chemical constituents, and safety.

Anticancer Effects

Synergistic Dose Permutation of Isolated Alkaloid and Sterol for Anticancer Effect on Young Swiss Albino Mice

Aljarba NH, Ali H, Alkahtani S.

Drug Des Devel Ther. 2021 Sep 23;15:4043-4052. PMID: 34588765

Introduction: Synergy is defined as an interaction of some substances that cooperate to give rise to the combined effect greater than the sum of their individual effects. It is a natural strategy that has evolved by nature to more efficacy with low cost. **Methods:** This study is designed to evaluate the chemopreventive effect of a combined drug sample which is prepared by mixing an equal portion of stigmasterol and palmatine isolated from *Azadirachta indica* and *Tinospora cordifolia* respectively at a concentration of 100 mg/kg and 200 mg/kg body weight during the whole concentration. **Results:** At the end of the study, it was found that this combined drug sample decreased the number of tumors and their size. This drug significantly reduced the serum level of glutamate pyruvate transaminase, alkaline phosphatase, glutamate oxalate transaminase, and bilirubin and enhanced the level of oxidative enzyme level of glutathione, superoxide dismutase, and catalase, and inhibit the level of lipid peroxides. **Discussion:** The result suggests that combined drug samples exhibit a chemopreventive effect which is better than the effect of individual drugs (stigmasterol and palmatine).

Screening of *Azadirachta indica* phytoconstituents as GSK-3 β inhibitor and its implication in neuroblastoma: molecular docking, molecular dynamics, MM-PBSA binding energy, and in-vitro study

Chandel S, Singh R, Gautam A, Ravichandiran V.

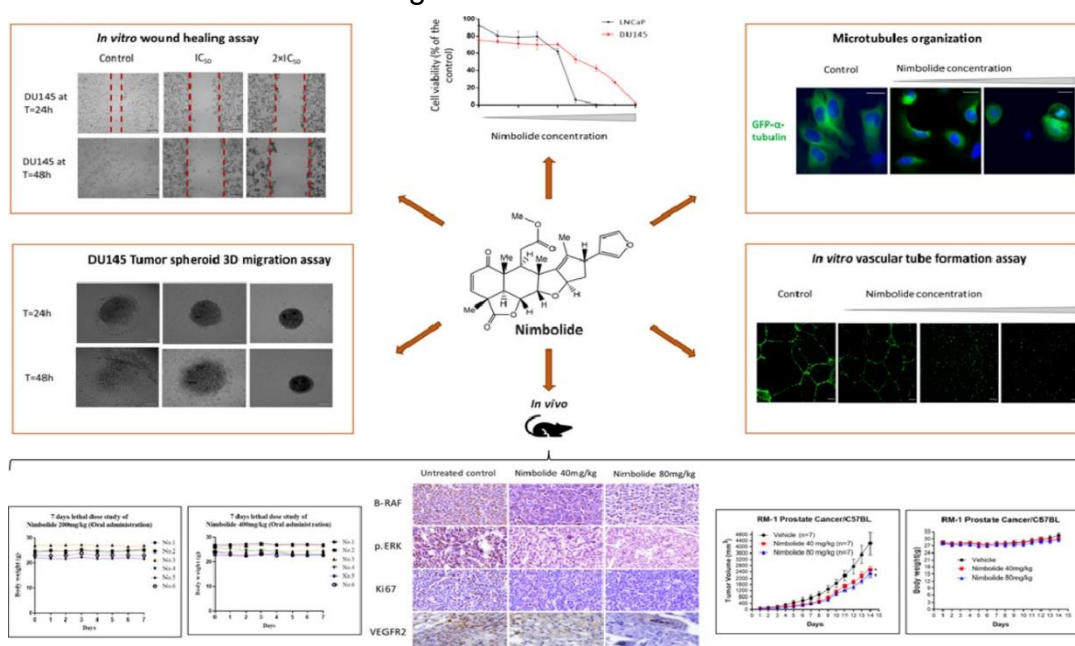
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Glycogen synthase kinase-3 (GSK-3), a constitutively active serine/threonine kinase, primary regulator of various cellular activities varying from glycogen metabolism to cell proliferation and regulation. GSK-3 β is associated with the pathogenesis of numerous human diseases, including cancer, metabolic disorder, and Alzheimer's disease. In this study, *Azadirachta indica* compounds were selected and further screened on the BOILED-Egg model. The compounds showing good GIT absorption were docked with the crystal structure of GSK-3 β . The compounds with high docking score were submitted for the molecular dynamic simulation (MDS) and Molecular Mechanics Poisson-Boltzmann Surface Area (MM-PBSA). Based upon the MDS and MM-PBSA study, gedunin showed the highest binding energy throughout the MDS process. Gedunin was isolated from the *Azadirachta indica*, and its efficacy on GSK-3 β inhibition was studied in the human neuroblastoma (SH-SY5Y) cells. Gedunin induced apoptosis and anti-proliferative activity by arresting G2/M phase, as evident by cell-cycle analysis. From immunoblot study, gedunin significantly enhanced the expression of an inhibitory form of GSK-3 β (p-GSK-3 β Ser9) in concentration-dependent manner. Our findings demonstrate that gedunin may act as an effective GSK-3 β inhibitor suggesting that this compound may be used for the management of neuroblastoma. Further preclinical and clinical investigation is desirable.

Nimbolide inhibits 2D and 3D prostate cancer cells migration, affects microtubules and angiogenesis and suppresses B-RAF/p.ERK-mediated in vivo tumor growth
Mahmoud N, Dawood M, Huang Q, Ng JPL, Ren F, Wong VKW, Efferth T.

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Background: Prostate cancer (PCa) is the most prominent malignancy among men worldwide. PCa cells have a high tendency to metastasize to various distant organs, and this activity is the main cause of PCa mortality. Previous studies showed that nimbolide a promising phytochemical constituent of neem exhibited potent anticancer activity however, its role against PCa tumorigenesis has not been fully elucidated. **Purpose:** Our work aims to explore the role of nimbolide in regulating the essential tumor-associated processes involved in the metastatic cascade in PCa cells. **Methods:** The cytotoxicity of nimbolide towards PCa cell lines was assessed by resazurin assays. The cell mobility and migration of nimbolide-treated DU145 cells were determined by wound healing and spheroid invasion assays. Tubulin network was visualized using U2OS cells and DU145 cells. The effect of nimbolide on E-cadherin, β -catenin, acetylated α -tubulin and HDAC6 protein expressions levels were measured by Western blot and angiogenesis by HUVEC tube-formation assay. Nimbolide antitumor effect was studied in a syngeneic model of murine prostate cancer. **Results:** Nimbolide negatively affected the migratory and invasive capacity of DU145 prostate cancer cells in 2D and 3D spheroid cultures. Interestingly, nimbolide induced downregulation of E-cadherin without any influence on the expression level of β -catenin. Additionally, we demonstrated that nimbolide influenced the microtubule network which was supported by the upregulation of acetylated α -tubulin and the reduction in HDAC6 protein. Moreover, the inhibitory effect of nimbolide on angiogenesis was clearly observed in HUVEC tube formation assay. In vivo experiments revealed the significant suppression of PCa growth and targeting of the B-RAF/p.ERK signaling pathway by nimbolide. **Conclusion:** Our results showed that nimbolide inhibited 2D and 3D prostate cancer cells migration and downregulated E-cadherin protein expression, a marker for metastatic chemoresistance and tumor recurrence. Nimbolide stabilized microtubules, combated angiogenesis and suppressed B.RAF/ERK-mediated in vivo tumor growth. Nimbolide may be considered as potential therapeutic agent for metastatic and advanced PCa patients and merits further investigations.



Neem- Ethnobotanical Analysis

Ethnobotanical study of plants used by the Munda ethnic group living around the Sundarbans, the world's largest mangrove forest in southwestern Bangladesh.

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Ethnopharmacological relevance: Indigenous knowledge of medicinal plants is an integral part of the primary health care (PHC) system in almost every society. For more than two centuries, Munda, a small ethnic group in Bangladesh, has lived around the Sundarbans, the world's largest mangrove forest. This mangrove is rich in biodiversity but is threatened by global climate change. Information on the therapeutic use of plants by Munda ethnic minorities remains completely unknown. Therefore, it needs urgent documentation. **Aim of the study:** The purpose of the study is (1) to search and compile data on the diversity of medicinal plants used by the Munda people for PHC needs, and (2) Quantitative analysis of these data to identify important medicinal plants and diseases related to treatment by this species. **Material and methods:** We conducted repeated field surveys and interviews among 79 Munda informants to collect ethnobotanical data. Informants were selected through random sampling techniques and interviewed using an open and semi-structured questionnaire. We reported the primary (absolute) data as use reports (URs) with frequency citation (FC). The International Classification of Primary Care-2 (ICPC-2) was followed to categorize the therapeutic use of medicinal plants, and quantitative analysis was performed using the FC and informant consensus factor (ICF). **Results:** The present study explored and compiled a total of 3199 medicinal URs for 98 medicinal plant species to treat 132 ailment conditions under sixteen (16) ICPC-2 pathological groups. The highest URs (948) were noted for the digestive (D) group treated by 69 plant species, where the highest ICF value was measured for the social problem (Z) disease category (ICF: 1.00). Of the recorded medicinal plants, 17 were identified as true Mangrove (MNG), 24 as Mangrove Associates (MNA), and 57 as Non-Mangrove (NMG) species. Fabaceae (13 species) represented the leading family, followed by Lamiaceae and Compositae (5 species). Herbs (43%) have shown dominant life forms, and the leaves (41%) were frequently used plant parts. The most commonly cited preparation method was juice (24%), and the prevalent mode of administration was oral (62%). *Azadirachta indica* A. Juss. was the most widely used therapeutic plant species based on FC (39) values. The comparative literature review study reveals that the practices of 15 plants and their ethnomedicinal use by the Munda people are still entirely unexplored and newly reported in Bangladesh. Additionally, therapeutic use of 2 species, *Brownlowia tersa* (L.) Kosterm., and *Dalbergia candenatensis* (Dennst.) Prain has not been previously reported worldwide. In addition, 51 plant species (52%) of the total plants studied enlisted on the IUCN Red List of Threatened Species. **Conclusion:** To our knowledge, this is the first ethnobotanical study on the Munda ethnic group in Bangladesh. This study indicates that Munda people still rely on medicinal plants for PHC and have a rich and varied traditional knowledge about the therapeutic use of plants. This study also warns of the high risk of the current availability status of plants in the study area. Therefore, this study calls for urgent steps to protect and conserve high-risk plants that can be done by taking both in-situ and ex-situ

measures. In addition, further phytochemical and pharmacological investigations of the important medicinal plants cited in the study have been suggested.

Quantitative Ethnobotanical Analysis of Medicinal Plants of High-Temperature Areas of Southern Punjab, Pakistan.

Usman M, Ditta A, Ibrahim FH, Murtaza G, Rajpar MN, Mehmood S, Saleh MNB, Imtiaz M, Akram S, Khan WR.

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Lack of proper infrastructure and the poor economic conditions of rural communities make them dependent on herbal medicines. Thus, there is a need to obtain and conserve the historic and traditional knowledge about the medicinal importance of different plants found in different areas of the world. In this regard, a field study was conducted to document the medicinal importance of local plants commonly used by the inhabitants of very old historic villages in Southern Punjab, Pakistan. In total, 58 plant species were explored, which belonged to 28 taxonomic families, as informed by 200 experienced respondents in the study area. The vernacular name, voucher number, plant parts used, and medicinal values were also documented for each species. Among the documented species, *Poaceae* remained the most predominant family, followed by *Solanaceae* and *Asteraceae*. The local communities were dependent on medicinal plants for daily curing of several ailments, including asthma, common cold, sore throat, fever, cardiovascular diseases, and digestive disorders. Among the reported species, leaves and the whole plant remained the most commonly utilized plant parts, while extracts (38.8%) and pastes (23.9%) were the most popular modes of utilization. Based on the ICF value, the highest value was accounted for wound healing (0.87), followed by skincare, nails, hair, and teeth disorders (0.85). The highest RFC value was represented by *Acacia nilotica* and *Triticum aestivum* (0.95 each), followed by *Azadirachta indica* (0.91). The highest UV was represented by *Conyza canadensis* and *Cuscuta reflexa* (0.58 each), followed by *Xanthium strumarium* (0.37). As far as FL was concerned, the highest value was recorded in the case of *Azadirachta indica* (93.4%) for blood purification and *Acacia nilotica* (91.1%) for sexual disorders. In conclusion, the local inhabitants primarily focus on medicinal plants for the treatment of different diseases in the very old historic villages of Southern Punjab, Pakistan. Moreover, there were various plants in the study area that have great ethnobotanical potential to treat various diseases, as revealed through different indices.

Neem: Applications in Industry

Eco-friendly approach towards isolation of colorant from Esfand for bio-mordanted silk dyeing.

Adeel S, Habib N, Batool F, Rahman A, Ahmad T, Amin N.

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Sustainability in all applied fields particularly in textiles is to protect our globe, environment, and community, where green dyed products are playing their role. For the current study, Esfand (*Peganum harmala*) has been explored using a green isolation tool, i.e., ultrasonic (U.S.) rays, and applied onto fabric. Different dyeing parameters have been explored statistically through response surface methodology by employing temperature (50-80°C), time (25-65 min), extract volume (15-55 mL), salt (1-5 g/100 mL), and dye bath pH (4-7) through series of experiments. For developing new shades, green mordants such as elaichi, neem, turmeric, and zeera have been utilized. It has been found that exposure of 35 mL extract of 7 pH containing 3 g/100 mL of salt as exhausting agent to U.S. rays for 30 min for the dyeing of silk at 70°C for 45 min has given maximum color strength with reddish-yellow shades. Color characteristics obtained in the CIE Lab system reveal that 5% of turmeric as meta bio-mordant has given good quality reddish-yellow shades. It is found that U.S. rays have not only good potential to isolate colorant followed by dyeing of silk under reduced condition but also the application of bio-mordants have made the process more greener, sustainable, and cleaner.



Characterization and application of dried neem leaf powder as a bio-additive for salt less animal skin preservation for tanneries.

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Sodium chloride (NaCl) is commonly used as a curing/preservative agent for raw hides and skins in tanneries and is removed through a soaking process with total dissolved solids (TDS) and other organic pollutants in effluent, causing significant pollution load to the environment. Hence, the present study evaluated to apply dried neem leaf powder (DNL) as an additive to reduce the usage of salt in skin processing and preservation. To make certain of DNL antimicrobial properties, solvent extracts were performed against proteolytic bacteria isolated from raw skins. Initial characterization of DNL revealed the presence of bioactive compounds nimbolide and dehydro salannol and acetone extract with 16.9-mm, 10-mm and 8-mm zone of inhibition against *Salmonella* sp., *E. coli* sp. and *Bacillus* sp. identified using phenotypic conventional biochemical screening method. Further, skin curing experiments were carried out using four different treatments of DNL

(10% 15%, 20% and 25% w/w) along with 15% w/w of conventional salt to obtain an optimum concentration for pilot-scale studies. Thus, the application of optimal DNL (15%) and salt (15%) resulted in no physical changes such as smell and hair slip and was taken for further studies for hydroxyproline activity, pollution load and organoleptic properties along compared with control 40% salt. DNL-aided salt less preservation of freshly flayed goat skins at ambient condition showed no hair slip or putrefaction during the preservation period with significant reduction of TDS (86%) and chloride (71%) in soak liquors compared to conventional salt preservation and enhanced organic load requiring additional treatment. However, the application of the organoleptic, physical and hydrothermal properties of resulting leathers produced from the DNL applied skins was on par with results of leather obtained from conventional salt. Thus, our results demonstrate DNL-aided salt less preservation method is able to reduce the amount of salt for preservation of goat skins significantly, leading to reduced salinity issues during leather processing.

