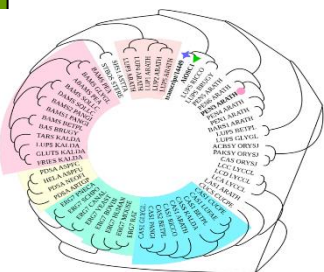
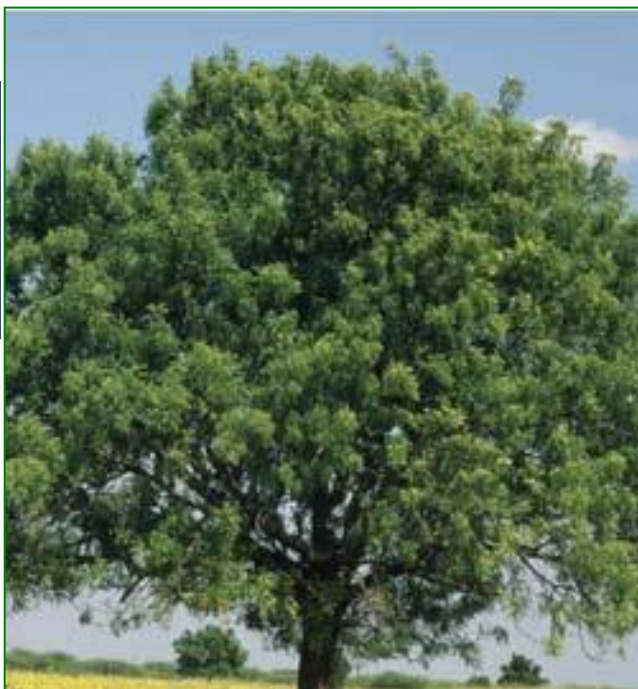




Neem Research Newsletter Volume 3, Issue 9, 2023



WORLD NEEM ORGANISATION (WNO)



From
The Editor's Desk.....

In this issue of the Newsletter, abstracts of several interesting findings from research on neem are presented. Chitosan neem nanocapsules can be used as a new versatile eco-friendly alternative for antibiotics in treating bacterial diseases affecting the aquaculture sector as revealed by enhanced immunity and disease resistance in Nile tilapia. Neem plant extract-assisted synthesis of nanoparticles was found to be useful in photocatalytic degradation of non-steroidal anti-inflammatory drugs that are frequently detected in aquatic environments due to their widespread usage and improper disposal practices. Nimbolide-based nanomedicine was demonstrated to inhibit breast cancer stem-like cells by epigenetic reprogramming. Epoxyzadiradione, another limonoid extracted from neem seed exerted anticancer potential against neuroblastoma. Gedunin was found to protect against monkeypox virus. Neem extract was shown to be effective in smear layer removal during root canal irrigation. Neem-silk fibroin hydrogel formulation was demonstrated as a therapeutically viable choice that might be utilized in novel formulations for managing chronic wounds. Neem leaf extract exerted immuno-stimulatory effect against highly pathogenic avian influenza in experimental chickens.

S. Nagini

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



Neem in Agriculture & Aquaculture

Efficacy of Insecticides against the Invasive Apricot Aphid, *Myzus mumecola*.

Tabet DH, Visentin E, Bonadio M, Bjeljic M, Reyes-Domínguez Y, Gallmetzer A, Spitaler U.

Insects. 2023 Sep 6;14(9):746. doi: 10.3390/insects14090746.PMID: 37754715

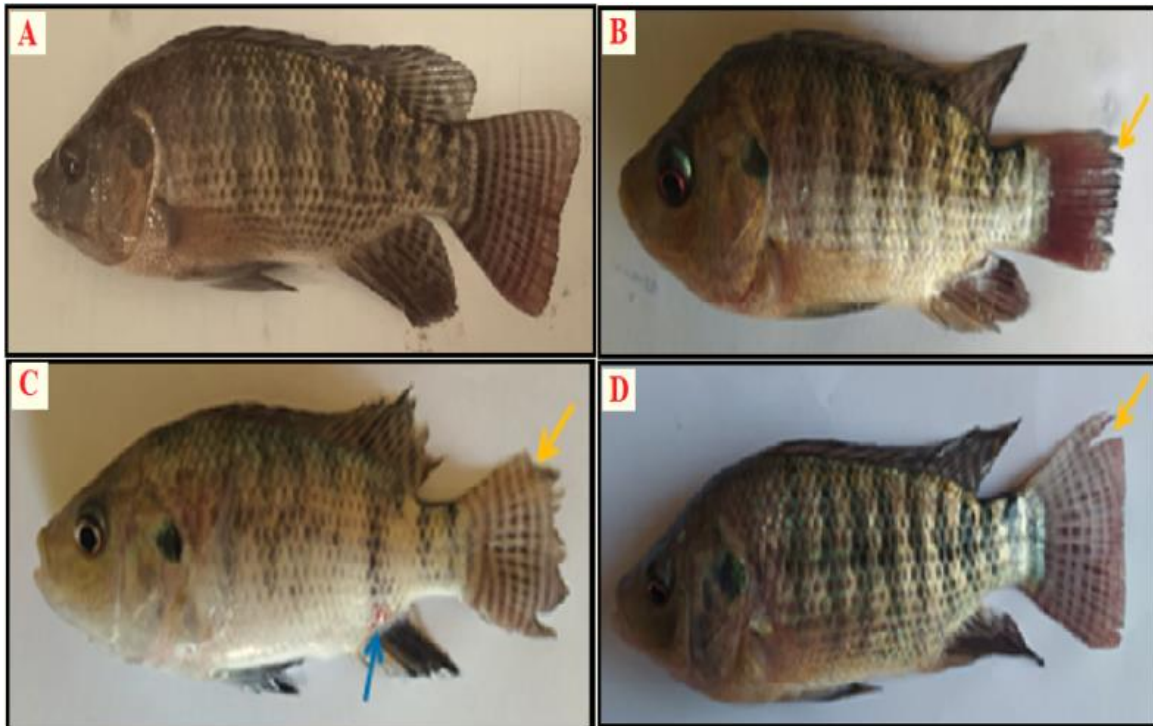
The invasive apricot aphid (*Myzus mumecola* Matsumura) is an important pest of apricot trees (*Prunus armeniaca* L.). In the presented study, laboratory bioassays using treated leaf disks of apricot were conducted to test the efficacy of twelve insecticides according to the maximum field dose. Additionally, dose-response curves were established for selected insecticides, and the effects on colony development were evaluated. Furthermore, a field trial was conducted to investigate the effectiveness of commonly used insecticides in apricot cultivation. The dose-response curves showed LC₅₀ values ranging from 0.08 mg/L for flupyradifurone, 0.15 mg/L for acetamiprid, 0.70 mg/L for etofenprox, 1.89 mg/L for sulfoxaflor, 2.64 mg/L for pirimicarb, 3.97 mg/L for deltamethrin, up to 6.79 mg/L for tau-fluvalinate. These aforementioned insecticides resulted in mortality rates ranging from 95 to 100% at the field dose. Azadirachtin, flonicamid, and pyrethrins showed mortality rates of 27 to 45%. Spirotetramat reduced the colony development and decreased the number of infested shoots by 86%. Spinosad, which is not recommended against aphids, showed minimal impact; reducing the number of exuviae in nymphs in the colony development bioassay. It can be concluded that the majority of the tested insecticides are effective against *M. mumecola*.

Chitosan neem nanocapsule enhances immunity and disease resistance in Nile tilapia (*Oreochromis niloticus*).

Ibrahim RE, Elshopakey GE, Abdelwarith AA, Younis EM, Ismail SH, Ahmed AI, El-Saber MM, Abdelhamid AE, Davies SJ, El-Murr A, Abdel Rahman AN.
Heliyon. 2023 Aug 22;9(9):e19354. doi: 10.1016/j.heliyon.2023.e19354. eCollection 2023 Sep.PMID: 37662722

Finding eco-friendly alternatives for antibiotics in treating bacterial diseases affecting the aquaculture sector is essential. Herbal plants are promising alternatives, especially when combined with nanomaterials. Neem (*Azadirachta indica*) leaves extract was synthesized using a chitosan nanocapsule. Chitosan neem nanocapsule (CNNC) was tested *in-vitro* and *in-vivo* against the *Aeromonas sobria* (*A. sobria*) challenge in Nile tilapia. A preliminary experiment with 120 Nile tilapia was conducted to determine the therapeutic dose of CNNC, which was established to be 1 mg/L. A treatment study was applied for seven days using 200 fish categorized into four groups (10 fish/replicate: 50 fish/group). The first (control) and second (CNNC) groups were treated with 0 and 1 mg/L CNNC in water without being challenged. The third (*A. sobria*) and fourth (CNNC + *A. sobria*) groups were treated with 0 and 1 mg/L CNNC, respectively, and challenged with *A. sobria* (1×10^7 CFU/mL). Interestingly, CNNC had an *in-vitro* antibacterial activity against *A. sobria*; the minimum inhibitory concentration and minimum bactericidal concentration of CNNC against *A. sobria* were 6.25 and 12.5 mg/mL, respectively. *A. sobria* challenge caused behavioral

alterations, skin hemorrhage, fin rot, and reduced survivability (60%). The infected fish suffered a noticeable elevation in the malondialdehyde level and hepato-renal function markers (aspartate aminotransferase, alanine aminotransferase, and creatinine). Moreover, a clear depletion in the level of the antioxidant and immune indicators (catalase, reduced glutathione, lysozymes, nitric oxide, and complement 3) was obvious in the *A. sobria* group. Treatment of the *A. sobria*-challenged fish with 1 mg/L CNNC recovered these parameters and enhanced fish survivability. Overall, CNNC can be used as a new versatile tool at 1 mg/L as a water treatment for combating the *A. sobria* challenge for sustainable aquaculture production.



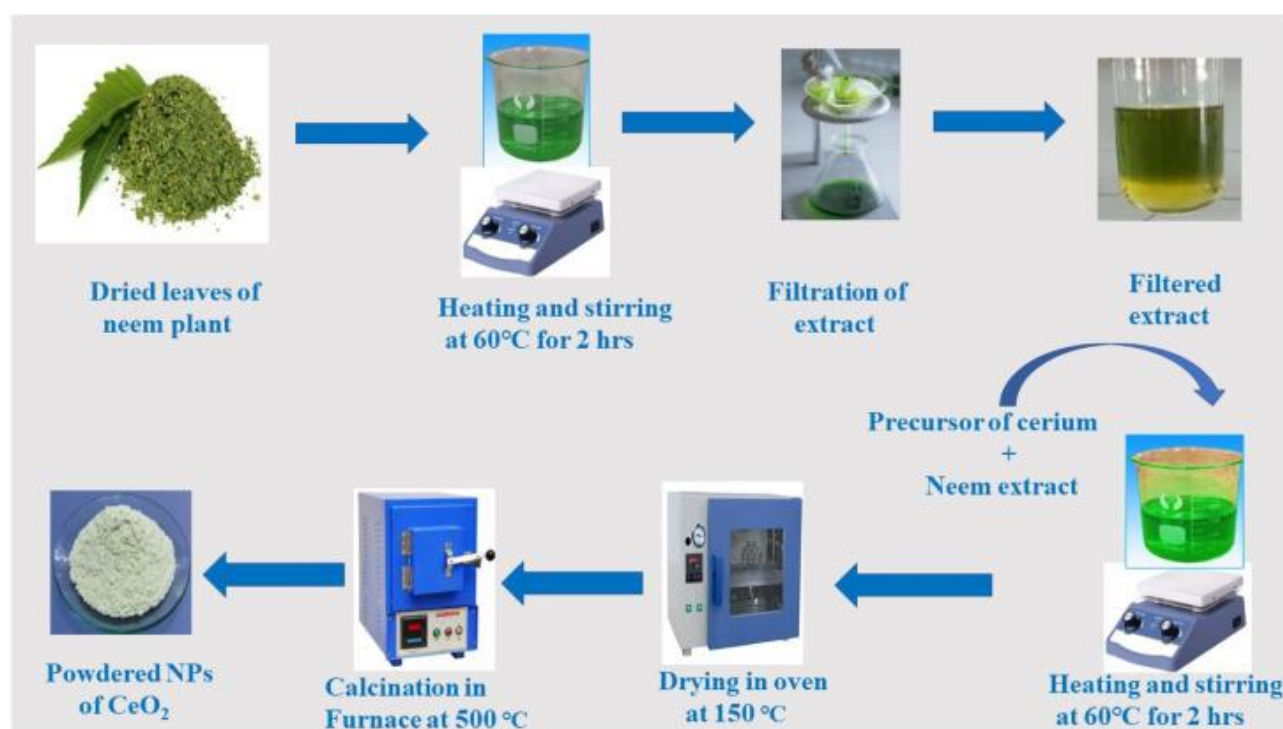
Effect of CNNC as water exposure on clinical observations of experimentally infected *O. niloticus* with *A. sobria* for seven days. (A) Fish of the control group or CNNC group demonstrating normal appearance. (B and C) Fish of the *A. sobria* group demonstrating skin ulcerations (blue arrows), body hemorrhages, and fin rot (yellow arrows). (D) Fish of the CNNC + *A. sobria* group demonstrating slight fin rot (yellow arrow).

Neem plant extract-assisted synthesis of CeO₂ nanoparticles for photocatalytic degradation of piroxicam and naproxen.

Quddus F, Shah A, Nisar J, Zia MA, Munir S.

RSC Adv. 2023 Sep 22;13(40):28121-28130. doi: 10.1039/d3ra04185a. eCollection 2023 Sep 18. PMID: 37746332

Piroxicam and naproxen are well-known non-steroidal anti-inflammatory drugs that are frequently detected in aquatic environments due to their widespread usage and improper disposal practices. This research investigates the photocatalytic degradation of these drugs by using CeO₂ nanoparticles. The nanoparticles were synthesized by using *Azadirachta indica* plant extract and were characterized through various characterization techniques such as UV-visible spectroscopy, FTIR spectroscopy, SEM, EDX, and XRD. The photocatalytic degradation of piroxicam and naproxen using CeO₂ nanoparticles led to the efficient removal of these pharmaceutical drugs in a short time duration with photodegradation efficiencies of 89% and 97% for naproxen and piroxicam, respectively. The photodegradation reaction was found to follow pseudo-order first-order kinetics. The recyclability of the catalyst was also studied for up to six cycles where the degradation efficiency was maintained at 100% till the 2nd cycle and was decreased by 11 and 13% for piroxicam and naproxen respectively after the 6th cycle. The current work focused on the achievement of sustainable development goals (SDGs) for water purification *via* environmentally benign nanoparticles to remedy water pollution as it is the most prevalent issue in developed and underdeveloped countries throughout the world.



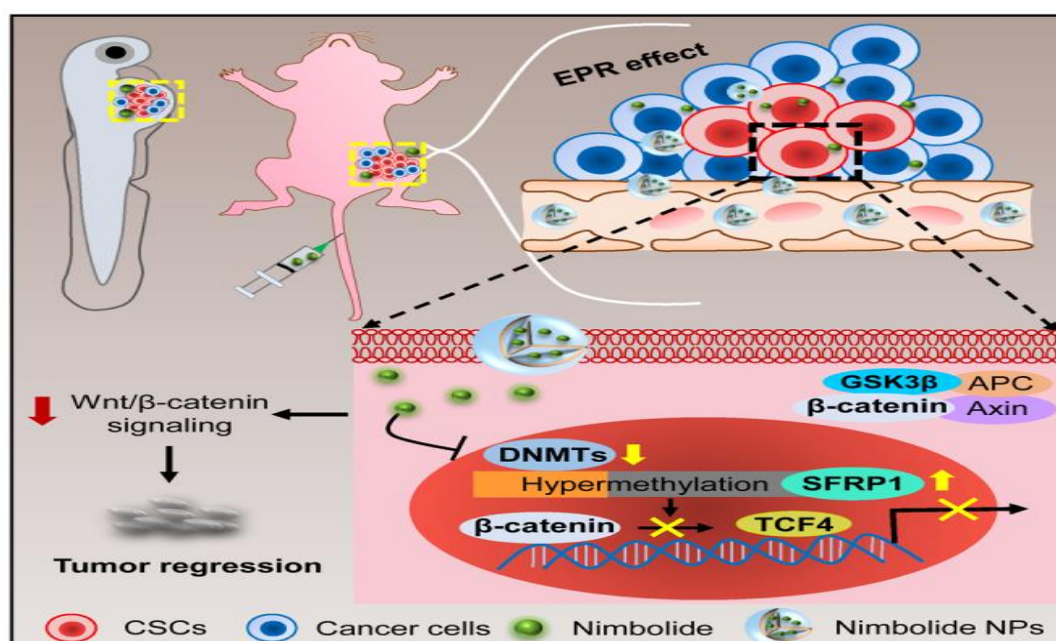
Neem for Human Health

Nimbolide-based nanomedicine inhibits breast cancer stem-like cells by epigenetic reprogramming of DNMTs-SFRP1-Wnt/ β -catenin signaling axis.

Mohapatra P, Madhulika S, Behera S, Singh P, Sa P, Prasad P, Swain RK, Sahoo SK.

Mol Ther Nucleic Acids. 2023 Sep 9;34:102031. doi: 10.1016/j.omtn.2023.102031. eCollection 2023 Dec 12. PMID: 37771911

Triple-negative breast cancer (TNBC) harbors a high percentage of breast cancer stem-like cells (BCSCs) that significantly contribute to poor prognosis, metastasis, and relapse of the disease. Thus, targeting BCSCs could be a promising approach to combat TNBC. In this context, we investigated nimbolide (Nim), a limonoid triterpenoid that has potent anticancer properties, but poor pharmacokinetics and low bioavailability limit its therapeutic application. So, to enhance the therapeutic potential of Nim, Nim-encapsulated poly(lactic-co-glycolic acid) (PLGA) nanoparticles (Nim NPs) were formulated and the anticancer stem cell (CSC) effects evaluated *in vitro* and *in vivo*. *In vitro* studies suggested that Nim NPs significantly inhibited several inherent characteristics of BCSCs, such as stemness, self-renewability, chemoresistance, epithelial-to-mesenchymal transition (EMT), and migration in comparison to native Nim. Next, the mechanism behind the anti-CSC effect of Nim was explored. Mechanistically, we found that Nim epigenetically restores tumor suppressor gene secreted frizzled-related protein 1 (SFRP1) expression by downregulating DNA methyltransferases (DNMTs), leading to Wnt/ β -catenin signaling inhibition. Further, *in vivo* results demonstrated that Nim NPs showed enhanced anti-tumor and anti-metastatic effects compared to native Nim in two preclinical models without any systemic toxicity. Overall, these findings provide proof of concept that Nim-based phytonanomedicine can inhibit BCSCs by epigenetic reprogramming of the DNMTs-SFRP1-Wnt/ β -catenin signaling axis.



Investigation of the anti-cancer potential of epoxyazadiradione in neuroblastoma: experimental assays and molecular analysis.

Chandel S, Bhattacharya A, Gautam A, Zeng W, Alka O, Sachsenberg T, Gupta GD, Narang RK, Ravichandiran V, Singh R.

J Biomol Struct Dyn. 2023 Sep 27:1-19. doi: 10.1080/07391102.2023.2262593. PMID: 37753734

Neuroblastoma, the most common childhood solid tumor, originates from primitive sympathetic nervous system cells. Epoxyazadiradione (EAD) is a limonoid derived from *Azadirachta indica*, belonging to the family Meliaceae. In this study, we isolated the EAD from *Azadirachta indica* seed and studied the anti-cancer potential against neuroblastoma. Herein, EAD demonstrated significant efficacy against neuroblastoma by suppressing cell proliferation, enhancing the rate of apoptosis and cycle arrest at the SubG₀ and G₂/M phases. EAD enhanced the pro-apoptotic Caspase 3 and Caspase 9 and inhibited the NF- κ B translocation in a dose-dependent manner. In order to identify the specific EAD target, a gel-free quantitative proteomics study on SH-SY5Y cells using Liquid Chromatography with tandem mass spectrometry was done in a dose-dependent manner, followed by detailed bioinformatics analysis to identify effects on protein. Proteomics data identified that Enolase1 and HSP90 were up-regulated in neuroblastoma. EAD inhibited the expression of Enolase1 and HSP90, validated by mRNA expression, immunoblotting, Enolase1 and HSP90 kit and flow-cytometry based bioassay. Molecular docking study, Molecular dynamic simulation, and along with molecular mechanics/Poisson-Boltzmann surface area analysis also suggested that EAD binds at the active site of the proteins and were stable throughout the 100 ns Molecular dynamic simulation study. Overall, this study suggested EAD exhibited anti-cancer activity against neuroblastoma by targeting Enolase1 and HSP90 pathways.

Antibacterial study of carbopol-mastic gum/silver nanoparticle-based topical gels with carvacrol/neem bark extract in vitro.

Zintle M, Siwaphiwe P, Marthe Carine F, Thierry Youmbi F, Derek Tantoh N, Suprakas Sinha R, Blessing Atim A.

J Wound Care. 2023 Sep 1;32(Sup9a):clxxxi-clxxxix. doi: 10.12968/jowc.2023.32.Sup9a.clxxxi.PMID: 37703219

Background: Resistance to antimicrobial drugs as a result of prolonged use usually results in clinical failure, especially in wound infections. Development of effective antimicrobial therapeutics for the management of infected wounds from a natural source with improved therapeutic effects is a pressing need. **Objective:** In this study, carbopol-mastic gum-based topical gels were loaded with silver nanoparticles in combination with either neem bark extract or carvacrol oil. The effect of combining silver nanoparticles with neem bark extract or the essential oil carvacrol in the prepared gel formulations was investigated on selected bacterial strains. **Method:** The prepared gels were characterised by Fourier transform infrared (FTIR) spectroscopy, transmission electron microscopy (TEM) and ultraviolet-visible (UV-vis) spectroscopy, followed by antimicrobial analysis against selected strains of bacteria. **Results:** There was no interaction between the loaded natural extract or essential oil and the polymer used for the preparation of the formulations, which was visible from the

FTIR spectra of the formulations. The gels were selective and effective against selected strains of bacteria. However, the combination of the silver nanoparticles with essential oil or natural extract in some of the gel formulations rendered the formulation ineffective against some of the bacterial strains. **Conclusion:** The gel formulations were effective against bacterial strains such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Enterococcus faecalis* which are the common causes of wound infections. Incorporation of silver nanoparticles into the topical formulations with natural extracts is usually a good approach to overcome antibiotic-resistant infections. However, the combination of antibacterial agents must be managed carefully.

Therapeutic Promises of Plant Metabolites against Monkeypox Virus: An In Silico Study.

Banik A, Ahmed SR, Shahid SB, Ahmed T, Tamanna HK, Marma H.

Adv Virol. 2023 Sep 2;2023:9919776. doi: 10.1155/2023/9919776. eCollection 2023. PMID: 37693295

The monkeypox virus was still spreading in May 2022, with the first case identified in a person with travel ties to Nigeria. Using molecular docking-based techniques, we evaluated the efficiency of different bioactive chemicals obtained from plants against the monkeypox virus. A total of 56 plant compounds were evaluated for antimonekypox capabilities, with the top four candidates having a higher binding affinity than the control. We targeted the monkeypox profilin-like protein, which plays a key role in viral replication and assembly. Among the metabolites, curcumin showed the strongest binding affinity with a value of -37.43 kcal/mol, followed by gedunin (-34.89 kcal/mol), piperine (-34.58 kcal/mol), and coumadin (-34.14 kcal/mol). Based on ADME and toxicity assessments, the top four substances had no negative impacts. Furthermore, four compounds demonstrated resistance to deformability, which was corroborated by normal mode analysis. According to the bioactivity prediction study, the top compound target class was an enzyme, membrane receptor, and oxidoreductase. Furthermore, the study discovered that wortmannin, a gedunin analogue, can behave as an orthopoxvirus. The study found that these bioactive natural drug candidates could potentially work as monkeypox virus inhibitors. We recommended further experimental validation to confirm the promising findings of the study.

Analysis of Inhibition Potential of Nimbin and its Analogs against NF-κB Subunits P50 and P65: A Molecular Docking and Molecular Dynamics Study.

Khan A, Singh D, Waidha K, Sisodiya S, Gopinath P, Hussian S, Tanwar P, Katare DP.

Anticancer Agents Med Chem. 2023 Sep 8. doi: 10.2174/1871520623666230908101204. PMID: 37694791

Background: Cancer remains the major cause of morbidity and mortality. The nuclear factor kappa-B (NF-κB) plays an indispensable role in cancer cell proliferation and drug resistance. The role of NF-κB is not only limited to tumor cell proliferation and suppression of apoptotic genes but it also induces EMT transition responsible for metastasis. Inhibition of the NF-κB pathway in cancer cells by herbal derivatives makes it a favorable yet promising target for cancer therapeutics. **Aim:** The purpose of the study is to explore the inhibition

potential of Nimbin and its analogs against NF- κ B subunits p50 and p65. **Methods:** In the present study, an herbal compound Nimbin and its derivative analogs were investigated to examine their impact on the p50 and p65 subunits of the NF- κ B signaling pathway using in-silico tools, namely molecular docking and simulation. **Results:** The molecular docking analysis revealed that Nimbin and its analogs may bind to p50 and p65 subunits with dG bind values ranging from -33.23 to -50.49Kcal/mol. Interestingly, molecular dynamic simulation for the NO5-p65 complex displayed a stable conformation and convergence when compared to the NO4-p50 complex. **Conclusion:** These results indicate that NO5 may have a potential inhibitory effect against NF- κ B subunit p65, which needs to be further validated in in-vitro and in-vivo systems. Also, the results obtained emphasize and pave the way for exploring the Nimbin scaffold against NF- κ B inhibition for cancer therapeutics.

***In vitro* antimicrobial and cytotoxic activity of Neem and Kirata herbal formulation mediated Silver nanoparticles.**

R R, Sp SD, B N, S R.

Bioinformation. 2022 Nov 30;18(11):1069-1074. doi: 10.6026/973206300181069. eCollection 2022.PMID: 37693082

Silver nanoparticles (AgNPs) gain great interest among noble metal nanoparticles due to their broad applications in medicine, dentistry, drug delivery, tissue and tumour imaging, biolabeling, and biosensing. The antibacterial, antifungal, antiviral, and antiparasitic activity of AgNPs is well documented in the literature. This study aimed to determine the antimicrobial and cytotoxic activity of Neem and Kirata herbal formulation-mediated silver nanoparticles against oral biofilm. The green synthesis of Neem and Kirata herbal formulation-mediated silver nanoparticles was done. The antimicrobial action against the strains of *Candida albicans*, *Staphylococcus aureus*, *Enterococcus faecalis*, and *Streptococcus mutans* were assessed. The results showed that the newly formulated nanoparticle had effective anti-microbial properties and decreased cytotoxic properties which make it advantageous for clinical applications and treatment modalities. It showed great potential for the nanoparticle in decreasing the bacterial effects and cytotoxic nature thereby providing future scope for clinical application in preventing oral biofilm formation and its deleterious effects.

Comparative Evaluation of Intracanal Smear Layer Removal by Different Root Canal Irrigants: A Scanning Electron Microscope Study.

Sudhakar S, Gupta N, Ghambir N, Singh R, Singh D.

Int J Clin Pediatr Dent. 2023 Jul-Aug;16(4):633-638. doi: 10.5005/jp-journals-10005-2648.PMID: 37731794

Aim: The purpose of the study is to compare and evaluate the efficacy of different root canal irrigants-100, 75, 50, and 25% *neem* extract, 100, 75, 50, and 25% apple cider vinegar (ACV), a combination of 5.25% sodium hypochlorite (NaOCl) and 17% ethylenediaminetetraacetic acid (EDTA), and saline on smear layer removal using a scanning electron microscope (SEM). **Materials and methods:** A total of 80 freshly extracted single-rooted teeth were collected and divided into 10 groups-group I: normal

saline (negative control), group II: NaOCl with EDTA (positive control), group III: 100% *neem* extract, group IV: 75% *neem* extract, group V: 50% *neem* extract, group VI: 25% *neem* extract, group VII: 100% ACV, group VIII: 75% ACV, group IX: 50% ACV, and group X: 25% ACV. The samples were irrigated with a specific group of irrigants, then split in a longitudinal axis and processed for analysis in an SEM. Microphotographs were obtained and scored according to Torabinejad et al. **Results:** Microphotographs were assessed and showed that 100% *neem* extract was similar to NaOCl with EDTA, followed by 75% *neem* extract and 100% ACV. **Conclusion:** This study showed that 100% *neem* extract removed the smear layer, similar to the NaOCl with EDTA.

Scanning Electron Microscopy Analysis of Smear Layer Removal Ability of Conventional Endodontic Irrigation Regimen, MTAD, and QMix™ Versus a Mixture of *Azadirachta indica* and *Citrus limon*: An In Vitro Study.

Meyappan N, Mahadevan M, Manimaran ND, Paulaiian B, Gopal R, Kumar N. *Cureus*. 2023 Aug 2;15(8):e42877. doi: 10.7759/cureus.42877. eCollection 2023 Aug. PMID: 37664257

Introduction: Smear layer removal from root canals aid in the penetration of both irrigants and endodontic sealer into the dentinal tubules, thereby improving the efficacy of endodontic treatment. The aim of this in vitro study was to compare the smear layer removal ability of a conventional endodontic irrigation regimen, MTAD (mixture of tetracycline, acid, and detergent), and QMix™ (Dentsply Sirona, Charlotte, North Carolina, United States) with that of a mixture of herbal irrigants, namely, aqueous extracts of *Azadirachta indica* (*neem*) and *Citrus limon* (*lemon*), evaluated using scanning electron microscopy (SEM). **Materials and methods:** We selected 40 extracted human premolar teeth for the study, which we randomly divided into five groups (eight samples each) according to irrigation solution: (i) Group A (normal saline); (ii) Group B (conventional endodontic regimen, 3% sodium hypochlorite (NaOCl) + 17% ethylenediamine tetraacetic acid (EDTA) + 2% chlorhexidine (CHX)); (iii) Group C (MTAD); (iv) Group D (QMix 2-in-1); and (v) Group E (aqueous extracts of *Azadirachta indica* and *Citrus limon*). After we prepared the canals with ProTaper Universal nickel-titanium (Ni-Ti) rotary files (Dentsply Sirona) and the respective irrigants, we split the teeth longitudinally to evaluate the amount of remnant smear layer in the coronal, middle, and apical thirds using SEM photomicrographs. We performed statistical analyses of the data using the Kruskal-Wallis and Mann-Whitney U tests, where the level of significance was set at 0.05. **Results:** The SEM analysis of the coronal third showed mean values of 3.83 in Group A, 3.67 in Group B, 2.79 in Group C, 3.63 in Group D, and 4.00 in Group E. The SEM analysis of the middle third showed mean values of 4.00 in Group A, 3.88 in Group B, 3.75 in Group C, 3.50 in Group D, and 3.50 in Group E. The SEM analysis of the apical third showed mean values of 3.92 in Group A, 3.63 in Group B, 3.71 in Group C, 3.88 in Group D, and 3.17 in Group E. Therefore, we found that there were significant statistical differences between the groups when an overall comparison was done for the coronal, middle, and apical third, with a p-value of 0.001. On multiple comparisons across the different tooth-section thirds. Groups A and B showed statistically significant differences in the apical third (p-value=0.017). Groups A and C showed statistically significant differences in the coronal third and middle third (p-values=0.001 and 0.010, respectively). Groups A and D showed statistically significant differences in the middle third (p-













value=0.001). Groups A and E showed statistically significant differences in all thirds (p-values=0.039, 0.001, and 0.001, respectively) Conclusion: The conventional needle irrigation with MTAD showed the highest level of smear layer removal ability on the root canal surface, followed by QMix 2-in-1, the *Azadirachta indica* leaf and *Citrus limon* extract mixture, and the conventional endodontic regimen. Normal saline showed the lowest smear layer removal effect.

Neem (*Azadirachta Indica*) and silk fibroin associated hydrogel: Boon for wound healing treatment regimen.

Nasrine A, Narayana S, Gulzar Ahmed M, Sultana R, Noushida N, Raunak Saliyan T, Almuqbil M, Almadani ME, Alshehri A, Alghamdi A, Alshehri S, Mohammed Basheeruddin Asdaq S.

Saudi Pharm J. 2023 Oct;31(10):101749. doi: 10.1016/j.jsps.2023.101749. Epub 2023 Aug 18. PMID: 37663591

Background & objectives: Wound healing is the complex physiological process of replacing damaged cells or tissue layers. The neem (*Azadirachta Indica*) has a variety of biological activities, which may hasten the rate at which the wound healing mechanism occurs. Silk fibroin is a biomaterial that is reported for its tissue regeneration activity. So, the present study was designed to assess the effectiveness of a hydrogel comprising neem and silk fibroin biomaterials for the treatment of wounds. **Methods:** Topical neem hydrogels (N-HG) with and without silk fibroin (N-SFB-HG) were prepared using neem extract, silk fibroin, and guar gum, which act by entrapping the components by forming a gel. Evaluation tests such as Fourier transform infrared spectroscopy (FT-IR), visual emergence, pH, rheological behavior, spreading capacity, drug content, skin irritation, anti-microbial action, *in vivo* wound healing activity, and stability were carried out. **Results:** The FT-IR results showed no chemical interaction between the constituents. The formed hydrogels had pH values of 5.87 ± 0.3 for N-HG and 5.76 ± 0.2 for N-SFB-HG. The preferred topical gel viscosity was observed in the N-HG (54.2 ± 3.2 cPs) and N-SFB-HG (59.9 ± 4.8 cPs) formulations. The formulated hydrogels were sterile and did not irritate the skin. The *in vivo* wound healing investigation results reveal that the N-SF-HG treatment speeds up the regeneration of the injured area faster when compared to control and N-HG treated groups. **Interpretation & conclusion:** These results support the efficacy of the topical hydrogel formulation, including neem and silk fibroin. Therefore, the neem-silk fibroin hydrogel formulation is a therapeutically viable choice that, following necessary clinical research, might be utilized in novel formulations for managing chronic wounds.

Time interval	Group-1 Control	Group-2 N-HG	Group-3 N-SFB-HG
0 th Day			
7 th Day			
14 th Day			
21 st Day			

Neem in Veterinary Science & Medicine

Evaluation of the immuno-stimulatory effect of aqueous neem (*Azadirachta indica*) leaf extract against highly pathogenic avian influenza (H5N8) in experimental chickens.

Hegazy AM, Hassanin O, Hemele MAM, Momenah MA, Al-Saeed FA, Shakak AO, El-Tarabily KA, El-Saadony MT, Tolba HMN.

Poult Sci. 2023 Aug 18;102(11):103043. doi: 10.1016/j.psj.2023.103043. PMID: 37741118

The recently detected clade 2.3.4.4 of the highly pathogenic avian influenza (HPAI) H5N8 virus in poultry encouraged us to study the efficacy of the 6 most extensively used saleable H5 poultry vaccinations (bivalent [AI + ND], Re-5 H5N1, H5N1, H5N3, monovalent AI, monovalent ND) with or without aqueous 8% neem (*Azadirachta indica*) leaf extract as an immunostimulant. One hundred thirty birds were randomly divided into 7 groups. Groups 1, 2, 3, 4, 5, and 6 were divided into 2 subgroups (G1a, G2a, G3a, G4a, G5a, G6a) and (G1b, G2b, G3b, G4b, G5b, G6b) with 10 birds each. Subgroups (G1a, G2a, G3a, G4a, G5a, G6a) received the (bivalent [AI + ND], Re-H5N1, H5N1, H5N3, monovalent AI, monovalent ND) vaccines, while subgroups (G1b, G2b, G3b, G4b, G5b, G6b) received the same previous vaccination but treated with neem leaf extract administrated 2 d before and after vaccination, and G7 with 10 birds was kept unvaccinated as positive control group. Clinical signs of the

challenged group showed conjunctivitis, closed eyes, cyanosis in comb and wattle, ocular discharge, and greenish diarrhea, while postmortem lesions showed congested trachea and lung, hemorrhage on the shank, proventriculus, and pancreas; gelatinous fluid submandibular, congestion of all organs (septicemia), mottled spleen. The clinical signs and lesions were mild in neem leaf extract treated with bivalent vaccine and Re-H5N1 while moderate in monovalent vaccine and H5N3 with or without neem leaf extract treated and reached severe in the group immunized with H5N1 with or without neem leaf extract treatment. The protection levels in the bivalent vaccine (AI + ND), Re-5 H5N1, and H5N3 treated with neem leaf extract, were 80%, 80%, and 60%, respectively, while bivalent vaccine (AI + ND), Re-5 H5N1 and H5N3 without treatment were 60%, 60%, and 40%, respectively. The virus shedding was prevented in groups vaccinated with bivalent vaccine and Re-H5N1 vaccine treated with neem leaf extract, while decreased in the group vaccinated with H5N3 with neem leaf extract and Re-H5N1 without neem leaf extract compared with H5N3, H5N1, and monovalent vaccine. The immunological response after vaccination was stronger in the bivalent vaccine group than in the other commercial vaccine groups treated with neem leaf extract, with geometric mean titer (GMTs) of 315.2 and 207.9 at the third and fourth weeks, respectively. The use of immunostimulant antiviral medicinal plants, such as neem, completely protected chicken flocks against HPAI (H5N8) and prevented AI virus shedding, leading us to the conclusion that the use of bivalent vaccines induces a higher immune response than other different commercial vaccines.

Antibacterial activity of medicinal plants on the management of mastitis in dairy cows: A systematic review.

Kaseke TB, Chikwambi Z, Gomo C, Mashingaidze AB, Murungweni C.

Vet Med Sci. 2023 Sep 19. doi: 10.1002/vms3.1268. PMID: 37725398

Background: Mastitis is a disease of economic importance in dairy production systems. The common management regime for mastitis is the use of synthetic antibiotics, giving a new problem of antibiotic resistance. There is, therefore, a need to prospect for alternatives to conventional antibiotics from herbal plants. **Objectives:** This systematic review evaluates the use of plants as alternatives for the control of mastitis in dairy cattle, focussing on the effectiveness of studied plants and plant-based products and possible implications on the use of these products in livestock health. **Methodology:** The PRISMA model was implemented with searches done in five electronic databases: Scopus, ScienceDirect, PubMed, Ovid and Research4Life. Data were extracted from 45 studies with 112 plant species from plant species belonging to 42 different families. The specific keywords were 'mastitis', 'dairy cows' and 'medicinal plants'. **Results:** The most cited plant species included *Allium sativum* L., *Azadirachta indica* and *Eucalyptus globulus* Labill with the latter further exploring its components. Microbial species causing mastitis mainly were *Staphylococcus aureus* and *Escherichia coli*. The extraction methods used included maceration approach using ethanol, methanol and water as solvents for phytochemicals and chromatographic techniques for essential oils. A few studies explored the mode of action, and toxicities of the herbal extracts as well as evaluating their efficacy in clinical trials using animal models. **Conclusion:** Plants with defined levels of phytochemicals were essential sources of antibacterials. Standardisation of analytical methods is required.