REVIEW ARTICLE

Exploring the Therapeutic Potential of *Azadirachta indica* (Neem): Recent Advances and Applications

Suresh Dhakar, Sachin K Jain, Harshal Tare

Faculty of Pharmacy, Oriental University, Indore, Madhya Pradesh, India.

Received: 18th September, 2023; Revised: 24th October, 2023; Accepted: 16th November, 2023; Available Online: 25th December, 2023

ABSTRACT

This review explains the therapeutic prospective of *Azadirachta indica* (Neem), a traditional medicinal tree in India, Southeast Asia, and Africa. Neem extracts have been found to have various therapeutic properties, including antimicrobial, antifungal, hepatoprotective, antiulcer, antifertility, and antinociceptive properties. Recent research has shown neem's potential as an antiviral agent, cancer treatment, and a source of antibiotic compounds. Neem oil nano hydrogel shows significant antimicrobial activity against various pathogens. The plant also has the potential to mitigate heavy metal pollution and develop a model for predicting soil remediation using neem leaves. Neem's inhibitory activity on papain-like protease of SARS-CoV-2 is also explored. Overall, neem's therapeutic potential is significant and its potential in healthcare and environmental remediation is highlighted.

Keywords: *Azadirachta indica*, Therapeutic properties, Pharmacological perspectives.

International Journal of Pharmaceutical Quality Assurance (2023); DOI: 10.25258/ijpqa.14.4.60

How to cite this article: Dhakar S, Jain SK, Tare H. Exploring the Therapeutic Potential of *Azadirachta indica* (Neem): Recent Advances and Applications. International Journal of Pharmaceutical Quality Assurance. 2023;14(4):1211-1213.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

The evergreen tree *Azadirachta indica*, most popularly known as neem. Because of its therapeutic characteristics, it has been utilized by Indians for centuries to cure a wide range of conditions.[1] Leaves, bark, fruit, flowers, oil, and gum from the neem tree are all listed in the aforementioned medical folklore for their purported ability to treat various diseases and ailments.[2] The review explores most recent work that has been done on neem extracts. While it is natural that starting materials and extraction procedures can vary widely, we will provide a brief summary of few of the most relevant bioactive chemicals frequently present in many extracts. We also stress that much of the current work is still experimental, which should always be taken into account when trying to create safer goods for people to consume. We searched academic databases (like PUBMED, Science Direct, and Elsevier) and commercial search engines (like Google, Google Patents, and Patenscope) to compile the information used in this literature review.

The usage of neem has led to its transformation into a "wonder tree" of Western medicine. It has usage in alternative medication for anything from inflammation and infection to fever, skin illness, and tooth decay.[3,4]

Acne, psoriasis, and eczema are just few of the epidermal dysfunctions that it helps.[5] Additionally, neem leaves have been shown to have characteristics against hyperglycemia,[6] viruses,[7] mutagenesis,[8] inflammation, malaria, and carcinogenesis. In addition to its antimicrobial, antifungal, hepatoprotective, antiulcer, antifertility, and antinociceptive properties, neem also has a number of other useful properties.[9-11]

Neem twigs can be used to eliminate bad breath, reduce tooth pain, and clean and polish teeth. The bark of the neem tree can kill microorganisms and prevent sweating. Some of the phytochemicals are potent in their ability to kill microorganisms. Azadirachtin, a component of neem, is effective against bacteria. Neem-based moisturizers have also been utilized in the past.

Recent Advances in *A. indica*

Recent (within the last three to four years) neem research is discussed. A worldwide healthcare crisis has resulted from the SARS-CoV-2 epidemic, with symptomatic therapy being the mainstay of care. The rising mortality toll necessitates the use of targeted antivirals, yet the Food and Drug Administration (FDA) only permits emergency use of remdesivir. To find small chemical inhibitors of the membrane and envelope proteins of SARS-CoV-2, scientists used docking and simulation techniques. Common chemicals were discovered to have a high affinity for binding to these proteins, indicating that they may be able to block viral assembly.[12]

The extract of the neem utilized for the treatment and prevention of cancer, is being studied for its anti-inflammatory

**Author for Correspondence: harshaltare51@gmail.com*

properties. Human leukemia cells had their NF-B activity, vitality, and IB kinase activity suppressed by the extract. Improved knowledge of the mechanisms of *A. indica* influences on pro-inflammatory cell signaling and apoptosis outcomes.[13]

Silver nanoparticles (AI-AgNPs) with a high yield and crystalline structure were synthesized using the leaves. Disc diffusion studies showed that the compound was effective at killing various bacteria. A viscous hydrogel with improved antibacterial characteristics was created by loading nanoparticles onto a biocompatible-biodegradable polymer (PF127). Hydrogel application improved the healing of wounds in mice without causing any harm to the skin. An easy green method for synthesizing AI-AgNPs with improved antimicrobial and free-radical scavenging activity is presented in the study.[14]

This study analyses the utilization of non-edible plant-based oil of *A. indica*, ethanol, and diesel fuels in IC engines. To evaluate the performance of *A. indica* oil and diesel, three blends were developed: D80B20, B80E20, and D60B20E20. Brake thermal efficiency (BTE) was shown to be higher using various fuels, and exhaust emissions were found to be lower when compared to pure diesel. It is suggested that the biodiesel blends be used in IC engines as a replacement fuel.[15]

This research shows a nano hydrogel derived from *A. indica* oil as a potential new source of antibacterial chemicals. Inhibition ranged from 50.23 to 82.57% when compared to diclofenac sodium, the gold standard.[16]

Nosocomial *Acinetobacter baumannii* is an antibiotic-resistant human infection. *A. baumannii*'s biofilm development is a major virulence factor since it is mediated by the *csgA* gene. This could be a unique infection-control target. To determine whether or not essential bio-compounds from *A. indica* have anti-biofilm activity against ESBL-generating strains of *A. baumannii*, *in-vitro* and *in-silico* investigations were conducted.[17]

The research describes an environmentally benign technique for creating AgNPs from silver nitrate and *A. indica* leaf extract. It was observed that 1 mM AgNO3, 60 mg/mL, 30 minutes, and 85°C produced the best results. Minimum inhibitory concentration studies showed that 15.6 g/mL of AgNPs was effective against both *Escherichia coli* and *Staphylococcus aureus*. The biomedical sector may benefit from this green and cheap technique.[18]

The nanoparticles were measured and found to be spherical with a diameter between 19.27 and 22.15 nm. The anti-inflammatory and anti-diabetic effects of the nanoparticles were moderately comparable to those of established therapies.[19]

Air, water, and land pollution, especially from heavy metals, have increased worldwide as a result of industrialization and population development. *A. indica* was tested to see if its powder might be used as a natural adsorbent to get rid of copper ions in water. The maximum percentage of copper removal was attained under optimized circumstances. According to these results, *A. indica* could be a good biomass to use in order to remove copper ions.[20]

Total petroleum hydrocarbon (TPH) degradation was tracked using the model while microorganisms were present in the reactor. Soil treated with 100 g of room-dried *A. indica* leaves showed the greatest remediation, with data showing a considerable reduction in polluting agents. The model was effectively utilized to predict TPH remediation behavior, enabling for monitoring of contaminated soil remediation.[21]

Research has been reported that looked into whether or not neem extracts have any effect on the new coronavirus SARS-CoV-2's papain-like protease (PLpro). All of the substances investigated shown respectable inhibitory action in molecular docking and molecular dynamics simulations, with desacetylgedunin (DCG) demonstrating the highest binding affinity.[22]

The research demonstrates the green manufacturing of copper oxide nanoparticles (CuO NPs) utilizing *A. indica* flower extract. Crystalline, round, and chemically unadulterated NPs were discovered. Different concentrations were also used to examine their cytotoxicity towards H9c2 cardiomyocyte cells during treatment. The results may help lessen the prevalence of organ failure and death overall.[23]

In the study reported, the antioxidant and anticancer activities of *A. indica* gum polysaccharide were isolated and purified. The carboxymethylated polysaccharide was utilised to create curcumin nanocarriers, which demonstrated potent cytotoxicity against MCF7 cancer cell lines despite lacking antibacterial activity.[24]

The research explores the prospective of leaves for phenol adsorption in refineries and chemical industries. The study found that neem leaves can effectively remove 97.5% of phenol when the pH, dose, time, concentration, and temperature are controlled. The adsorption mechanism was supported by various models, and the adsorption process was non-random, exothermic, and spontaneous. The study recommends safe disposal of the adsorbent through incineration.[25]

CONCLUSION

A. indica (Neem) has therapeutic potential in traditional medicine, offering health benefits like addressing epidermal dysfunctions and viral infections. It has been integrated into modern Western medicine for treating inflammatory diseases and cancer. Neem's antimicrobial properties make it useful for wound healing and infections. Its eco-friendly applications include silver nanoparticle synthesis and heavy metal removal. Neem's antiviral potential is promising, particularly in inhibiting the SARS-CoV-2 protease. Its anti-inflammatory properties make it a potential candidate for cancer treatment. Neem's potential extends to biomedical applications. This work gives recent work done on *A. indica*, which is very helpful for further research.

REFERENCES

1. Latif MJ, Hassan SM, Mughal SS, Aslam A, Munir M, Shabbir N, Mushtaq M, Perveiz S. Therapeutic potential of *Azadirachta indica* (neem) and their active phytoconstituents against diseases prevention. J. ChemCheml Sci. 2020;10(3):98-110.

2. Kumar VS, Navaratnam V. Neem (*Azadirachta indica*): Prehistory to contemporary medicinal uses to humankind. Asian Pacific journal of tropical biomedicine. 2013 Jul 1;3(7):505-14.
3. Athavale VB. Dentistry in Ayurveda. Chaukhamba Sanskrit Pratishthan; 1999.
4. Kumar D, Rahal A, Malik JK. Neem extract. InNutraceuticals 2016 Jan 1 (pp. 585-597). Academic Press.
5. Subapriya R, Nagini S. Medicinal properties of neem leaves: a review. Current Medicinal Chemistry-Anti-Cancer Agents. 2005 Mar 1;5(2):149-56.
6. Bisht S, Sisodia SS. Anti-hyperglycemic and antidyslipidemic potential of *Azadirachta indica* leaf extract in STZ-induced diabetes mellitus. J Pharm Sci Res. 2010 Oct 1;2(10):622-7.
7. Parida MM, Upadhyay C, Pandya G, Jana AM. Inhibitory potential of neem (*Azadirachta indica*Juss) leaves on dengue virus type-2 replication. Journal of ethnopharmacology. 2002 Feb 1;79(2):273-8.
8. Vinod V, Tiwari PK, Meshram GP. Evaluation of mutagenic and antimutagenic activities of neem (*Azadirachta indica*) seed oil in the in vitro A
9. Gupta SC, Prasad S, Tyagi AK, Kunnumakkara AB, Aggarwal BB. Neem (*Azadirachta indica*): An indian traditional panacea with modern molecular basis. Phytomedicine. 2017 Oct 15;34:14-20.
10. Atawodi SE, Atawodi JC. *Azadirachta indica* (neem): a plant of multiple biological and pharmacological activities. Phytochemistry reviews. 2009 Oct;8:601-20.
11. Ahmad S, Maqbool A, Srivastava A, Gogol S. Biological detail and therapeutic effect of *Azadirachta indica* (neem tree) products-a review. Evidence Based Med. Healthcare. 2019;6(22):1607-12.
12. Borkotoky S, Banerjee M. A computational prediction of SARS-CoV-2 structural protein inhibitors from *Azadirachta indica* (Neem). Journal of Biomolecular Structure and Dynamics. 2021 Jul 24;39(11):4111-21.
13. Schumacher M, Cerella C, Reuter S, Dicato M, Diederich M. Anti-inflammatory, pro-apoptotic, and anti-proliferative effects of a methanolicneem (*Azadirachta indica*) leaf extract are mediated via modulation of the nuclear factor-κB pathway. Genes & nutrition. 2011 May;6(2):149-60.
14. Chinnasamy G, Chandrasekharan S, Koh TW, Bhatnagar S. Synthesis, characterization, antibacterial and wound healing efficacy of silver nanoparticles from *Azadirachta indica*. Frontiers in microbiology. 2021 Feb 19;12:611560.
15. Sathish T, Mohanavel V, Arunkumar M, Rajan K, Soudagar ME, Mujtaba MA, Salmen SH, Al Obaid S, Fayaz H, Sivakumar S. Utilization of *Azadirachta indica* biodiesel, ethanol and diesel blends for diesel engine applications with engine emission profile. Fuel. 2022 Jul 1;319:123798.
16. Kaur S, Sharma P, Bains A, Chawla P, Sridhar K, Sharma M, Inbaraj BS. Antimicrobial and anti-inflammatory activity of low-energy assisted nanohydrogel of *Azadirachta indica* oil. Gels. 2022 Jul 11;8(7):434.
17. Jaisankar AI, Girija AS, Gunasekaran S, Priyadharsini JV. Molecular characterisation of csgA gene among ESBL strains of *A. baumannii* and targeting with essential oil compounds from *Azadirachta indica*. Journal of King Saud University-Science. 2020 Dec 1;32(8):3380-7.
18. Asimuddin M, Shaik MR, Adil SF, Siddiqui MR, Alwarthan A, Jamil K, Khan M. *Azadirachta indica* based biosynthesis of silver nanoparticles and evaluation of their antibacterial and cytotoxic effects. Journal of King Saud University-Science. 2020 Jan 1;32(1):648-56.
19. Chi NT, Narayanan M, Chinnathambi A, Govindasamy C, Subramani B, Brindhadevi K, Pimpimon T, Pikulkaew S. Fabrication, characterization, anti-inflammatory, and anti-diabetic activity of silver nanoparticles synthesized from *Azadirachta indica* kernel aqueous extract. Environmental Research. 2022 May 15;208:112684.
20. Al Moharbi SS, Devi MG, Sangeetha BM, Jahan S. Studies on the removal of copper ions from industrial effluent by *Azadirachta indica* powder. Applied Water Science. 2020 Jan;10(1):23.
21. Ukpaka C, Eno O. Modeling of *Azadirachta indica* leaves powder efficiency for the remediation of soil contaminated with crude oil. Chemistry International. 2020 Sep 16;7(1):62-70.
22. Baildya N, Khan AA, Ghosh NN, Dutta T, Chattopadhyay AP. Screening of potential drug from *Azadirachta indica* (Neem) extracts for SARS-CoV-2: An insight from molecular docking and MD-simulation studies. Journal of molecular structure. 2021 Mar 5;1227:129390.
23. Jayakodi S, Shanmugam R, Almutairi BO, Almutairi MH, Mahboob S, Kavipriya MR, Gandusekar R, Nicoletti M, Govindarajan M. *Azadirachta indica*-wrapped copper oxide nanoparticles as a novel functional material in cardiomyocyte cells: An ecotoxicity assessment on the embryonic development of Daniorerio. Environmental Research. 2022 Sep 1;212:113153.
24. Samrot AV, Angalene JL, Roshini SM, Stefi SM, Preethi R, Raji P. Purification, characterization and exploitation of *Azadirachta indica* gum for the production of drug loaded nanocarrier. Materials Research Express. 2020 May 4;7(5):055007.
25. Mandal A, Bar N, Das SK. Phenol removal from wastewater using low-cost natural bioadsorbentneem (*Azadirachta indica*) leaves: Adsorption study and MLR modeling. Sustainable Chemistry and Pharmacy. 2020 Sep 1;17:100308.