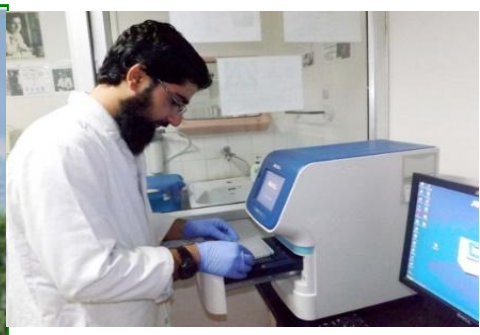
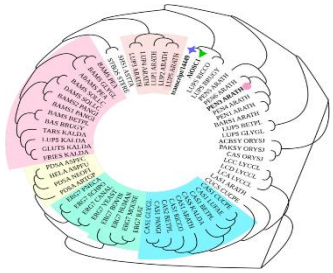
Neem Research Newsletter

Volume 4, Issue 4, 2024





From

The Editor's Desk……

This issue of the newsletter contains abstracts of interesting findings from research conducted on neem in diverse areas. Neem extract was found to be highly effective as an eco-friendly, sustainable approach for the management of pests that affect tomato production. Bromine conjugated nimbolide was demonstrated to exhibit potent antibacterial efficacy in Rohu fish. A one-step ultrasonication technique for generating biomass carbon dots from neem bark powder was developed that could recover valuable cationic organic dye compounds from contaminated environments. Evaluation of dust pollution on specific plant species near and around the marble mining site in Rajasthan, India indicated that neem exhibited highest air pollution tolerance index and effective dust capturing capacity at all sites and could therefore serve as potential pollution sink. Neem nanoformulation was shown to be a potential tool for malaria control through reduction in the vector longevity and reproductive capacity, possibly leading to decreased vector population densities. Neem was found to be a popular choice for the treatment of parasitic worm infections in an ethnobotanical survey conducted in Bangladesh. Neem exerted antimicrobial effects against dental infections and in restorative dentistry. The molecular mechanisms underlying the therapeutic effects of nimbolide in chronic diseases are comprehensively reviewed. The mechanistic basis for the immunomodulatory effects of neem leaf glycoprotein was unraveled. Neem extract was found to enhance the immune status of broiler chickens.

S. Nagini

Core Founding Member, WNO
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Interactions between Bacillus thuringiensis and selected plant extracts for sustainable management of Phthorimaea absoluta.

Ochieng TA, Akutse KS, Ajene IJ, Kilalo DC, Muiru M, Khamis FM.

Sci Rep. 2024 Apr 23;14(1):9299. doi: 10.1038/s41598-024-60140-4.PMID: 38653843

Phthorimaea absoluta is a global constraint to tomato production and can cause up to 100% yield loss. Farmers heavily rely on synthetic pesticides to manage this pest. However, these pesticides are detrimental to human, animal, and environmental health. Therefore, exploring eco-friendly, sustainable Integrated Pest Management approaches, including biopesticides as potential alternatives, is of paramount importance. In this context, the present study (i) evaluated the efficacy of 10 Bacillus thuringiensis isolates, neem, garlic, and fenugreek; (ii) assessed the interactions between the most potent plant extracts and B. thuringiensis isolates, and (iii) evaluated the gut microbial diversity due to the treatments for the development of novel formulations against P. absoluta. Neem recorded the highest mortality of 93.79 ± 3.12% with an LT_{50} value of 1.21 ± 0.24 days, Bt HD263 induced 91.3 ± 3.68% mortality with LT_{50} of 2.63 ± 0.11 days, compared to both Bt 43 and fenugreek that caused < 50% mortality. Larval mortality was further enhanced to 99 ± 1.04% when Bt HD263 and neem were combined. Furthermore, the microbiome analyses showed that Klebsiella, Escherichia and Enterobacter had the highest abundance in all treatments with Klebsiella being the most abundant. In addition, a shift in the abundance of the bacterial genera due to the treatments was observed. Our findings showed that neem, garlic, and Bt HD263 could effectively control P. absoluta and be integrated into IPM programs after validation by field efficacy trials.

Host Plant Modulated Physio-Biochemical Process Enhances Adaptive Response of Sandalwood (*Santalum album* L.) under Salinity Stress.

Verma K, Kumar A, Kumar R, Kumar N, Kumar A, Bhardwaj AK, Verma RC, Sharma P.

Plants (Basel). 2024 Apr 22;13(8):1162. doi: 10.3390/plants13081162.PMID: 38674572

Salinity is one of the most significant abiotic stress that affects the growth and development of high-value tree species, including sandalwood, which can also be managed effectively on saline soils with the help of suitable host species. Therefore, the current investigation was conducted to understand the physiological processes and antioxidant mechanisms in sandalwood along the different salinity gradients to explore the host species that could support sandalwood growth in salt-affected agro-ecosystems. Sandalwood seedlings were grown with ten diverse host species with saline water irrigation gradients (EC_{iw}~3, 6, and 9 dS m^{-1}) and control (EC_{iw}~0.82 dS m^{-1}). Experimental findings indicate a decline in the chlorophyll content (13-33%), relative water content (3-23%), photosynthetic (27-61%) and transpiration rate (23-66%), water and osmotic potential (up to 137%), and ion dynamics (up to 61%) with increasing salinity levels. Conversely, the carotenoid content (23-43%), antioxidant activity (up to 285%), and membrane injury (82-205%) were enhanced with increasing salinity stress. Specifically, among the hosts, *Dalbergia sissoo* and *Melia dubia* showed a minimum reduction in chlorophyll content, relative water content, and plant water relation and gas exchange

parameters of sandalwood plants. Surprisingly, most of the host tree species maintained K^+/Na^+ of sandalwood up to moderate water salinity of EC_{iw}~6 dS m^{-1}; however, a further increase in water salinity decreased the K^+/Na^+ ratio of sandalwood by many-fold. Salinity stress also enhanced the antioxidative enzyme activity, although the maximum increase was noted with host plants *M. dubia*, followed by *D. sissoo* and *Azadirachta indica*. Overall, the investigation concluded that sandalwood with the host *D. sissoo* can be successfully grown in nurseries using saline irrigation water and, with the host *M. dubia,* it can be grown using good quality irrigation water.

Delineating the role of host plants in regulating the water and salinity stress induced changes in sandalwood roots.

Sharma A, Verma K, Kumar A, Rani S, Chauhan K, Battan B, Kumar R.

3 Biotech. 2024 May;14(5):133. doi: 10.1007/s13205-024-03979-8. Epub 2024 Apr 22.PMID: 38660477

The interaction of root hemi-parasite (sandalwood) with its hosts is crucial for establishing successful plantations under abiotic stresses. In the present study, we explored the best possible host for sandalwood along with its effect on sandalwood physiology in terms of water and nutrients. Interactive effects of host species (*Alternanthera sp.*, *Azadirachta indica*, *Dalbergia sissoo*, *Melia dubia*, and *Aquilaria malaccensis*) with sandalwood were observed under eight treatments {100% best available water (BAW); 100% BAW + nutrient medium; 50% water deficit; 50% water deficit + nutrient medium; 100% saline water (EC_{iw} 8ds/m); 100% saline water (EC_{iw} 8ds/m) + nutrient medium; 50% water deficit + saline water (EC_{iw} 8ds/m); and 50% water deficit + saline water (EC_{iw} 8ds/m) + nutrient medium}. A significant change in morpho-physiological traits of sandalwood roots was observed under different stress conditions, which were slightly improved through external supply of nutrient medium. *Dalbergia sissoo* (Shisham) and *Melia dubia* (Dek) seemed to be the best host plants providing better environment for sandalwood growth and development, i.e., higher plant height (59.7 and 53.68 cm) and collar diameter (3.24 and 3.07 mm) under stresses by maintaining water and ionic balance. Root length is an important parameter that was reduced by 27.58%, 19.22%, and 36.3% under water deficit, salinity, and combined stress of water deficit and salinity. Sandalwood grown with *D. sissoo* and *M. dubia* maintained the lowest Ψw (- 1.38 MPa) and Ψs (- 1.47 and - 1.48 MPa), respectively. In addition, sandalwood cultivated with *D. sissoo* and *A. indica* had higher accumulation of soluble proteins (0.48 and 0.42 mg/g) and soluble sugars (98.56 and 91.04 mg/g) in their roots. Results also showed that sandalwood roots had higher K^+/Na^+ with compatible host, i.e., with *A. indica* (1.85) and *D. sissoo* (1.83) than other studied hosts. It was also observed that sandalwood plants could not grow and survive alone under stress conditions even with application of nutrient medium. Based on the morphological traits, it was observed that sandalwood grown with hosts, *Dalbergia sissoo* and *Melia dubia,* was able to tolerate stress conditions better than other studied hosts. We can further recommend growing sandalwood with *D. sissoo* and *M. dubia* as a viable option to endure adverse environmental conditions.

Compatibility of Entomopathogenic Nematodes with Chemical Insecticides for the Control of *Drosophila suzukii* (Diptera: Drosophilidae).

Dias SDC, de Brida AL, Jean-Baptiste MC, Leite LG, Ovruski SM, Lee JC, Garcia FRM.

Plants (Basel). 2024 Feb 25;13(5):632. doi: 10.3390/plants13050632.PMID: 38475479

The spotted-wing drosophila, *Drosophila suzukii* (Matsumura) (Diptera: Drosophilidae), is a pest that reduces the productivity of small fruits. Entomopathogenic nematodes (EPNs) and chemical insecticides can suppress this pest, but the compatibility of the two approaches together requires further examination. This laboratory study evaluated the compatibility of *Steinernema brazilense* IBCBn 06, *S. carpocapsae* IBCBn 02, *Heterorhabditis amazonensis* IBCBn 24, and *H. bacteriophora* HB with ten chemical insecticides registered for managing *D. suzukii* pupae. In the first study, most insecticides at the recommended rate did not reduce the viability (% of living infective juveniles (IJs)) of *S. braziliense* and both *Heterorhabditis* species. The viability of *S. carpocapsae* was lowered by exposure to spinetoram, malathion, abamectin, azadirachtin, deltamethrin, lambda-cyhalothrin, malathion, and spinetoram after 48 h. During infectivity bioassays, phosmet was compatible with all the EPNs, causing minimal changes in infectivity (% pupal mortality) and efficiency relative to EPN-only controls, whereas lambda-cyhalothrin generally reduced infectivity of EPNs on *D. suzukii* pupae the most, with a 53, 75, 57, and 13% reduction in infectivity efficiency among *H. bacteriophora, H. amazonensis, S. carpocapsae*, and *S. brazilense*, respectively. The second study compared pupal mortality caused by the two most compatible nematode species and five insecticides in various combinations. Both *Heterorhabditis* species caused 78-79% mortality among *D. suzukii* pupae when used alone, and were tested in combination with spinetoram, malathion, azadirachtin, phosmet, or novaluron at a one-quarter rate. Notably, *H. bacteriophora* caused 79% mortality on *D. suzukii* pupae when used alone, and 89% mortality when combined with spinetoram, showing an additive effect. Novaluron drastically reduced the number of progeny IJs when combined with *H. amazonensis* by 270 IJs and *H. bacteriophora* by 218. Any adult flies that emerged from EPN-insecticide-treated pupae had a shorter lifespan than from untreated pupae. The combined use of *Heterorhabditis* and compatible chemical insecticides was promising, except for novaluron.

Efficacy of conventional and organic pesticides following ingestion by Delia radicum (Diptera: Anthomyiidae).

Dugger CD, Lightle D, Matteson M, Rasmussen A, Buckland K.

J Econ Entomol. 2024 Apr 12;117(2):524-528. doi: 10.1093/jee/toae030.PMID: 38402493

Cabbage maggot (CM) (Delia radicum L.) is a devastating pest of Brassicaceae crops throughout the world, including the Willamette Valley in western Oregon, USA. Chemical control methods for this pest are limited, with reduction or elimination of chlorpyrifos tolerances and expensive alternative chemistries; therefore, there is an increasing need for novel chemical control options. Adult feeding, a strategy used with insecticide-treated baits for other fly species, has yet to be tested as an option for a chemical control delivery for cabbage maggot. Treated bait can exploit the feeding behavior of CM and expose them to insecticides in a field setting. In this study, the efficacy of 5 organic and 5 conventional

insecticides was compared in laboratory bioassays of treated bait stations in Aurora, Oregon, USA. The mortality of adult female cabbage maggot flies was assessed over time following ingestion of insecticides. Among organic insecticides tested, spinosad was highly effective 4 h after exposure, while pyrethrins + azadirachtin was moderately effective following 18 h after exposure. Flies exposed to conventional-use pesticides zeta-cypermethrin and bifenthrin had high mortality 1.75 h after exposure, while spinetoram had moderate efficacy 2 h after exposure. Insecticides identified with high or moderate efficacy may have the potential for use in baits or lure formulations that could be used to augment the control of cabbage maggots in field settings.

Br-nanoconjugate enhances the antibacterial efficacy of nimbolide against Flavobacterium columnare infection in Labeo rohita: A nanoinformatics approach.

Mishra S, Garg P, Srivastava S, Srivastava P.

Microb Pathog. 2024 Apr;189:106575. doi: 10.1016/j.micpath.2024.106575. Epub 2024 Feb 27.PMID: 38423405

Background: The bacterial pathogen, Flavobacterium columnare causes columnaris disease in Labeo rohita globally. Major effects of this bacterial infection include skin rashes and gill necrosis. Nimbolide, the key ingredient of the leaf extract of Azadirachta indica possesses anti-bacterial properties effective against many microorganisms. Nano-informatics plays a promising role in drug development and its delivery against infections caused by multi-drug-resistant bacteria. Currently, studies in the disciplines of dentistry, food safety, bacteriology, mycology, virology, and parasitology are being conducted to learn more about the wide anti-virulence activity of nimbolide. **Methods:** The toxicity of nimbolide was predicted to determine its dosage for treating bacterial infection in Labeo rohita. Further, comparative 3-D structure prediction and docking studies are done for nimbolide conjugated nanoparticles with several key target receptors to determine better natural ligands against columnaris disease. The nanoparticle conjugates are being designed using in-silico approaches to study molecular docking interactions with the target receptor. **Results:** Bromine conjugated nimbolide shows the best molecular interaction with the target receptors of selected species ie L rohita. Nimbolide comes under the class III level of toxic compound so, attempts are made to reduce the dosage of the compound without compromising its efficiency. Further, bromine is also used as a common surfactant and can eliminate heavy metals from wastewater. **Conclusion:** The dosage of bromine-conjugated nimbolide can be reduced to a non-toxic level and thus the efficiency of the Nimbolide can be increased. Moreover, it can be used to synthesize nanoparticle composites which have potent antibacterial activity towards both gram-positive and gram-negative bacteria. This material also forms a good coating on the surface and kills both airborne and waterborne bacteria.

Neem biomass derived carbon quantum dots synthesized via one step ultrasonification method for ecofriendly methylene blue dye removal.

Waseem Basha Z, Muniraj S, Senthil Kumar A.

Sci Rep. 2024 Apr 27;14(1):9706. doi: 10.1038/s41598-024-59483-9.PMID: 38678104

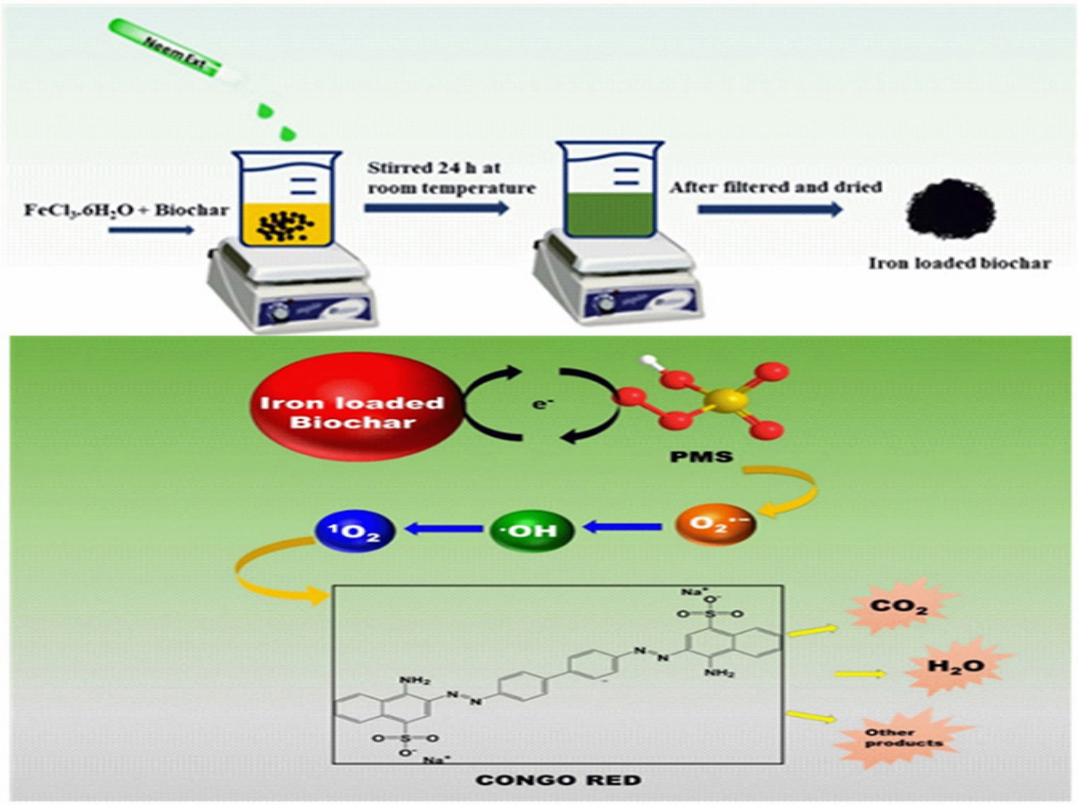
This article presents a one-step ultrasonication technique for generating biomass carbon dots (BCDs) from neem bark (Azadirachta indica) powder. The BCDs were characterized using modern techniques such as UV-Vis, FTIR, Raman, XRD, HRTEM, FESEM, EDAX, and Zeta potential analyses. Unlike traditional nanocomposite bed systems, this study utilized BCDs as a liquid-phase adsorbent for the regenerative adsorption of the environmentally harmful dye, methylene blue (MB), through an in-situ precipitation reaction. This involved the formation of BCDs-MB adduct via an electrostatic mechanism. The adsorption capacity and percentage of removal were remarkable at 605 mg g^{-1} and 64.7% respectively, exceeding various solid-based adsorption methods in the literature. The Langmuir isotherm and pseudo-second-order kinetics model provided an excellent fit for this system. The calculated thermodynamic parameter, Gibbs free energy change (ΔG) was negative, indicating a spontaneous, exothermic, and physisorption-based mechanism. The regenerative capacity of our system was further demonstrated by successfully extracting and recovering the MB dye (64%) using ethyl alcohol as the solvent. This method provides an efficient means of recovering valuable cationic organic dye compounds from contaminated environments.

Role of biochar in superoxide-dominated dye degradation in catalyst-activated peroxymonosulphate process.

Nandana E, Dwivedi AH, Nidheesh PV.

Chemosphere. 2024 Apr 8;356:141945. doi: 10.1016/j.chemosphere.2024.141945. PMID: 38599333

In recent times, the application of biochar (BC) as an upcoming catalyst for the elimination of recalcitrant pollutants has been widely explored. Here, an iron loaded bamboo biochar activated peroxymonosulphate (PMS) process was tested for removing Congo red (CR) dye from water medium. The catalyst was synthesized using a green synthesis method using neem extracts and characterized using SEM, FTIR, and XRD. The effects of various operating parameters, including solution pH, catalyst dosage, and pollutant dosage, on dye degradation efficiency were examined. The results showed that at the optimized conditions of 300 mg L^{-1} PMS concentration, 200 mg L^{-1} catalyst dosage, and pH 6, about 89.7% of CR dye (initial concentration 10 ppm) was removed at 60 min of operation. Scavenging experiments revealed the significant contribution of $O_2^{\bullet-}$, $^{\bullet}OH$, and $^1O_2$ for dye degradation, with a major contribution of $O_2^{\bullet-}$. The activation of PMS was mainly done by biochar rather than iron (loaded on biochar). The catalyst was highly active even after four cycles.



Evaluation of the effects of dust pollution on specific plant species near and around the marble mining site in Rajasthan, India.

Tarannum N, Rathore N, Natwadiya A, Kumar S, Chaudhary N.

Environ Sci Pollut Res Int. 2024 Apr 29. doi: 10.1007/s11356-024-33449-w. PMID: 38683429

Airborne particles (dust pollution) pose a significant threat to both human and plant populations. Plant leaves act as crucial biofilters, capturing significant amounts of air pollution; this characteristic offers a valuable tool to measure local pollution levels and assess individual plant species' ability to intercept and mitigate harmful dust particles. The present study was carried out to assess the effect of responses of various plant species to dust pollution near and around the marble mining site comprising residential site, highway area, and Central University of Rajasthan as control. The anticipated pollution index, air pollution tolerance index (APTI), dust absorption capacity, metal accumulation index (MAI), and biochemical factors were used to evaluate plant responses. Azadirachta indica A. Juss. demonstrated the highest (29.0) and Vachellia nilotica L. showed lowest (5.6) APTI, respectively. A. indica showed maximum MAI values in comparison to other plant species situated at residential site. Additionally, monitoring of particulate matter (PM_{10}) observed to highest at highway, followed by mining, residential, and control sites. Overall A. indica representing highest APTI and effective dust capturing capacity at all sites could serve as potential pollution sinks. V. nilotica, with its very low APTI, can be marked as biomonitoring tool for detecting dust pollution.

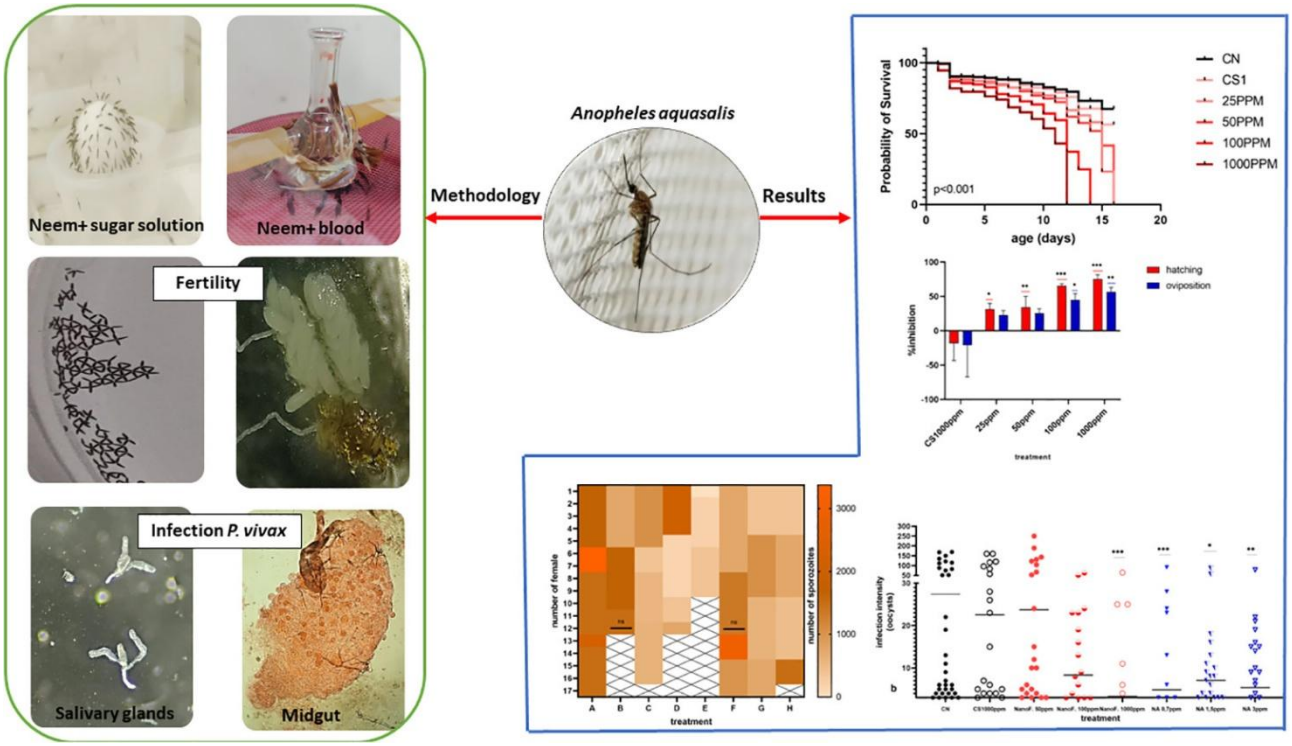
Neem for Human Health

Effect of nanoformulation Azadirachta indica on some factors associated with the vectorial capacity and competence of Anopheles aquasalis experimentally infected with Plasmodium vivax.

Aguirre PAU, Martins KM, López CDD, Sánchez FO, Castaño AT, Velásquez CMR, Vidal AP.

Acta Trop. 2024 Apr 18:107223. doi: 10.1016/j.actatropica.2024.107223. Online ahead of print.PMID: 38642694

Malaria remains a highly prevalent infectious disease worldwide, particularly in tropical and subtropical regions. Effectively controlling of mosquitoes transmitting of Plasmodium spp. is crucial in to control this disease. A promising strategy involves utilizing plant-derived products, such as the Neem tree (Azadirachta indica), known for its secondary metabolites with biological activity against various insect groups of agricultural and public health importance. This study investigated the effects of a nanoformulation prototype Neem on factors linked to the vector competence of Anopheles aquasalis, a malaria vector in Latin America. Different concentrations of the nanoformulation were supplied through sugar solution and blood feeding, assessing impacts on longevity, fecundity, fertility, and transgenerational survival from larvae to adults. Additionally, the effects of the Neem nanoformulation and NeemAZAL® formulation on the sporogonic cycle of P. vivax were evaluated. Overall, significant impacts were observed at 100 ppm and 1,000 ppm concentrations on adult survival patterns and on survival of the F1 generation. A trend of reduced oviposition and hatching rates was also noted in nanoformulation-consuming groups, with fertility and fecundity declining proportionally to the concentration. Additionally, a significant decrease in the infection rate and intensity of P. vivax was observed in the 1,000 ppm group, with a mean of 3 oocysts per female compared to the control's 27 oocysts per female. In the commercial formulation, the highest tested concentration of 3 ppm yielded 5.36 oocysts per female. Concerning sporozoite numbers, there was a reduction of 52% and 87% at the highest concentrations compared to the control group. In conclusion, these findings suggest that the A. indica nanoformulation is a potential as a tool for malaria control through reduction in the vector longevity and reproductive capacity, possibly leading to decreased vector population densities. Moreover, the nanoformulation interfered with the sporogonic development of P. vivax. However, further basic research on Neem formulations, their effects, and mechanisms of action is imperative to gain a more specific perspective for safe field implementation.



Anthelmintic screening of Bangladeshi medicinal plants and related phytochemicals using in vitro and in silico methods: An ethnobotanical perspective.

Khairuzzaman M, Hasan MM, Ali MT, Mamun AA, Akter S, Nasrin P, Islam MK, Nahar AU, Sarker DK, Hamdi OAA, Uddin SJ, Seidel V, Shilpi JA.

J Ethnopharmacol. 2024 Jun 28;328:118132. doi: 10.1016/j.jep.2024.118132. Epub 2024 Mar 31.PMID: 38565411

Ethnopharmacological relevance: Infections caused by parasitic worms or helminth continue to pose a great burden on human and animal health, particularly in underdeveloped tropical and subtropical countries where they are endemic. Current anthelmintic drugs present serious limitations and the emergence of drug resistance has made it increasingly challenging to combat such infections (helminthiases). In Bangladesh, medicinal plants are often used by indigenous communities for the treatment of helminthiases. Knowledge on such plants along with screening for their anthelmintic activity has the potential to lead to the discovery of phytochemicals that could serve as novel molecular scaffolds for the development of new anthelminthic drugs. **Aim of the study:** The purpose of this study was i) to conduct an ethnobotanical survey to gather data on Bangladeshi medicinal plants used in the treatment of helminthiases, ii) to test plants with the highest use values for their in vitro anthelmintic activity, and iii) to carry out in silico screening on phytochemicals present in the most active plant extract to investigate their ability to disrupt β-tubulin function in helminths. **Methods:** The ethnobotanical survey was conducted across three sub-districts of Bangladesh, namely Mathbaria, Phultala and Khan Jahan Ali. The in vitro screening for anthelmintic activity was performed in a motility test using adult Haemonchus contortus worms. Virtual screening using PyRx was performed on the phytochemicals reported from the most active plant, exploring their interactions with the colchicine binding site of the β-tubulin protein target (PDB ID: 1SA0).

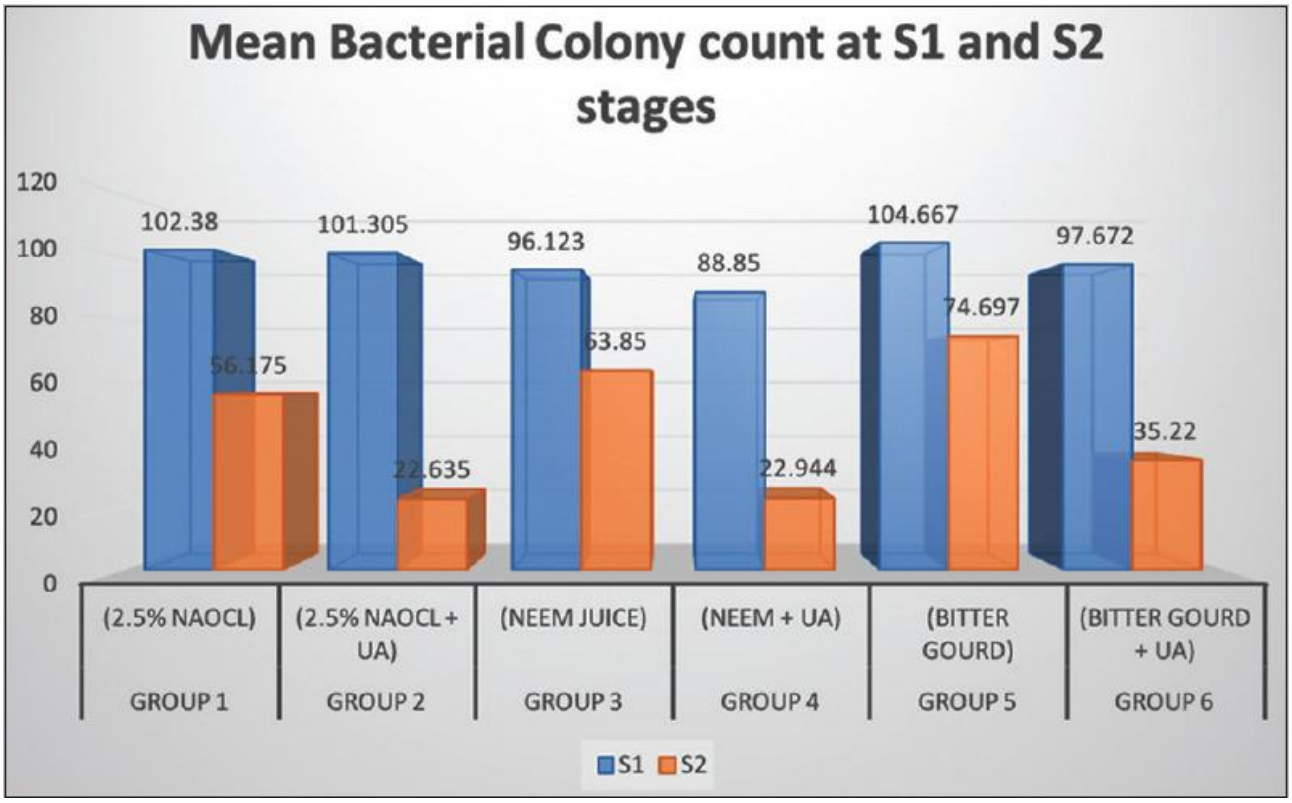
Results: The survey respondents reported a total of 32 plants for treating helminthiases. Based on their use values, the most popular choices were Ananas comosus (L.) Merr., Azadirachta indica A.Juss., Carica papaya L., Citrus maxima (Burm.) Merr., Curcuma longa L., Momordica charantia L., Nigella sativa L. and Syzygium cumini (L.) Skeels. In vitro anthelmintic testing revealed that A. indica leaves and bark had the highest activity with LC_{50} values of 16 mg/mL in both cases. Other plant extracts also exhibited good anthelmintic activity with LC_{50} values ranging from 16 to 52 mg/mL, while the value for albendazole (positive control) was 8.39 mg/mL. The limonoids nimbolide and 28-deoxonimbolide showed a binding affinity of -8.9 kcal/mol, and satisfied all drug-likeness parameters. The control ligand N-deacetyl-N-(2-mercaptoacetyl)colchicine had a binding affinity of -6.9 kcal/mol. **Conclusion:** Further in silico and in vitro studies are warranted on the identified limonoids to confirm the potential of these derivatives as novel drug templates for helminthiases. The current study supports the need for an ethnobotanical survey-based approach to discover novel drug templates for helminthiases.

Antimicrobial efficacy of two commercially available herbal products with and without ultrasonic activation in primary endodontic infections: A randomized clinical trial.

Palwankar D, Garg A, Tandan M, Bhasin P, Sachdeva A, Palwankar P.

J Conserv Dent Endod. 2024 Mar;27(3):305-309. doi: 10.4103/JCDE.JCDE_308_23. Epub 2024 Mar 6.PMID: 38634027

Background: Effective irrigation is crucial for successful endodontic treatment. Traditional irrigants like sodium hypochlorite (NaOCl) have been widely used, but there is a growing interest in exploring natural alternatives for their potential antimicrobial properties. **Objective:** The study aims to compare the antimicrobial efficacy of Neem, Bitter Gourd, and NaOCl, with and without ultrasonic activation in managing primary endodontic infections. **Materials and methods:** Ninety patients were randomly assigned six groups (*n* = 15) Group 1: NaOCl, Group 2: NaOCl with passive ultrasonic irrigation (PUI), Group 3: Neem juice, Group 4: Neem juice with PUI, Group 5: Bitter gourd juice, and Group 6: Bitter gourd juice with PUI. Bacteriological samples were collected before (S1) and after (S2) shaping, plated on brain heart infusion agar, and colony counting was done after 24 h. **Statistical analysis used:** Shapiro-Wilk test, one-way ANOVA, *post hoc* Tukey analysis, and paired *t*-test. **Results:** All the groups demonstrated a significant reduction in bacterial count. Groups with PUI (2, 4, 6) demonstrated higher mean bacterial reduction than their counterparts without PUI (1, 3, 5). **Conclusion:** Neem and Bitter gourd juices, particularly when used with PUI, demonstrated antimicrobial efficacy comparable to NaOCl with PUI.



Comparative Evaluation of Antimicrobial Effectiveness and Compressive Strength in Neem and Lemongrass-Modified Glass Ionomer Cement: An In Vitro Study.

Jaikumar Ram A, Paulraj J, V K, Shanmugam R, Maiti S.

Cureus. 2024 Mar 15;16(3):e56234. doi: 10.7759/cureus.56234.PMID: 38618412

Background Glass ionomer cement (GIC) demonstrates biocompatibility and fluoride ion release, indicating their potential to inhibit a wide range of bacteria, although this remains uncertain. Lemongrass and neem are recognized for their potent antimicrobial activity against numerous pathogenic microorganisms. The objective of the study is to evaluate the antimicrobial effectiveness and compressive strength of GIC modified with neem and lemongrass. Methodology Lemongrass and neem were incorporated into conventional GIC at varying concentrations. Group I - neem-modified GIC (0.5%, 1%, 2%), group II - lemongrass-modified GIC (0.5%, 1%, 2%), and group III (non-modified GIC as a control group). The disk-shaped specimens were then compared to unmodified GIC (control). Antimicrobial effectiveness was assessed using the minimal inhibitory concentration (MIC) assay against *Streptococcus mutans* and *Lactobacillus*. Compressive strength was assessed using a Universal Testing Machine, with a crosshead speed set to 0.5 mm per minute. Statistical analysis was conducted with a significance level set at $p < 0.05$. Results Neem modification displayed superior antimicrobial effectiveness against both *Streptococcus mutans* and *Lactobacillus* at all concentrations when compared to the control, with 2% showing the least mean value of 0.262. In contrast, lemongrass modification exhibited a significant difference in effectiveness against *Streptococcus mutans* but no difference against *Lactobacillus*. Neem modification demonstrated superior performance compared to lemongrass ($p < 0.05$). Both modified groups showed no significant impact on compressive strength. Conclusions Neem-modified GIC

demonstrated the highest antimicrobial efficacy against *Streptococcus mutans* and *Lactobacillus* without altering its compressive strength. This suggests its potential as a promising alternative material in restorative dentistry. Additional in vivo investigations are needed to assess the extended-term effectiveness of the material.

Efficacy of Ozone, UV Radiation, Herbal and Glutaraldehyde Method for Sterilisation of Elastomeric Impression Materials for Orthodontic and Prosthodontic procedures.

Ashil AM, Sharma A, Faiz MK, Garhnayak M, Mathar MI, Anupama T, Mahalakshmi G, Sharma T.

J Pharm Bioallied Sci. 2024 Feb;16(Suppl 1):S717-S719. doi: 10.4103/jpbs.jpbs_962_23. Epub 2024 Feb 29.PMID: 38595356

Objectives: The objectives of the current study was to evaluate the disinfection efficacy of ozone, ultraviolet (UV) radiation, herbal and glutaraldehyde method for sterilization of elastomeric impression materials. **Materials and methods:** Disinfection of elastomeric impression material was performed with each of the disinfection methods: ozone, UV radiation, herbal, and glutaraldehyde. Later microbiological analysis was performed and the colony-forming units were evaluated and compared. **Results:** The highest disinfection efficacy was found with glutaraldehyde, followed by ozone and UV radiation, and the least with neem herbal rinse. Intergroup comparison was highly significant. **Conclusion:** Dry gaseous ozone and UV radiation can be used effectively for the disinfection of impressions.

In vitro antibacterial activity of antibiotics and plant essential oils against Escherichia coli MTCC443 supported through the molecular docking and pharmacokinetics study.

Jain S, Shukla AK, Panwar S, Kumar R, Kumar A.

Biotechnol Appl Biochem. 2024 Apr 16. doi: 10.1002/bab.2583. PMID: 38627930

Most of the Escherichia coli turned into serious pathogens or developed antibiotic resistance, mainly due to their ability to show different phenotypic traits. In order to overcome the resistance to these antibiotics, the use of essential oils (EOs) is of great significance against highly pathogenic microorganisms. This study has been made to compare the in vitro antibacterial activity and further validated the same through the molecular docking study of 13 antibiotics such as ciprofloxacin, chloramphenicol, erythromycin, ampicillin, cefotaxime, rifampicin, kanamycin, vancomycin, streptomycin, penicillin, nalidixic acid, trimethoprim, and polymyxin, and 10 EOs such as garlic, tulsi, neem, clove, thyme, peppermint, coriander, tea, lavender, and eucalyptus against the target protein (DNA gyrase) of E. coli MTCC443. E. coli Microbial Type Culture Collection 443 was found to be highly sensitive to ciprofloxacin (zone of inhibition [ZOI], 2.5 cm ±0.1) and chloramphenicol (ZOI, 1.8 cm ±0.1), whereas garlic oil (ZOI, 5.5 cm ±0.1) and coriander oil (ZOI, 4.4 cm ±0.1) were found comparatively most effective. Further, the in silico investigation observed the same; ciprofloxacin (binding affinity: -7.2 kcal/mol) and chloramphenicol (binding affinity: -6.6 kcal/mol). Penicillin (binding affinity: -4.2 kcal/mol) and polymyxin (binding affinity: -0.3 kcal/mol) were found to be least effective against the tested microbe, whereas vancomycin (binding affinity: +0.8 kcal/mol) had no effect on it. Garlic (binding affinity: -7.8 kcal/mol), coriander (binding affinity: -6.8 kcal/mol), peppermint

(binding affinity: -6.2 kcal/mol), and neem (binding affinity: -6.2 kcal/mol) oil exhibited the potent antibacterial activity against E. coli MTCC443, whereas thyme (binding affinity: -6.1 kcal/mol), tea tree (binding affinity: -4.9 kcal/mol), and tulsi (binding affinity: -3.8 kcal/mol) oil were observed moderately effective. Eucalyptus (binding affinity: -2.9 kcal/mol) and lavender (binding affinity: -2.8 kcal/mol) oil were found to be the least effective among all the oils tested. The pharmacokinetics and networking were performed to the pharmacology of the potential compounds.

Herb Extracellular Vesicle-Chitosan-PEGylated Graphene Oxide Conjugate Delivers Estrogen Receptor α Targeting siRNA to Breast Cancer Cells.

Saroj S, Us P, Patil S, Paul D, Saha S, Ali A, Pal S, Lochab B, Rakshit T.

ACS Appl Bio Mater. 2024 Apr 17. doi: 10.1021/acsabm.3c01108. PMID: 38630629

Herb-based extracellular vesicles (EV), inherently replete with bioactive proteins, RNA, lipids, and other medicinal compounds, are noncytotoxic and uniquely capable of cellular delivery to meet the ever-stringent challenges of ongoing clinical applications. EVs are abundant in nature, affordable, and scalable, but they are also incredibly fragile and stuffed with many biomolecules. To address the low drug binding abilities and poor stability of EVs, we demonstrated herb-based EVs (isolated from neem, mint, and curry leaves) conjugated with chitosan (CS) and PEGylated graphene oxide (GP) that led to their transformation into robust and efficient vectors. The designed conjugates successfully delivered estrogen receptor α (ERα1)-targeting siRNA to breast cancer MCF7 cells. Our data revealed that neem-based EV-CS-GP conjugates were most efficient in cellular siRNA delivery, which could be attributed to hyaluronic acid-mediated recognition of neem EVs by MCF7 cells via CD44 receptors. Our approach shows a futuristic direction in designing clinically viable, sustainable, nontoxic EV-based vehicles that can deliver a variety of functional siRNA cargos.

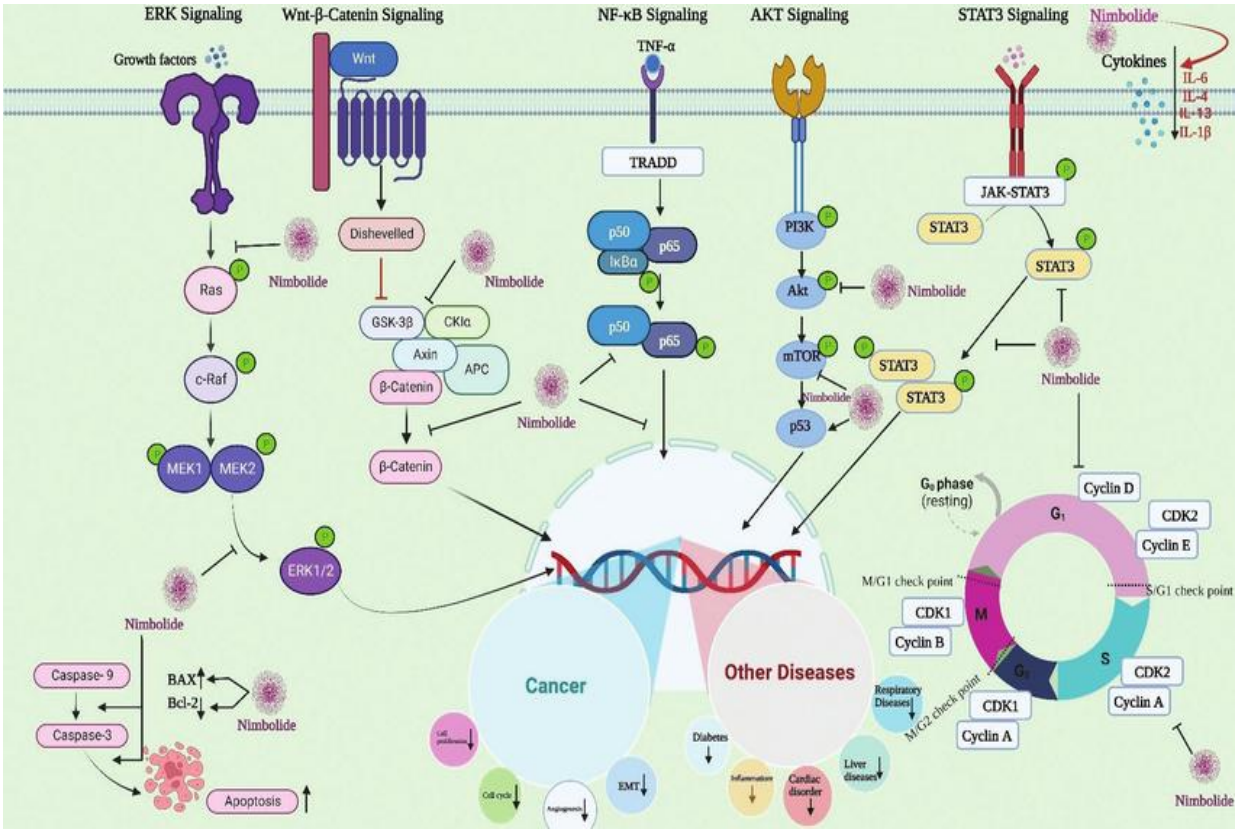
Nimbolide: promising agent for prevention and treatment of chronic diseases (recent update).

Rajendran P, Renu K, Abdallah BM, Ali EM, Veeraraghavan VP, Sivalingam K, Rustagi Y, Abdelsalam SA, Ibrahim RIH, Al-Ramadan SY.

Food Nutr Res. 2024 Mar 18;68. doi: 10.29219/fnr.v68.9650.PMID: 38571915

Background: Nimbolide, a bioactive compound derived from the neem tree, has garnered attention as a potential breakthrough in the prevention and treatment of chronic diseases. Recent updates in research highlight its multifaceted pharmacological properties, demonstrating anti-inflammatory, antioxidant, and anticancer effects. With a rich history in traditional medicine, nimbolide efficacy in addressing the molecular complexities of conditions such as cardiovascular diseases, diabetes, and cancer positions it as a promising candidate for further exploration. As studies progress, the recent update underscores the growing optimism surrounding nimbolide as a valuable tool in the ongoing pursuit of innovative therapeutic strategies for chronic diseases. **Methods:** The comprehensive search of the literature was done until September 2020 on the MEDLINE, Embase, Scopus and Web of Knowledge databases. **Results:** Most studies have shown the Nimbolide is one of the most potent limonoids derived from the flowers and leaves of neem (Azadirachta indica), which is widely used to treat a variety of human diseases. In chronic diseases, nimbolide reported to modulate the key signaling pathways, such as Mitogen-activated protein kinases (MAPKs), Wingless-related integration site-β (Wnt-

β)/catenin, NF-κB, PI3K/AKT, and signaling molecules, such as transforming growth factor (TGF-β), Matrix metalloproteinases (MMPs), Vascular Endothelial Growth Factor (VEGF), inflammatory cytokines, and epithelial-mesenchymal transition (EMT) proteins. Nimbolide has anti-inflammatory, anti-microbial, and anti-cancer properties, which make it an intriguing compound for research. Nimbolide demonstrated therapeutic potential for osteoarthritis, rheumatoid arthritis, cardiovascular, inflammation and cancer. **Conclusion:** The current review mainly focused on understanding the molecular mechanisms underlying the therapeutic effects of nimbolide in chronic diseases.



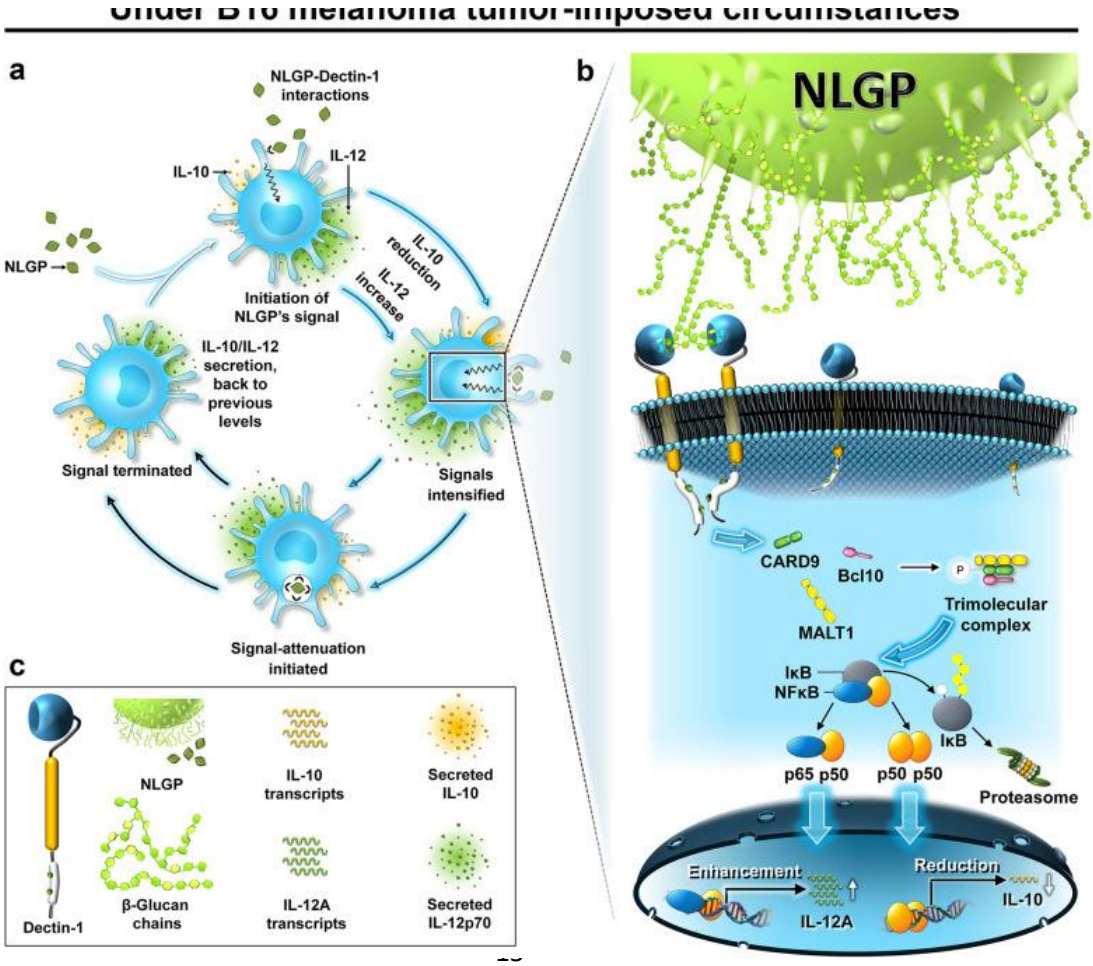
Neem leaf glycoprotein binding to Dectin-1 receptors on dendritic cell induces type-1 immunity through CARD9 mediated intracellular signal to NFkappaB.

Ganguly N, Das T, Bhuniya A, Guha I, Chakravarti M, Dhar S, Sarkar A, Bera S, Dhar J, Dasgupta S, Saha A, Ghosh T, Das J, Sk UH, Banerjee S, Laskar S, Bose A, Baral R.

Cell Commun Signal. 2024 Apr 23;22(1):237. doi: 10.1186/s12964-024-01576-z.PMID: 38649988

Background: A water-soluble ingredient of mature leaves of the tropical mahogany 'Neem' (Azadirachta indica), was identified as glycoprotein, thus being named as 'Neem Leaf Glycoprotein' (NLGP). This non-toxic leaf-component regressed cancerous murine tumors (melanoma, carcinoma, sarcoma) recurrently in different experimental circumstances by boosting prime antitumor immune attributes. Such antitumor immunomodulation, aid cytotoxic T cell (T_c)-based annihilation of tumor cells. This study focused on identifying and characterizing the signaling gateway that initiate this systemic immunomodulation. In search of this gateway, antigen-presenting cells (APCs) were explored, which activate and induce the cytotoxic thrust in T_c cells. **Methods:** Six

glycoprotein-binding C-type lectins found on APCs, namely, MBR, Dectin-1, Dectin-2, DC-SIGN, DEC205 and DNGR-1 were screened on bone marrow-derived dendritic cells from C57BL/6 J mice. Fluorescence microscopy, RT-PCR, flow cytometry and ELISA revealed Dectin-1 as the NLGP-binding receptor, followed by verifications through RNAi. Following detection of β-Glucans in NLGP, their interactions with Dectin-1 were explored in silico. Roles of second messengers and transcription factors in the downstream signal were studied by co-immunoprecipitation, western blotting, and chromatin-immunoprecipitation. Intracellularization of FITC-coupled NLGP was observed by processing confocal micrographs of DCs. **Results:** Considering extents of hindrance in NLGP-driven transcription rates of the cytokines IL-10 and IL-12p35 by receptor-neutralization, Dectin-1 receptors on dendritic cells were found to bind NLGP through the ligand's peripheral β-Glucan chains. The resulting signal phosphorylates PKCδ, forming a trimolecular complex of CARD9, Bcl10 and MALT1, which in turn activates the canonical NFκB-pathway of transcription-regulation. Consequently, the NFκB-heterodimer p65:p50 enhances Il12a transcription and the p50:p50 homodimer represses Il10 transcription, bringing about a cytokine-based systemic-bias towards type-1 immune environment. Further, NLGP gets engulfed within dendritic cells, possibly through endocytic activities of Dectin-1. **Conclusion:** NLGP's binding to Dectin-1 receptors on murine dendritic cells, followed by the intracellular signal, lead to NFκB-mediated contrasting regulation of cytokine-transcriptions, initiating a pro-inflammatory immunopolarization, which amplifies further by the responding immune cells including T_c cells, alongside their enhanced cytotoxicity. These insights into the initiation of mammalian systemic immunomodulation by NLGP at cellular and molecular levels, may help uncovering its mode of action as a novel immunomodulator against human cancers, following clinical trials.



Immunological studies on the effects of toltrazuril and neem extract in broiler chickens suffering from coccidiosis.

Kairy MH, Fadel HAE, Aleim AEAFAE, Gad GN, Youssef FEZA, Ibrahim AM, SaadEldin WF.

Open Vet J. 2024 Jan;14(1):341-349. doi: 10.5455/OVJ.2024.v14.i1.31. Epub 2024 Jan 31.PMID: 38633167

Background: The prevalence of avian coccidiosis in the poultry industry has grown, resulting in substantial financial losses from high mortality, stunted growth, reduced productivity, and expensive medical expenses. **Aim:** The purpose of the current study was to assess the immunological effects of neem leaf extract and toltrazuril on broilers that had contracted coccidiosis. **Methods:** In this investigation, 100 one-day-old Cobb broiler chicks without sexes were employed. The chicks were divided into five equal groups, with 20 birds in each. On the 14th day of life, the birds in groups 2, 3, 4, and 5 received an oral inoculation with 1 × 10^{5} sporulated oocysts of *Eimeria tenella* (*E. tenella*) (field isolate). The first group (Gp), which consists of 20 healthy broilers, served as a negative control. Gp (2) contains experimentally infected broilers and nontreated (served as a positive control). Gp (3) contains experimentally infected broilers treated with toltrazuril (1 ml/l drinking water) for two consecutive days. Gp (4) contains experimentally infected broilers treated with neem leaf extract 4% (50 ml/l drinking water) for 5 successive days, and Gp (5) contains experimentally infected broilers treated with toltrazuril (1 ml/l drinking water) and a half dose of neem leaves extract 4% (25 ml/l drinking water) for 5 successive days. For the purpose of estimating body weight growth and feed conversion ratio, each broiler was weighed separately at the start of the trial and again on the 1st and 10th day after treatment. In addition to obtaining intestinal samples for immunohistochemistry, blood samples were also obtained for immunological examination. **Results:** As compared to the negative control group, the experimentally infested broilers with *E. tenella* showed significant decreases in serum nitric oxide, lysosome, phagocytic percent, and phagocytic index, along with significant increases in white blood cells (WBCs), lymphocyte, heterophilis, eosinophilis, basophilis, monocyte, serum total protein, γ globulin, fibrinogen, and haptoglobin. When compared to the control positive group, experimentally infested broilers treated with either neem or toltrazuril alone or in combination demonstrated significant increases in serum total protein, nitric oxide, lysozyme, phagocytic percent, and phagocytic index, but significant decreases in WBCs, lymphocytes, heterophile, eosinophile, basophile, and monocyte. The intestinal peroxidase stain of broilers infected with *E. tenella* exhibited a significant positive expression for CD4, but the infected broilers treated with toltrazuril and half a dosage of neem displayed a negative expression for CD4, identical to the negative control. **Conclusion:** The broiler chickens infested with *E. tenella* may have a variety of negative impacts on their immune systems and immunohistopathological findings. Nonetheless, toltrazuril and neem extract, either separately or in combination, function as anticoccidial medications that may enhance the broiler chicks' immune state.