



# Anti-Microbial Effects Of *Azadirachta Indica*: A Review

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## ABSTRACT

*Azadirachta indica* is a member of Mahogany family. It is a sacred gift of nature. *Azadirachta indica* is used in India as an age-old treatment for diverse medical conditions. The Latinized name of neem is “*Azadirachta indica*,” *Azad* means “free,” *dirakht* means “tree,” and *i-Hind* means “of Indian origin.” Thus, it literally means “The free tree of India.”<sup>1</sup> *Azadirachta indica* recognized around the world as a broad-spectrum pesticide and fertilizer, neem has applications in agriculture and beyond. Currently, the antimicrobial activities of *Azadirachta indica* are being explored through research in the fields of dentistry, food safety, bacteriology, mycology, virology, and parasitology.<sup>2</sup> This plant is highly abundant in flavonoids, polyphenols, diterpenoids, triterpenoids, limonoids, tannins, coumarin, nimbolide, azadirachtin, azadirone, azadiradione, and gedunin. Some parts of *Azadirachta indica*, including the leaves in various forms, have been used for wound healing or as a repellent.<sup>3</sup> Neem fruits, leaves, bark, and roots have specific virtues. They have been traditionally used for a huge part of human history and are documented in Sanskrit texts. Due to human activity in trade and travel the plant species has been distributed around the globe and is cultivated in many tropical, and subtropical regions.<sup>4</sup>

**Key Words:** *Azadirachta indica*, Anti microbial activity, Phytochemicals, Microorganisms

## INTRODUCTION

the antimicrobial activity of *A. indica* against common endodontic pathogens, such as, *Streptococcus mutans*, *Enterococcus faecalis*, *Staphylococcus aureus*, and *Candida albicans*, has been well-studied. For example, 7.5% aqueous neem leaf extract was sufficient to inhibit the growth of *E. faecalis*, *S. mutans*, and *C. albicans*. The methanolic extract of *A. indica* showed antimicrobial activity against a three-week-old polymicrobial dental biofilm grown on extracted human teeth consisting of *S. mutans*, *E. faecalis*, *S. aureus* and *C. albicans*. gastrointestinal pathogens, which include foodborne and diarrhea-causing organisms cause morbidity and mortality all over the world. some of the traditional uses of neem are antidiarrheal, antacid, and antiulcer; this has led to a large body of research that has investigated the antibacterial properties of neem products against pathogens such as *Salmonella spp.*, *Shigella spp.*, *E. coli*, *Listeria monocytogenes*, and *Bacillus cereus*.<sup>5</sup> The methanolic extracts of Neem contain antibacterial activity against several microbes like *Vibrio cholera* and chloroform extracts against *E. coli*, *Bacillus subtilis*, *Enterococcus faecalis* and *Streptococcus faecalis*.<sup>6</sup> The seed oil of neem is used to treat certain chronic skin diseases, ulcers, different types of metritis, leprosy, gum and dental problems. But neem seed oil is capable of generate toxicity when given orally. Neem plant contains a large quantity of biologically active compounds that are chemically diverse and structurally variable with more than 140 compounds isolated from different parts of the tree. The compounds such as Quercetin and  $\beta$ -sitosterol, were the first polyphenolic flavonoids extracted and purified from neem fresh leaves and possess antibacterial and antifungal properties. The Leaf extracts of neem possess potent antidermatophytic activity against *Microsporum nanum*, *Trichophyton rubrum*, *T. violaceum*, and *Epidrmophyton floccosum*. The same extracts were found to have considerable inhibitory action on a broad spectrum of microorganisms

like *C. albicans*, *C. tropicalis*, *Neisseria gonorrhoea*, multi-drug resistant *Staphylococcus aureus*, urinary tract *E. coli*, *Herpes simplex-2* and HIV viruses.<sup>7</sup>

The neem have been used in herbal medicine for the treatment of different diseases, particularly cancer. The hepatic anti-oxidant activity of neem mediates its anti cancer effects. The administration of neem extract is capable of induce oncostatic activity via several mechanism including; suppression of the NF- $\kappa$ B pathway, increased expression of tumor suppressor, decreased expression of oncogenes, and increased apoptosis in cancerous cells. So neem plays a vital role in the prevention of cancer cell growth via the hepatic anti-oxidant activities and the application of neem extract reduce the growth of cancer cells.<sup>8</sup> The anticancer properties of neem have been investigated in detail from several scientific angles. Regular use of neem and its preparations were capable to prevent the onset of cancer. Neem and neem preparations can prevent the growth of cancer cells by several mechanisms like prevention of proliferation and growth of cancer cells, cell cycle arrest and apoptosis, interference with growth factor signaling, inhibition of angiogenesis, and decrease of tumor cell invasion and migration. The curative effects of this plant is due to the presence of numerous chemical constituents present in various parts of the plant. The constituents include azadirachtin, gedunin, nimbidin, nimbidol, nimbin, salannin, and quercetin. Many parts of neem such as stem, leaves, flowers, fruits, and seeds have already proven for the anticancer effects. However the anticancer effects of neem and neem preparations largely depend on the soil, climate and extraction methods. The regular consumption of neem oil can prevent the presence of cancer cells and especially the onset of breast cancer.<sup>9</sup> The leaf extract of neem is capable of regulating the genes involved in cellular development and functions. There by they can regulate the stimulatory effect of vascular endothelial growth factor and results in exerting strong antiangiogenic effects. Azadirachtin is a major constituent of neem found in neem seeds. It is a secondary metabolite of neem and is a feeding deterrent for insects and arthropods, a valuable pesticide, and is also very useful in preventing cancer progression. Nimbolide is found in many parts of the neem plant especially in leaves and flowers. Nimbolide is a triterpene which is useful in prevention and treatment of many diseases but is also useful for its anticancer activity. Many studies shown, nimbolide have its tumorigenesis and metastasis inhibitor effect. Nimbolide shows its anticancer effects by several mechanisms like suppression of proinflammatory pathways, increased apoptosis and growth arrest, and to the inhibition of carcinogenic activation and antioxidant effects.<sup>10</sup> Neem components cause cancer cells death by inducing apoptosis and promoting autophagy. Neem seed and leaf extracts have been studied for their increased apoptotic effects in various human cancers such as leukaemia, prostate, cervical, and breast cancers. Neem components such as Azadirachtin and Nimbolide have double acting in their mechanism of action against cancer causing cells. They inhibit carcinogen activation and simultaneously induce activation carcinogen detoxification.<sup>11</sup> The upregulation of certain marker enzymes, such as alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase results in Skin tumor. Treatment with aqueous leaf extract of neem can induce significant decrease in the activity of these marker enzymes. The aqueous leaf extract of neem reduced oxidative stress by decreasing lipid peroxidation levels and by enhancing the reduced glutathione contents and activities of various antioxidant enzymes.<sup>12</sup> The neem seeds extracts have shown that some limonoids exhibit potent and active inhibitory effects against melanogenesis in B16 melanoma cells. Azadirachtin exerts a potent inhibitory effect on in vivo two-stage mouse skin carcinogenesis.<sup>13</sup> The presence of various flavonoids in addition to limonoids in neem flower exhibit considerable melanogenesis-inhibitory activities.<sup>14</sup>

In recent years, many constituents from Neem have been shown considerable beneficial against various neurological disorders. The neem extract exhibit protective effect against various disorders like Alzheimer's and Parkinson's disease, mood disorders, ischemic-reperfusion injury. This neuroprotective effect of neem are primarily mediated by their anti-oxidant, anti-inflammatory and anti-apoptotic activities along with their ability to modulate signaling pathways.<sup>15</sup>

The neem extract have shown some antifilarial activity also. Ethanolic extract of neem leaves are rich in polyphenols and possesses strong filaricidal activity against *S. cervi*. This antifilarial activity generated due to increase in the level of reactive oxygen species. Therefore, the ethanolic extract of neem induced increased ROS production possibly have positive correlation with up regulation of pro-apoptotic genes.<sup>16</sup>

The aqueous extract of Neem bark have been shown considerable antisecretory and antiulcer effects. The extract can inhibit pylorus-ligation and drug induced acid secretion. The bark extract is equipotent to ranitidine but more potent than omeprazole in inhibiting pylorus-ligation induced acid secretion. It also shown some gastroprotection against stress ulcer by significantly preventing adhered mucus and

endogenous glutathione depletion. By significantly blocking lipid peroxidation It prevents oxidative damage of the gastric mucosa.<sup>17</sup>

## CONCLUSION

*Azadirachta indica* is a member of Mahogany family recognized around the world as a broad-spectrum pesticide and fertilizer. Currently, the antimicrobial activities of *Azadirachta indica* are being explored through research in the fields of dentistry, food safety, bacteriology, mycology, virology, and parasitology. Neem (*Azadirachta indica*) has been used medicinally for thousands of years. It has many potential uses. This plant is highly abundant in flavonoids, polyphenols, diterpenoids, triterpenoids, limonoids, tannins, coumarin, nimbolide, azadirachtin, azadirone, azadiradione, and gedunin. Some parts of *Azadirachta indica*, including the leaves in various forms, have been used for wound healing or as a repellent. The various extracts of neem plant contains several protective effects in the body. It possess antibacterial activity, antifungal activity, anti cancer activity, anti filarial activity and anti inflammatory activity. It also possess some protective effects in gastrointestinal activity and skin infections.

## REFERENCE

1. Singaravelu S, Sankarapillai J, Sasidharn Chandrakumari A, Sinha P. Effect of *Azadirachta indica* Crude Bark Extracts Concentrations against Gram-Positive and Gram-Negative Bacterial Pathogens. J Pharm Bioallied Sci. 2019 Jan-Mar;11(1):33-37. doi: 10.4103/jpbs.JPBS\_150\_18. PMID: 30906137; PMCID: PMC6394162.
2. Wylie MR, Merrell DS. The Antimicrobial Potential of the Neem Tree *Azadirachta indica*. Front Pharmacol. 2022 May 30;13:891535. doi: 10.3389/fphar.2022.891535. PMID: 35712721; PMCID: PMC9195866.
3. Dutt Y, Pandey RP, Dutt M, Gupta A, Vibhuti A, Raj VS, Chang CM, Priyadarshini A. Silver Nanoparticles Phytofabricated through *Azadirachta indica*: Anticancer, Apoptotic, and Wound-Healing Properties. Antibiotics (Basel). 2023 Jan 9;12(1):121. doi: 10.3390/antibiotics12010121. PMID: 36671322; PMCID: PMC9855199.
4. Hummel HE, Langner SS, Leithold G, Schmutterer H. Neem: Unusually Versatile Plant Genus *Azadirachta* With Many Useful And So Far Insufficiently Exploited Properties For Agriculture, Medicine, And Industry. Commun Agric Appl Biol Sci. 2014;79(2):211-28. PMID: 26084100.
5. Wylie MR, Merrell DS. The Antimicrobial Potential of the Neem Tree *Azadirachta indica*. Front Pharmacol. 2022 May 30;13:891535. doi: 10.3389/fphar.2022.891535. PMID: 35712721; PMCID: PMC9195866.
6. Oscar Herrera-Calderon<sup>1,\*</sup>, Kainat Ejaz<sup>2</sup>, Mahnoor Wajid<sup>3</sup>, Muzzamil Shehzad<sup>4</sup>, Johnny Aldo Tinco-Jayo<sup>5</sup>, Edwin Enciso-Roca<sup>5</sup>, Cesar Franco-Quino<sup>6</sup>, Ricardo Ángel Yuli-Posadas<sup>7</sup>, Victor Chumpitaz-Cerrate<sup>8</sup>. *Azadirachta indica*: Antibacterial Activity of Neem Against Different Strains of Bacteria and their Active Constituents as Preventive in Various Diseases. Pharmacogn J. 2019;11(6)Suppl:1597-1604
7. Mahmoud DA, Hassanein NM, Youssef KA, Abou Zeid MA. Antifungal activity of different neem leaf extracts and the nimonol against some important human pathogens. Braz J Microbiol. 2011 Jul;42(3):1007-16. doi: 10.1590/S1517-838220110003000021. Epub 2011 Sep 1. PMID: 24031718; PMCID: PMC3768785.
8. Iman M, Taheri M, Bahari Z. The anti-cancer properties of neem (*Azadirachta indica*) through its antioxidant activity in the liver: its pharmaceuticals and toxic dosage forms. A literature review. J Complement Integr Med. 2021 May 10;19(2):203-211. doi: 10.1515/jcim-2021-0009. PMID: 33964199.
9. Zingue S, Kamga Silihe K, Fouba Bourfane I, Boukar A, Tueche AB, Njuh AN, Njamen D. Potential of Regular Consumption of Cameroonian Neem (*Azadirachta indica* L.) Oil for Prevention of the 7,12-Dimethylbenz(a)anthracene-Induced Breast Cancer in High-Fat/Sucrose-Fed Wistar Rats. Evid Based Complement Alternat Med. 2019 Apr 7;2019:2031460. doi: 10.1155/2019/2031460. PMID: 31080481; PMCID: PMC6475536.
10. Moga MA, Bălan A, Anastasiu CV, Dimienescu OG, Neculoiu CD, Gavriș C. An Overview on the Anticancer Activity of *Azadirachta indica* (Neem) in Gynecological Cancers. Int J Mol Sci. 2018 Dec 5;19(12):3898. doi: 10.3390/ijms19123898. PMID: 30563141; PMCID: PMC6321405.
11. Agrawal S, Bablani Popli D, Sircar K, Chowdhry A. A review of the anticancer activity of *Azadirachta indica* (Neem) in oral cancer. J Oral Biol Craniofac Res. 2020 Apr-Jun;10(2):206-209. doi: 10.1016/j.jobcr.2020.04.007. Epub 2020 Apr 18. PMID: 32489822; PMCID: PMC7254467.

12. Paul R, Prasad M, Sah NK. Anticancer biology of *Azadirachta indica* L (neem): a mini review. *Cancer Biol Ther.* 2011 Sep 15;12(6):467-76. doi: 10.4161/cbt.12.6.16850. Epub 2011 Sep 15. PMID: 21743298.
13. Kikuchi T, Ishii K, Noto T, Takahashi A, Tabata K, Suzuki T, Akihisa T. Cytotoxic and apoptosis-inducing activities of limonoids from the seeds of *Azadirachta indica* (neem). *J Nat Prod.* 2011 Apr 25;74(4):866-70. doi: 10.1021/np100783k. Epub 2011 Mar 7. PMID: 21381696.
14. Kitdamrongtham W, Ishii K, Ebina K, Zhang J, Ukiya M, Koike K, Akazawa H, Manosroi A, Manosroi J, Akihisa T. Limonoids and flavonoids from the flowers of *Azadirachta indica* var. *siamensis*, and their melanogenesis-inhibitory and cytotoxic activities. *Chem Biodivers.* 2014 Jan;11(1):73-84. doi: 10.1002/cbdv.201300266. PMID: 24443427.
15. Sandhir R, Khurana M, Singhal NK. Potential benefits of phytochemicals from *Azadirachta indica* against neurological disorders. *Neurochem Int.* 2021 Jun;146:105023. doi: 10.1016/j.neuint.2021.105023. Epub 2021 Mar 20. PMID: 33753160.
16. Mukherjee N, Mukherjee S, Saini P, Roy P, Sinha Babu SP. Antifilarial effects of polyphenol rich ethanolic extract from the leaves of *Azadirachta indica* through molecular and biochemical approaches describing reactive oxygen species (ROS) mediated apoptosis of *Setaria cervi*. *Exp Parasitol.* 2014 Jan;136:41-58. doi: 10.1016/j.exppara.2013.11.006. Epub 2013 Nov 23. PMID: 24275557.
17. Bandyopadhyay U, Biswas K, Chatterjee R, Bandyopadhyay D, Chattopadhyay I, Ganguly CK, Chakraborty T, Bhattacharya K, Banerjee RK. Gastroprotective effect of Neem (*Azadirachta indica*) bark extract: possible involvement of H(+)-K(+)-ATPase inhibition and scavenging of hydroxyl radical. *Life Sci.* 2002 Nov 1;71(24):2845-65. doi: 10.1016/s0024-3205(02)02143-4. PMID: 12377267.

