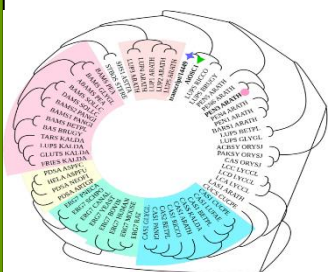


# Neem Research Newsletter

## Volume 2, Issue 4, 2022



**WORLD NEEM ORGANISATION (WNO)**



From  
The Editor's Desk.....

Neem Greetings! This issue of the newsletter features several research and review articles on neem in diverse fields. Zinc-coated urea was found to be best suited in terms of enhancing the productivity and quality of rice grown in anaerobic conditions compared to other forms of urea. Scientists report the complete chloroplast genome of the genus *Azadirachta* that could pave way for applications. Co-pyrolysis of neem wood bark and low density polyethylene was demonstrated to increase the yield and quality of bio-oil. The dermato-cosmetic effects of neem have been highlighted in a narrative review. Bioinformatic approaches have provided leads to explore the inhibitory effects of neem phytochemicals against porcine reproductive and respiratory syndrome virus. Neem seed derived carbon nanocapsules were shown to induce death of breast cancer cells. Neem leaf glycoprotein documented to influence dendritic cell functions and confer T cell mediated cytotoxicity could be harnessed to combat COVID-19, emphasizing the tenet that in the age of drug repurposing, lessons learnt from cancer could well be extrapolated for the management of novel diseases. The material properties of neem/glass hybrid fibre that could be used for industrial applications were analysed.

S. Nagini

Core Founding Member, WNO  
Chief Scientific Coordinator &

Regional Director, South India



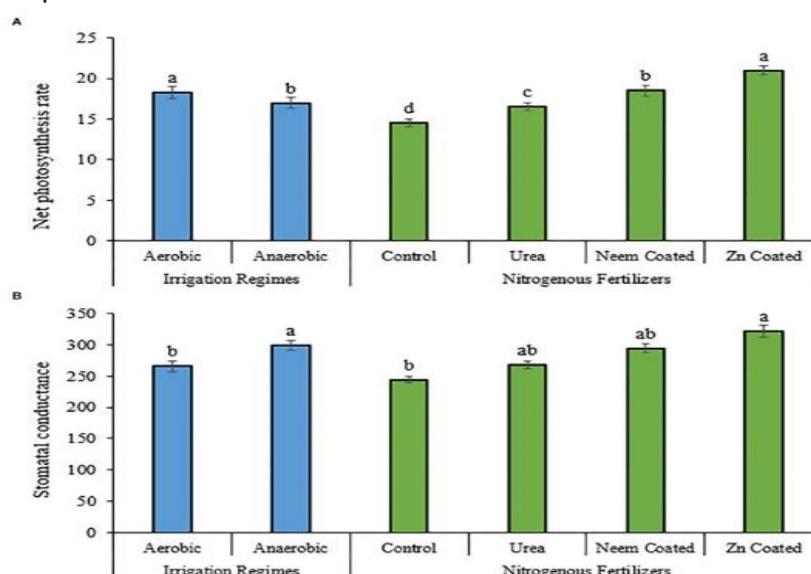
# Neem in Agriculture

## Nitrogenous Fertilizer Coated With Zinc Improves the Productivity and Grain Quality of Rice Grown Under Anaerobic Conditions.

Wahid MA, Irshad M, Irshad S, Khan S, Hasnain Z, Ibrar D, Khan AR, Saleem MF, Bashir S, Alotaibi SS, Matloob A, Farooq N, Ismail MS, Cheema MA.

*Front Plant Sci.* 2022 Jun 28;13:914653. doi: 10.3389/fpls.2022.914653. eCollection 2022. PMID: 35837462

An ample quantity of water and sufficient nutrients are required for economical rice production to meet the challenges of ever-increasing food demand. Currently, slow-release nitrogenous fertilizers for efficient inputs utilization and maximum economic yield of field crops are in the limelight for researchers and farmers. In this study, we evaluated the comparative efficacy of conventional urea and coated urea (zinc and neem) on rice grown under aerobic and anaerobic regimes in greenhouse conditions. For the aerobic regime, field capacity was maintained at 80-100% to keep the soil aerated. On the other hand, for the anaerobic regime, pots were covered with a polythene sheet throughout the experimentation to create flooded conditions. All forms of urea, conventional and coated (zinc and neem), improved plant growth, gas exchange, yield, yield contributing parameters, and quality characteristics of rice crop. However, better performance in all attributes was found in the case of zinc-coated urea. Gas exchange attributes (photosynthetic rate, 30%, and stomatal conductance 24%), yield parameters like plant height (29%), tillers per plant (38%), spikelets per spike (31%), grains per panicle (42%), total biomass (53%), and grain yield (45%) were recorded to be maximum in rice plants treated with zinc-coated urea. The highest grain and straw nitrogen contents, grain protein contents, and grain water absorption ratio were also found in plants with zinc-coated urea applications. In irrigation practices, the anaerobic regime was found to be more responsive compared to the aerobic regime regarding rice growth, productivity, and quality traits. Thus, to enhance the productivity and quality of rice grown in anaerobic conditions, zinc-coated urea is best suited as it is more responsive when compared to other forms of urea.

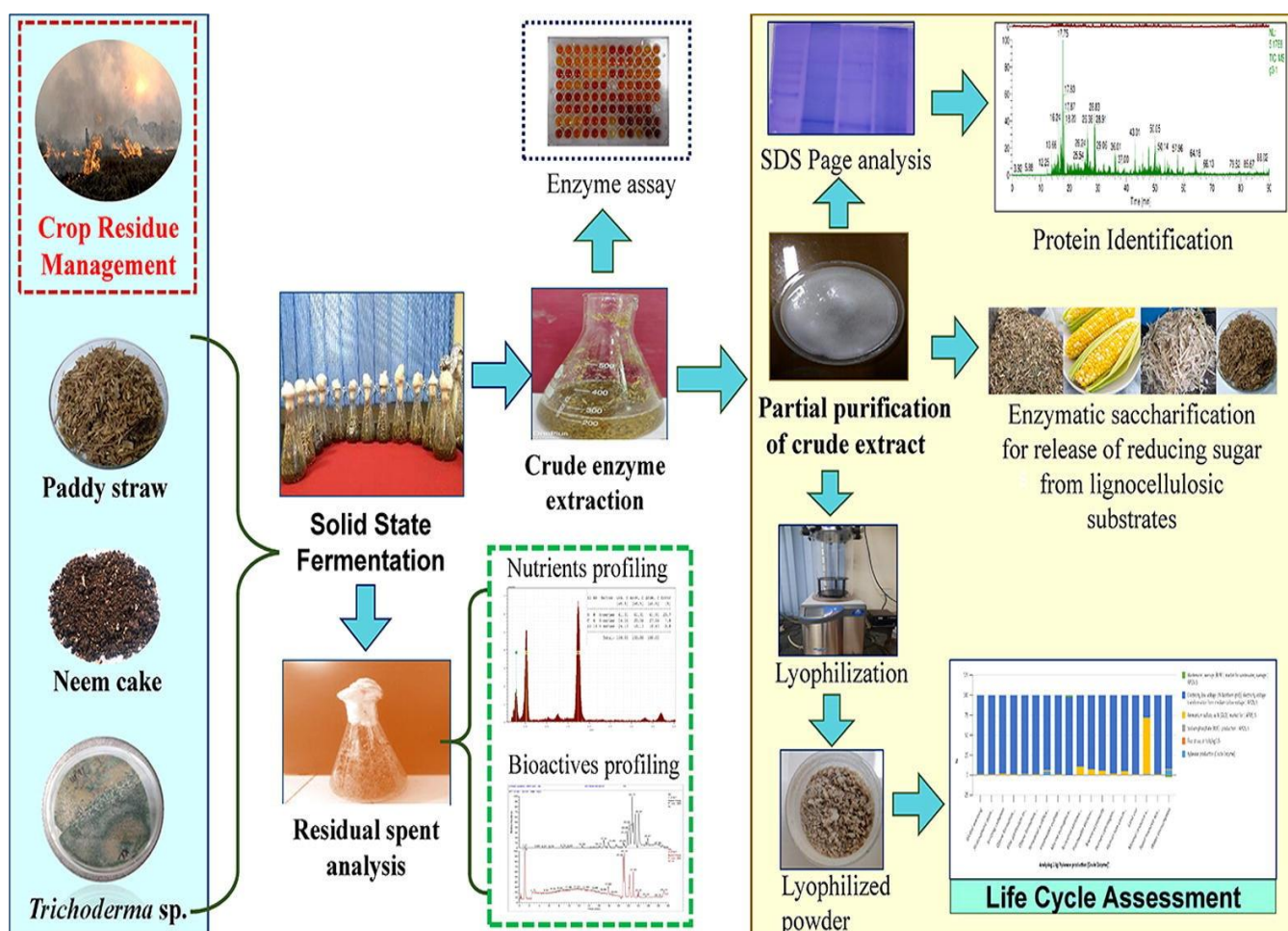


# Melioration of Paddy Straw to produce cellulase-free xylanase and bioactives under Solid State Fermentation and deciphering its impact by Life Cycle Assessment.

Singh G, Samuchiwal S, Hariprasad P, Sharma S.

Bioresour Technol. 2022 Jun 28;360:127493. doi: 10.1016/j.biortech.2022.127493. Online ahead of print. PMID: 35777645

Aiming towards zero waste management of Paddy straw (PS), the study offers a novel route for production of cellulase-free xylanase, using consortia of *Trichoderma* spp. under Solid State Fermentation (SSF) of PS valorized using nitrogen rich de-oiled neem cake (NC). Life Cycle Assessment (LCA) for enzyme production, performed using SimaPro software, depicted adverse impacts due to electricity consumption (92.84%) and use of ammonium sulphate salt (6.17%). Nonetheless, employing renewable energy and reducing salt consumption could help minimize these impacts. OHR-LCMS study of the partially purified enzyme revealed the presence of  $\beta$ -xylanase and  $\alpha$ -L-Arabinofuranosidase. Enzymatic saccharification of various substrates enhanced the release of reducing sugars (mg/g) from corn cob ( $137.54 \pm 0.96$ ), pine needle ( $41.43 \pm 1$ ), sugarcane bagasse ( $105.17 \pm 0.7$ ), and PS ( $76.66 \pm 1.29$ ), demonstrating its applicability in the biofuel domain. LC-MS, ICMPS, and EDX profiling of the residual spent unravelled the manifestation of bioactives, minerals, and silica, playing an essential role as biopesticide and biofertilizer.



## Can omic tools help generate alternative newer sources of edible seed oil?

Rangan P, Maurya R, Singh S.

*Plant Direct*. 2022 Jun 7;6(6):e399. doi: 10.1002/pld3.399. eCollection 2022

Jun.PMID: 35774621

There are three pathways for triacylglycerol (TAG) biosynthesis: De novo TAG biosynthesis, phosphatidylcholine-derived biosynthesis, and cytosolic TAG biosynthesis. Variability in fatty acid composition is mainly associated with phosphatidylcholine-derived TAG pathway. Mobilization of TAG-formed through cytosolic pathway into lipid droplets is yet unknown. There are multiple regulatory checkpoints starting from acetyl-CoA carboxylase to the lipid droplet biogenesis in TAG biosynthesis. Although a primary metabolism, only a few species synthesize oil in seeds for storage, and less than 10 species are commercially exploited. To meet out the growing demand for oil, diversifying into newer sources is the only choice left. The present review highlights the potential strategies targeting species like *Azadirachta*, *Callophyllum*, *Madhuca*, *Moringa*, *Pongamia*, *Ricinus*, and *Simarouba*, which are not being used for eating but are otherwise high yielding (ranging from 1.5 to 20 tons per hectare) with seeds having a high oil content (40-60%). Additionally, understanding the toxin biosynthesis in *Ricinus* and *Simarouba* would be useful in developing toxin-free oil plants. Realization of the importance of cell cultures as "oil factories" is not too far into the future and would soon be a commercially viable option for producing oils in vitro, round the clock.

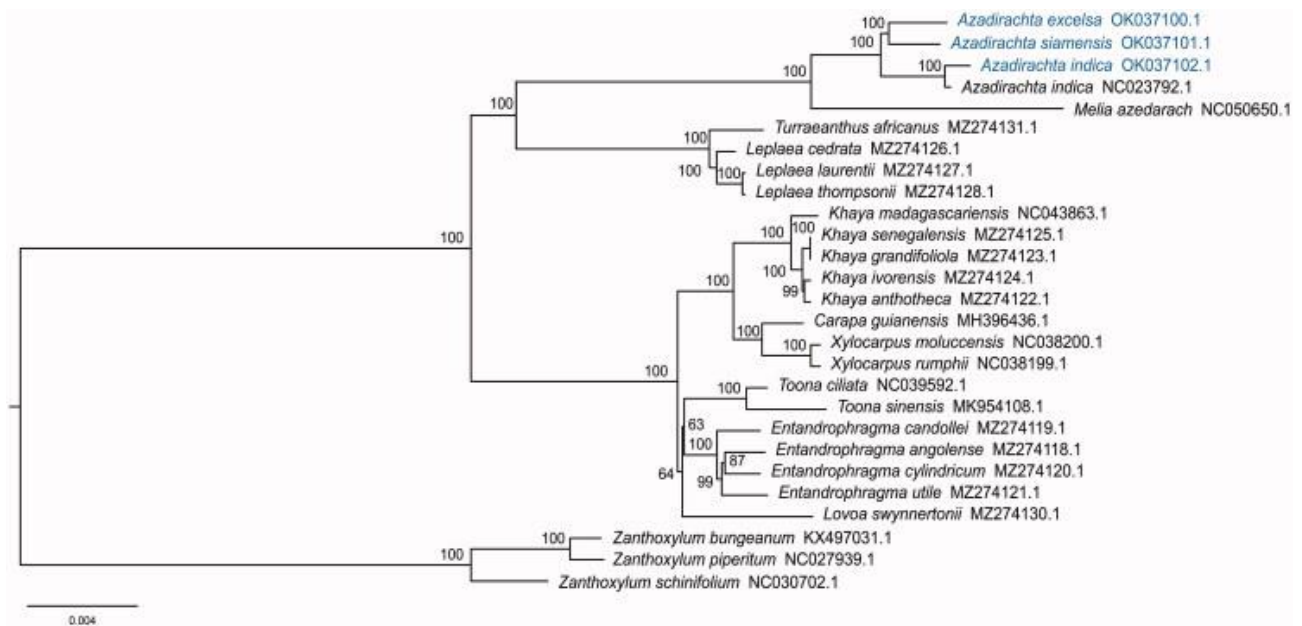
# Neem- Genome Analysis

## The complete chloroplast genome of the genus *Azadirachta*.

He ST, Wu JC, Zheng YX, Zhang YP, Li SH, Peng XM.

*Mitochondrial DNA B Resour.* 2022 Jul 14;7(7):1267-1269. doi: 10.1080/23802359.2022.2095230. eCollection 2022. PMID: 35859717

*Azadirachta* consists of 2 species and 1 variety indigenous to the tropical areas of the Indo-Malayan region. They are evergreen trees for multi-purpose utilization featured by containing azadirachtin. The complete chloroplast (cp) genome of *Azadirachta indica*, *A. indica* var. *siamensis* and *Azadirachta excelsa* were reported in this study, which was 160,876 bp, 160,477 bp, and 160,361 bp in length respectively. The whole cp genomes encode 131 genes (37 tRNA genes, 8 rRNA genes, and 86 protein-coding genes) in both *A. indica* and *A. excelsa*, while *A. indica* var. *siamensis* do not have the *rrn4.5S* gene in the inverted repeat regions. The phylogenetic analysis indicated that *A. indica* var. *siamensis* and *A. excelsa* were closely related and *A. indica* was separated from these two species, which suggested that *A. siamensis* could be a species rather than a variety.



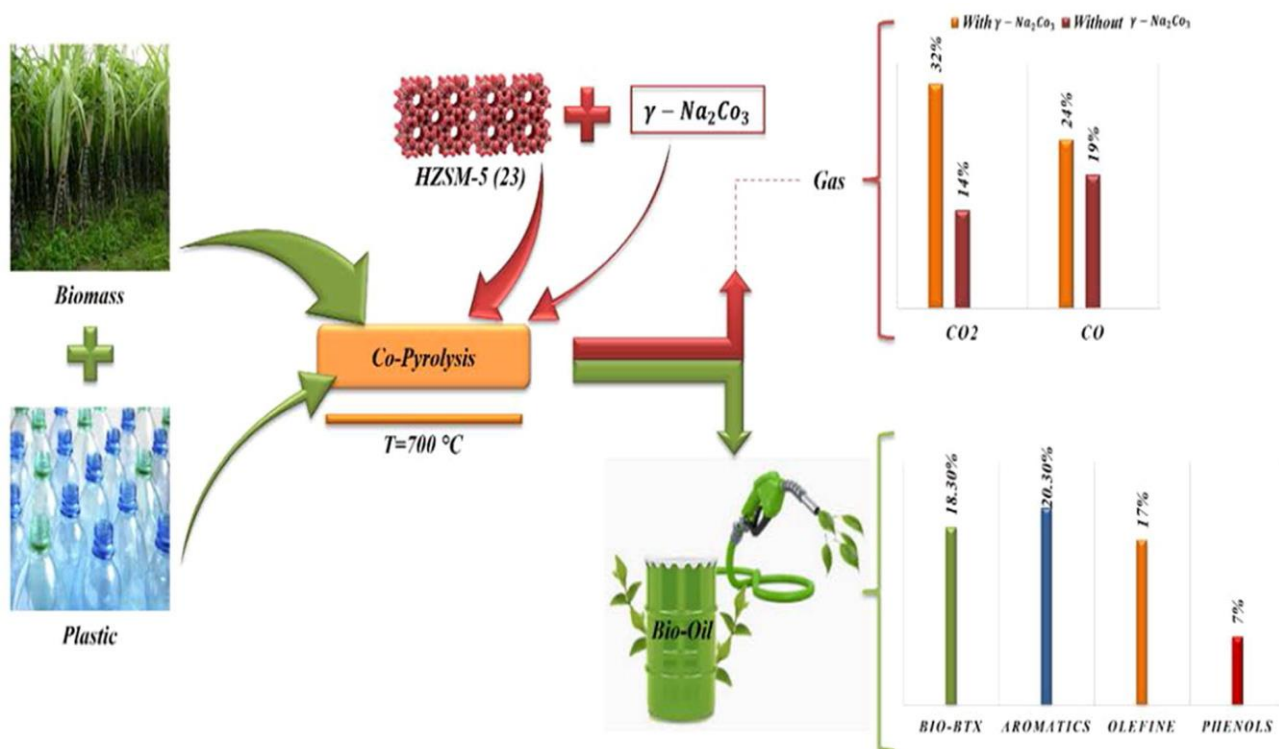
# Neem For Sustainable Environment

**Co-pyrolysis of neem wood bark and low-density polyethylene: influence of plastic on pyrolysis product distribution and bio-oil characterization.**

**Kaushik VS, Dhanalakshmi CS, Madhu P, Tamilselvam P.**

*Environ Sci Pollut Res Int.* 2022 Jul 13. doi: 10.1007/s11356-022-21746-1. Online ahead of print. PMID: 35831654

In this study, the investigation on the effect of plastic during co-pyrolysis with biomass was carried out in a fixed reactor. Pyrolysis of neem wood bark (NB), low density polyethylene (LDPE) and their blends at different ratios was performed in order to evaluate the product distribution. The effects of reaction temperature and NB-to-LDPE blend ratio on product distribution and the chemical compositions of pyrolysis oil were examined. The co-pyrolysis of NB and LDPE increased the yield and quality of the bio-oil. The experiments were conducted under different LDPE addition percentages such as 20%, 40%, 50%, 60% and 80%. Under the optimum experimental condition of 60% addition of LDPE and a temperature of 450 °C, the maximum yield of bio-oil (64.8 wt%) and hydrocarbon (75.2%) was achieved with the lowest yield of oxygenated compounds. The calorific value of the co-pyrolysis oil was found to be higher than that of the NB pyrolysis oil. The relationship between NB and LDPE during co-pyrolysis was validated with the help of gas chromatography-mass spectrometry (GC-MS) analysis, which showed decreased oxygenated compounds.



## **A comparative analysis on CI turbine act and emissions resorting to a novel antioxidant preservative**

**MA Lamba, MG Tamrakar, MH Gaur**

*Telematique, 2022 - provinciajournal.com vol 21, Issue 1. 523-535.*

The use of ordinary strength beginnings and environmental contamination belonging to the exercise of these strength sources form biodiesel as a tenable replacement to the engine. Biodiesel can be taken advantage of as an active replacement for fossil engines as allure possessions are equivalent to engines. The primary hurt of the biodiesel is the allure of lower decay soundness and prone to microbial growth that debases the properties of biodiesel all along the volume. By any means, these issues may be overwhelmed by increasing appropriate additional stuff to the biodiesel. The non-consumable neem lubricate is an individual of the feedstocks taken advantage of for biodiesel in India. The neem biodiesel has lower disintegration steadiness and accordingly accumulating sensible additives is fundamental. The eucalyptus lubricate has better container support and microbial hindrance characteristics and as a consequence, it was employed as an additional substance in this place of work. The impact of containing this additional substance biodiesel characteristics, engine outflows, and killing were contemplated. The engine tests were experienced on a pressure start engine at differing burdens with various consolidations of eucalyptus lubricate. The motor demonstration shows that the warm influence of the engine accompanying biodiesel is lower than the fuel while the engine smog emanations like HC, CO, and smoke were lower accompanying the biodiesel. The exercise of eucalyptus lubricate as an added entity to the biodiesel at complete burden builds the engine warm output by 3.08%. Likewise, it produces unhappy engine exhaust discharges other than NO<sub>x</sub> efflux.



# Neem For Human Health

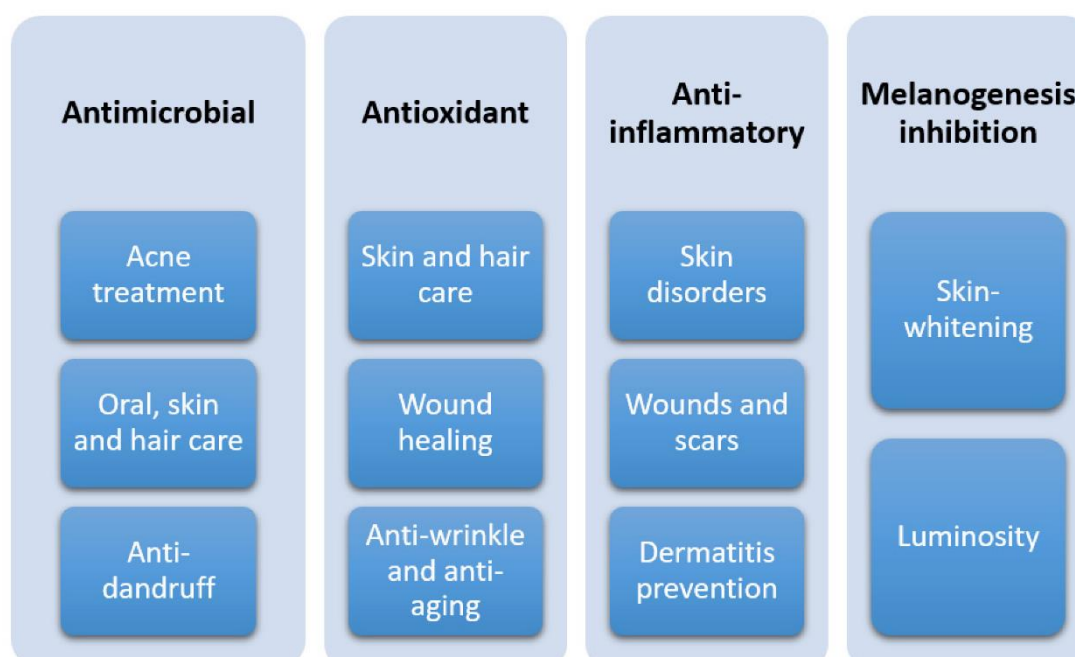
## Dermatocosmetic Effects

***Azadirachta indica* (Neem) as a Potential Natural Active for Dermocosmetic and Topical Products: A Narrative Review.**

**Baby AR, Freire TB, Marques GdA, Rijo P, Lima FV, Carvalho JCMd, Rojas J, Magalhães WV, Velasco MVR, Morocho-Jácome AL.**

*Cosmetics*. 2022; 9(3):58. <https://doi.org/10.3390/cosmetics9030058>

*Azadirachta indica* (Neem) is a large tree that is native to India and is traditionally used due to its several properties, mainly to treat skin diseases, as well as its “herbicide” activity. Its bark, leaves, seeds, fruits and flowers are widely used in medicinal treatment due to the presence of active secondary metabolites with biological effects, mainly limonoids and tetranortriterpenoids, such as azadirachtin. Thus, *A. indica* was studied in a variety of conditions, such as anticancer, antiseptic, anti-inflammatory and chemopreventive agents, as well as a biopesticide. Furthermore, differentiated cell tissue in *A. indica* cultivation was reported to produce active metabolites for different purposes. However, only a few studies have been developed regarding its potential use in cosmetics. For instance, most studies explained the antimicrobial properties in health conditions, such as acne, dandruff and personal health care. Here, we summarized not only the most common cosmetic claims to treat acne but also mitigating other skin disorders related to inflammatory and oxidant processes in recent in vivo studies and patents to aid researchers and industrialists to select *A. indica* derivatives as novel cosmetic ingredients.



# Antiviral Effects

## COVID-19 imparted immune manifestation can be combated by NLGP: Lessons from cancer research

Bose A, Baral R.

*Cytokine* 2022; 158:155980

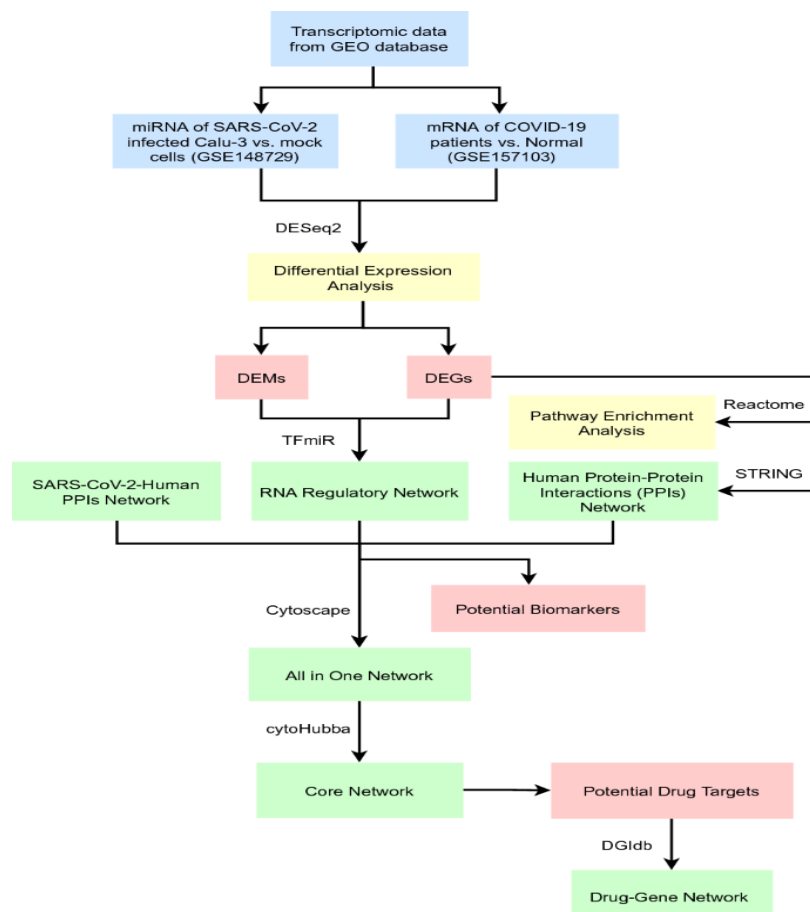
SARS-CoV-2 easily infects human monocytes, macrophages and possibly dendritic cells (DCs), causing dysfunctions of these important antigen presenting cells (APCs). Observed DC dysfunctions facilitate improper antigen presentation, which obviously results T cell anergy, exhaustion and apoptosis, thus, may be contributing significantly in SARS-CoV-2 infection associated lymphopenia. Neem Leaf Glycoprotein or NLGP has enormous role in altered DC functions, thereby, offering optimum T cell mediated cytotoxicity, as experienced from cancer system. Such NLGP guided correction of altered DCs might also be effective to generate proper SARS-CoV-2-specific effector and central memory T cells.

## SARS-CoV-2 potential drugs, drug targets, and biomarkers: a viral-host interaction network-based analysis.

Samy A, Maher MA, Abdelsalam NA, Badr E.

*Sci Rep.* 2022 Jul 13;12(1):11934. doi: 10.1038/s41598-022-15898-w.PMID: 35831333

COVID-19 is a global pandemic impacting the daily living of millions. As variants of the virus evolve, a complete comprehension of the disease and drug targets becomes a decisive duty. The Omicron variant, for example, has a notably high transmission rate verified in 155 countries. We performed integrative transcriptomic and network analyses to identify drug targets and diagnostic biomarkers and repurpose FDA-approved drugs for SARS-CoV-2. Upon the enrichment of 464 differentially expressed genes, pathways regulating the host cell cycle were significant. Regulatory and interaction networks featured hsa-mir-93-5p and hsa-mir-17-5p as blood biomarkers while hsa-mir-15b-



5p as an antiviral agent. MYB, RRM2, ERG, CENPF, CIT, and TOP2A are potential drug targets for treatment. HMOX1 is suggested as a prognostic biomarker. Enhancing HMOX1 expression by neem plant extract might be a therapeutic alternative. We constructed a drug-gene network for FDA-approved drugs to be repurposed against the infection. The key drugs retrieved were members of anthracyclines, mitotic inhibitors, anti-tumor antibiotics, and CDK1 inhibitors. Additionally, hydroxyquinone and digitoxin are potent TOP2A inhibitors. Hydroxyurea, cytarabine, gemcitabine, sotalol, and amiodarone can also be redirected against COVID-19. The analysis enforced the repositioning of fluorouracil and doxorubicin, especially that they have multiple drug targets, hence less probability of resistance.

### **Therapeutic role of traditionally used Indian medicinal plants and spices in combating COVID-19 pandemic situation.**

**Nath M, Debnath P.**

*J Biomol Struct Dyn.* 2022 Jun 30:1-20. doi: 10.1080/07391102.2022.2093793. Online ahead of print. PMID: 35773779

The coronavirus disease (COVID-19) caused by SARS-CoV-2 is a big challenge and burning issue to the scientific community and doctors worldwide. Globally, COVID-19 has created a health disaster and adversely affects the economic growth. Although some vaccines have already emerged, no therapeutic medication has yet been approved by FDA for the treatment of COVID-19 patients. Traditionally, we have been using different medicinal plants like neem, tulsi, tea, and many spices like garlic, ginger, turmeric, black seed, onion, etc. for the treatment of flu-like diseases. In this paper, we are highlighting the recent research progress in the identification of natural products from the Indian medicinal plants and spices that have potential inhibition properties against SARS-CoV-2. This study will provide an initiative to stimulate further research by providing useful guidance to the medicinal chemists for designing new protease inhibitors effective against SARS-CoV-2 in future.

## **Anti-inflammatory Effects**

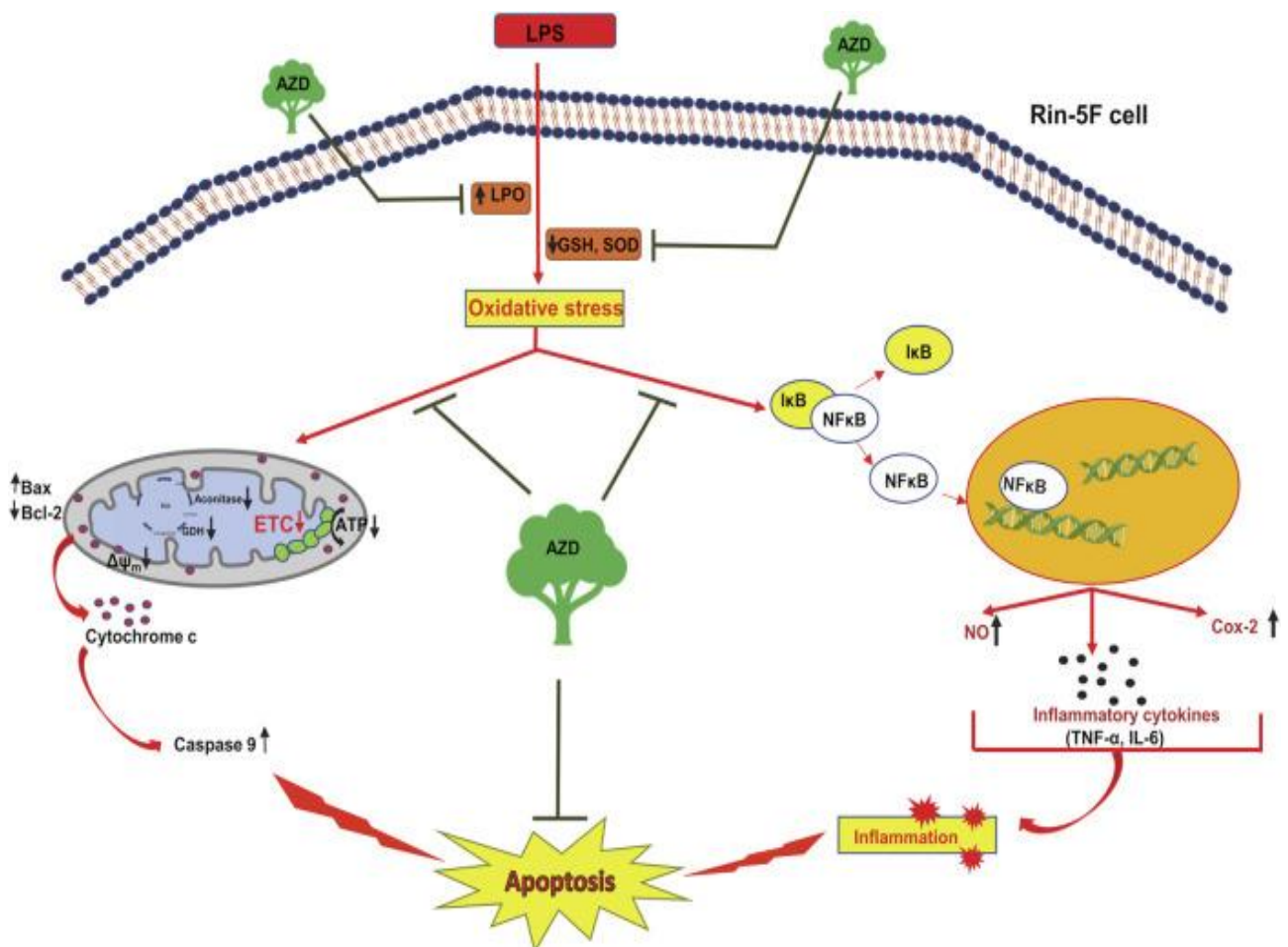
### **Alterations in Inflammatory Cytokines and Redox Homeostasis in LPS-Induced Pancreatic Beta-Cell Toxicity and Mitochondrial Stress: Protection by Azadirachtin.**

**John A, Raza H.**

*Front Cell Dev Biol.* 2022 Jun 20;10:867608. doi: 10.3389/fcell.2022.867608. eCollection 2022. PMID: 35794865

Inflammation and redox imbalance are hallmarks of cancer, diabetes, and other degenerative disorders. Pathophysiological response to these disorders leads to oxidative stress and mitochondrial dysfunction by alterations and reprogramming in cellular signaling and metabolism. Pancreatic beta cells are very sensitive to the inflammatory and altered nutrient signals and hence play a crucial role in diabetes and cancer. In this study, we treated insulin-secreting pancreatic beta cells, Rin-5F, with the bacterial endotoxin, LPS (1 µg/ml) to induce an inflammatory response *in vitro* and then treated the cells with a known anti-inflammatory, anticancer and antioxidant phytochemical, azadirachtin (AZD, 25 µM for 24 h). Our results demonstrated lipid peroxidation and nitric oxide production causing increased

nitro/oxidative stress and alterations in the activities of anti-oxidant enzymes, superoxide dismutase and catalase after LPS treatment. Pro-inflammatory responses caused by translocation of nuclear factor kappa B and release of inflammatory cytokines were also observed. These changes were accompanied by GSH-dependent redox imbalance and alterations in mitochondrial membrane potential and respiratory complexes enzyme activities leading to mitochondrial respiratory dysfunction, reduced ATP synthesis, and intrinsic caspase-9 mediated apoptosis. Caspase-9 was activated due to alterations in Bcl-2 and Bax proteins and release of cytochrome c into the cytosol. The activities of oxidative stress-sensitive mitochondrial matrix enzymes, aconitase, and glutamate dehydrogenase were also inhibited. Treatment with AZD showed beneficial effects on the recovery of antioxidant enzymes, inflammatory responses, and mitochondrial functions. GSH-dependent redox homeostasis also recovered after the treatment with AZD. This study may help in better understanding the etiology and pathogenesis of inflammation-induced disorders in pancreatic beta cells to better manage therapeutic strategies.



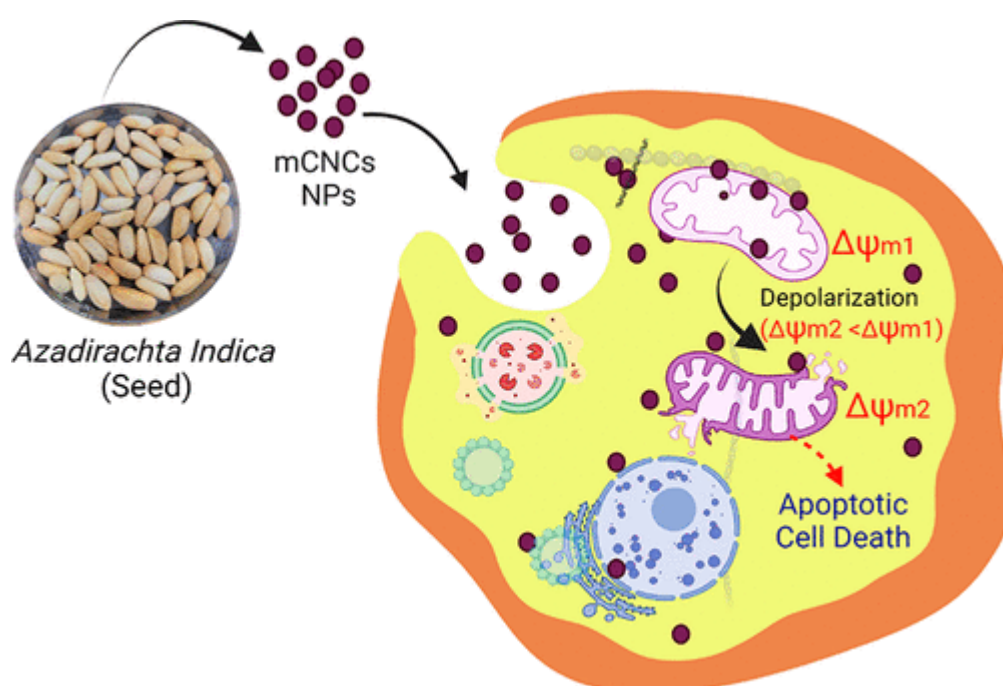
## Anticancer Effects

### ***Azadirachta indica* Seed Derived Carbon Nanocapsules: Cell Imaging, Depolarization of Mitochondrial Membrane Potential, and Dose-Dependent Control Death of Breast Cancer.**

**Maity S, Tomar MS, Wasnik K, Patra S, Modak MD, Gupta PS, Pareek D, Singh M, Paik P.**

*ACS Biomater Sci Eng.* 2022 Jul 27. doi: 10.1021/acsbomaterials.2c00463. Online ahead of print. PMID: 35892286

In this work, a series of mesoporous carbon nanocapsules (mCNS) of size below 10 nm have been prepared from *Azadirachta indica* seeds with a very easy and cost-effective approach. These nanocapsules can emit red and green light and are effective for cell imaging. Further, these carbon nanocapsules are biocompatible toward the normal healthy cells, however, they possess modest cytotoxicity against the MCF-7 (human breast cancer) and triple-negative breast cancer (TNBC) (MDA-MB-231 breast cancer cells), and the rate of killing cancer cells strongly depends on the dose of mCNCs. Further, the mitochondrial membrane potential and apoptosis assay were performed to analyze the therapeutic significance of these nanocapsules to kill breast cancer. Results showed that these carbon nanocapsules can depolarize the mitochondrial membrane potential alone (without using conventional drugs) and can change the physiological parameters and cellular metabolic energy of the cancer cells and kill them. The apoptosis results confirmed the death of breast cancer cells in the form of apoptosis and necrosis. Moreover, the results suggested that the porous carbon nanocapsules (mCNCs) reported herein can be used as a potential candidate and useful for the theranostic applications such as for cancer cell detection and therapy without using any conventional drugs.



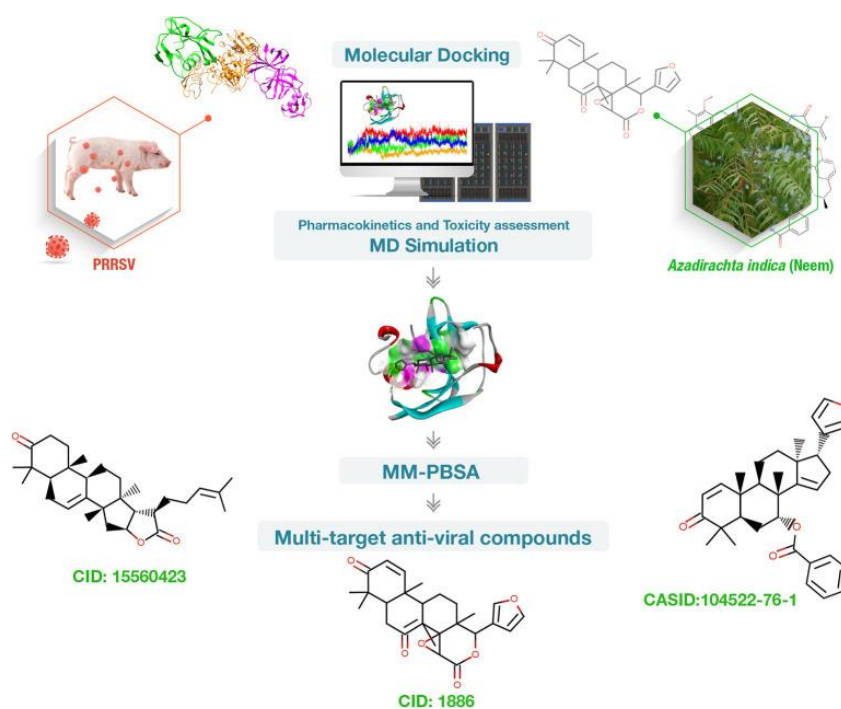
# Neem for Animal Health

## Investigating Multi-Target Antiviral Compounds by Screening of Phytochemicals From Neem (*Azadirachta indica*) Against PRRSV: A Vetinformatics Approach.

Pathak RK, Kim DY, Lim B, Kim JM

Front Vet Sci. 2022 Jun 16;9:854528. doi: 10.3389/fvets.2022.854528. eCollection 2022. PMID: 35782555

Porcine reproductive and respiratory syndrome virus (PRRSV) is a global health problem for pigs. PRRSV is highly destructive and responsible for significant losses to the swine industry. Vaccines are available but incapable of providing adequate and long-term protection. As a result, effective and safe strategies are urgently needed to combat the virus. The scavenger receptor cysteine-rich domain 5 (SRCR5) in porcine CD163, non-structural protein 4 (Nsp4), and Nsp10 are known to play significant roles in PRRSV infection and disease development. Therefore, we targeted these proteins to identify multi-target antiviral compounds. To identify potent inhibitors, molecular docking of neem phytochemicals was conducted; three compounds [7-deacetyl-7-oxogedunin (CID:1886), Kulactone (CID:15560423), and Nimocin (CASID:104522-76-1)] were selected based on the lowest binding energy and multi-target inhibitory nature. The efficacy and safety of the selected compounds were revealed through the pharmacokinetics analysis and toxicity assessment. Moreover, 100 ns molecular dynamics (MD) simulation was performed to evaluate the stability and dynamic behavior of target proteins and their docked complexes with selected compounds. Besides, molecular mechanics Poisson-Boltzmann surface area method was used to estimate the binding free energy of each protein-ligand complex obtained from the MD simulations and validate the affinities of selected compounds to target proteins. Based on our analysis, we concluded that the identified multi-target compounds can be utilized as lead compounds for the development of natural drugs against PRRSV. If further validated in clinical studies, these compounds can be used individually or in combination against the virus.



## Neem- Industrial Applications

### **Characterization of material properties of green polymer composite**

**AF Ahmed, S Sivaganesan**

*Materials Today: Proceedings, 2022 (in press) <https://doi.org/10.1016/j.matpr.2022.07.213>*

The composite materials are being utilized for many industrial applications. With the advent of academic research, many composite materials are introduced in the market by incorporating bio waste materials. The current paper addresses the tribological behaviour of epoxy composite reinforced with hybrid fibre such as glass and neem along with the incorporation of rice husk ash. The green epoxy composite was prepared using compression moulding by varying neem/glass hybrid fibre ratio between 10 and 40 wt% and keeping 2% (by wt.) of rice husk filler as constant. The tribological characteristics was studied through the conduct of pin on disc wear test instrument. Wear resistance of the composite due to the functional parameters such as load, sliding distance and speed were investigated.