

International Journal of Pharmacognosy and Pharmaceutical Sciences



ISSN Print: 2706-7009
ISSN Online: 2706-7017
IJPPS 2022; 4(2): 01-05
www.pharmacognosyjournal.net
Received: 13-06-2022
Accepted: 26-06-2022

Archana Seethapathy
Research Scholar, Department
of Biosciences and Sericulture,
Sri Padmavati Mahila
Visvavidyalayam (SPMVV),
Tirupati, Andhra Pradesh,
India

Suvarna Latha Anchapakkula
Assistant Professor,
Department of Biosciences and
Sericulture, (SPMVV),
Tirupati, Andhra Pradesh,
India

Nagalakshamma Kataru
Professor, Department of
Biosciences and Sericulture,
(SPMVV), Tirupati, Andhra
Pradesh, India

Corresponding Author:
Archana Seethapathy
Research Scholar, Department
of Biosciences and Sericulture,
Sri Padmavati Mahila
Visvavidyalayam (SPMVV),
Tirupati, Andhra Pradesh,
India

The extracts of neem (*Azadirachta indica*) as a source of potential antimicrobial agent: An overview

**Archana Seethapathy, Suvarna Latha Anchapakkula and
Nagalakshamma Kataru**

DOI: <https://doi.org/10.33545/27067009.2022.v4.i2a.37>

Abstract

Plants have been a source of herbal remedies throughout the history of mankind. Various medicinal plants have been used for years in daily life to treat diseases all over the world. Screening of medicinal plants for bioactive compounds leads to development of less expensive new antimicrobial agents with improved safety and efficacy. *Azadirachta indica* (neem) is a multipurpose tree with multiple health benefits. Different parts of the plant are shown to exhibit antimicrobial effects against a wide variety of microorganisms. Neem (*Azadirachta indica*) is recognized as a medicinal plant well known for its antibacterial, antimalarial, antiviral, Antiulcer, Antidermatic, larvicidal, Anti-inflammatory, properties. Neem has become valuable plant in the world which shows the solutions for hundreds to thousands problems. The parts of Neem tree such as Root, bark, leaf, flower, seed and fruit together possesses biological activities. Various compounds have been obtained from various parts of neem such as Margolone, margolonone and isomargolonone are tri-cyclic diterpenoids isolated from stem bark are shown to exhibit antibacterial activity. Nimbidin and nimbolide from seed oil show antifungal, antimalarial and antibacterial activity including inhibition of Mycobacterium tuberculosis. However presence of high concentrations of azadirachtins, quercetin and β -sitosterol in *A. indica* leaves might be responsible for strong antibacterial and antifungal activity compared with bark and seed. It is possible that neem may take a role as an adjuvant to the use of antibiotics or as a replacement of current antibiotics. In the present review the antimicrobial activity in different parts of neem tree has been reported.

Keywords: *Azadirachta indica*, antimicrobial agent, antibacterial and antifungal activity

Introduction

The plant product or natural products show an important role in diseases prevention and treatment through the enhancement of antioxidant activity, inhibition of bacterial growth, and modulation of genetic pathways. The therapeutic role of number of plants in diseases management is still being enthusiastically researched due to their less side effect and affordable properties. It has been accepted that drugs based on allopathy are expensive and also exhibit toxic effect on normal tissues and on various biological activities. It is a largely accepted fact that numerous pharmacologically active drugs are derived from natural resources including medicinal plants^[1, 2].

Neem ingredients are applied in Ayurveda, Unani, Homeopathy, and modern medicine for the treatment of many infectious, metabolic diseases^[3, 4]. Different types of preparation based on plants or their constituents are very popular in many countries in diseases management. In this vista, neem (*Azadirachta indica*), a member of the Meliaceae family, commonly found in India, Pakistan, Bangladesh, and Nepal, has therapeutic implication in diseases cure and formulation based on the fact that neem is also used to treat various diseases. *Azadirachta indica* has complex of various constituents including nimb in, nimbidin, nimbolide, and limonoids and such types of ingredients play role in diseases management through modulation of various genetic pathways and other activities. Quercetin and β -sitosterol were first polyphenolic flavonoids purified from fresh leaves of neem and were known to have antifungal and antibacterial activities^[5, 6]. Numerous biological and pharmacological activities have been reported including antibacterial^[7], antifungal^[8], and anti-inflammatory. Earlier investigators have confirmed their role as anti-inflammatory,

antiarthritic, antipyretic, hypoglycemic, antigastric ulcer, antifungal, antibacterial, and antitumour activities [9-12] and the various therapeutics role of neem and its active ingredients in the diseases prevention and treatment through the modulation of various biological pathways.

Table 1: Taxonomic position of *Azadirachta indica* (neem).

Order: Rutales
Suborder: Rutinae
Family: Meliaceae
Subfamily: Melioideae
Tribe: Melieae
Genus: *Azadirachta*
Species: *indica*

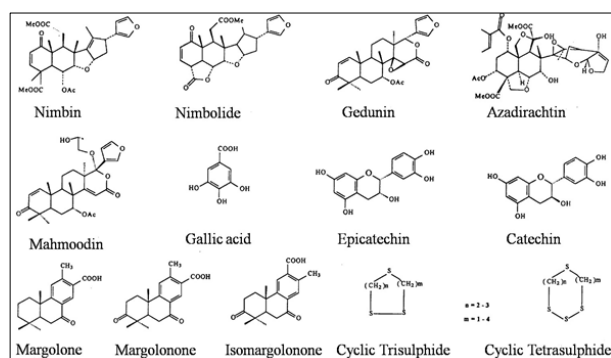
Botanical Description of Neem

Neem tree belongs to the family Meliaceae which is found in abundance in tropical and semitropical regions like India, Bangladesh, Pakistan, and Nepal. It is a fast-growing tree with 20–23m tall and trunk is straight and has a diameter around 4-5 ft. The leaves are compound, imparipinnate, with each comprising 5–15 leaflets. Its fruits are green drupes which turn golden yellow on ripening in the months of June–August.

Active Compounds of *Azadirachta indica* L. (Neem)

Azadirachta indica L. (neem) shows therapeutics role in health management due to rich source of various types of ingredients.

The most important active constituent is azadirachtin and the others are nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbin, gedunin, salannin, and quercetin. Leaves contain ingredients such as nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione, and nimbiol. Quercetin and β sitosterol, polyphenolic flavonoids, were purified from neem fresh leaves and were known to have antibacterial and antifungal properties and seeds hold valuable constituents including gedunin and *Azadirachta* [23].



Nimbin Nimbin is a triterpenoid isolated from Neem. Nimbin is thought to be responsible for much of the biological activities of neem oil, and is reported to have anti-inflammatory, antipyretic, fungicidal, antihistamine and antiseptic properties [24]. Azadirachtin, a chemical compound belonging to the limonoid group, is a secondary metabolite present in neem seeds. It is a highly oxidized tetranortriterpenoid which boasts a plethora of oxygen-bearing functional groups, including an enol ether, acetal,

hemiacetal, tetra-substituted epoxide and a variety of carboxylic esters [24].

Gedunin Gedunine is an organic compound that is classified with the meliacines and as such with the triterpenoids. The substance is found in trees from the Mahogany family (Meliaceae), including the neem *Azadirachta indica*, the krappa (*Carapa guianensis*) and the tiana (*Entandrophragma angolense*). It also occurs in the mangrove *Xylocarpus granatum*. The medicinal effects of gedunine have been shown against filariasis, cancer, gastric ulcers and malaria. It also has an effect against the dengue mosquito, *Culex quinquefasciatus* and the European corn borer [24].

Mechanism of Action of Active Compounds

Neem (*Azadirachta indica*), a member of the Meliaceae family, has therapeutics implication in the diseases prevention and treatment. But the exact molecular mechanism in the prevention of pathogenesis is not understood entirely. It is considered that *Azadirachta indica* shows therapeutic role due to the rich source of antioxidant and other valuable active compounds such as azadirachtin, nimbolinin, nimbin, nimbidin, nimbidol, salannin, and quercetin. Possible mechanism of action of *Azadirachta indica* is presented as follows.

Neem (*Azadirachta indica*) plants parts shows antimicrobial role through inhibitory effect on microbial growth/potentiality of cell wall breakdown. Azadirachtin, a complex tetranortriterpenoid limonoid present in seeds, is the key constituent responsible for both anti-feedant and toxic effects in insects [18]. Results suggest that the ethanol extract of neem leaves showed *in vitro* antibacterial activity against both *Staphylococcus aureus* and MRSA with greatest zones of inhibition noted at 100% concentration [19]. Neem plays role as free radical scavenging properties due to rich source of antioxidant. Azadirachtin and nimbolide showed concentration-dependent antiradical scavenging activity and reductive potential in the following order: nimbolide > azadirachtin > ascorbate [20].

Neem ingredient shows effective role in the management of cancer through the regulation of cell signaling pathways. Neem modulates the activity of various tumour suppressor genes (e.g., p53, pTEN), angiogenesis (VEGF), transcription factors (e.g., NF- κ B), and apoptosis (e.g., bcl2, bax). Neem also plays role as anti-inflammatory via regulation of proinflammatory enzyme activities including cyclooxygenase (COX), and lipoxygenase (LOX) enzyme.

Therapeutic Implications of Neem and Its Various Ingredients in Health Management

Active constituents play role in the diseases cure via activation of anti-oxidative enzyme, rupture the cell wall of bacteria and play role as chemo preventive through the regulation of cellular pathways.

Antimicrobial Effect

Neem and its ingredients play role in the inhibition of growth of numerous microbes such as viruses, bacteria, and pathogenic fungi. The role of neem in the prevention of microbial growth is described individually as follows.

Antibacterial Activity

A study was performed to evaluate antimicrobial efficacy of herbal alternatives as endodontic irrigants and compared

with the standard irrigant sodium hypochlorite and finding confirmed that leaf extracts and grape seed extracts showed zones of inhibition suggesting that they had antimicrobial properties [25]. Furthermore, leaf extracts showed significantly greater zones of inhibition than 3% sodium hypochlorite [26].

The antibacterial activity of neem extracts against 21 strains of foodborne pathogens was evaluated and result of the study suggested the neem extracts possess compounds containing antibacterial properties that can potentially be useful to control foodborne pathogens and spoilage organisms [27]. Another experiment was made to evaluate the antibacterial activity of the bark, leaf, seed, and fruit extracts of *Azadirachta indica* (neem) on bacteria isolated from adult mouth and results revealed that bark and leaf extracts showed antibacterial activity against all the test bacteria used [28]. Furthermore, seed and fruit extracts showed antibacterial activity only at higher concentrations. Antiviral Activity.

Results showed that neem bark (NBE) extract significantly blocked HSV-1 entry into cells at concentrations ranging from 50 to 100 $\mu\text{g}/\text{mL}$ [28]. Furthermore, blocking activity of NBE was noticed when the extract was preincubated with the virus but not with the target cells suggesting a direct anti-HSV-1 property of the neem bark [29]. Leaves extract of neem (*Azadirachta indica* A. Juss.) (NCL-11) has shown virucidal activity against coxsackie virus B-4 as suggested via virus inactivation and yield reduction assay besides interfering at an early event of its, replication cycle [30].

Antifungal Activity

Experiment was made to evaluate the efficacy of various extracts of neem leaf on seed borne fungi *Aspergillus* and *Rhizopus* and results confirmed that growth of both the fungal species was significantly inhibited and controlled with both alcoholic and water extract. Furthermore, alcoholic extract of neem leaf was most effective as

compared to aqueous extract for retarding the growth of both fungal species [31]. Another finding showed the antimicrobial role of aqueous extracts of neem cake in the inhibition of spore germination against three sporulating fungi such as *C. lunatus*, *H. pennisetti*, and *C. gloeosporioides* f. sp. *Mangifera* [32] and results of the study revealed that, methanol and ethanol extract of *Azadirachta indica* showed growth inhibition against *Aspergillus flavus*, *Alternaria solani*, and *Cladosporium* [33]. Aqueous extracts of various parts of neem such as neem oil and its chief principles have antifungal activities and have been reported by earlier investigators [34-36]. A study was undertaken to examine the antifungal activity of *Azadirachta indica* L. against *Alternaria solani* Sorauer and results confirmed that ethyl acetate fraction was found most effective in retarding fungal growth with MIC of 0.19 mg and this fraction was also effective than fungicide (Metalaxyl +mancozeb) as the fungicide has MIC of 0.78mg [37].

Antimalarial Activity

Experiment was made to evaluate the antimalarial activity of extracts using *Plasmodium berghei* infected albino mice and results revealed that neem leaf and stem bark extracts reduced the level of parasitemia in infected mice by about 51–80% and 56–87%, respectively, [38] and other studies showed that azadirachtin and other limonoids available in neem extracts are active on malaria vectors [39-41]. Another finding based on crude acetone/water (50/50) extract of leaves (IRAB) was performed to evaluate the activity against the asexual and the sexual forms of the malaria parasite, *Plasmodium falciparum*, *in vitro* and results showed that, in separate 72-hour cultures of both asexual parasites and mature gametocytes treated with IRAB (0.5microg/mL), parasite numbers were less than 50% of the numbers in control cultures, which had 8.0% and 8.5% parasitemia, respectively [42].

Table 1: Biological activities of some neem compounds [43-45]

S. No	Compound Name	Source	Biological activity
1	Nimbidin	Seed oil	Anti-inflammatory Antiarthritic Diuretic Hypoglycaemic Antifungal Spermicidal Antigastric ulcer Antibacterial Antipyretic
2	Sodium nimbidate	Seed oil	Anti-inflammatory
3.	Azadirachtin	Seed oil	Antimalarial
4.	Nimbin	Seed oil	Spermicidal
5.	Nimbolide	Seed oil	Antimalarial
			Antibacterial
6.	Gedunine	Seed oil	Antimalarial
			Antifungal
7.	. Mahmoodin	Seed oil	Antibacterial
8.	Gallic acid (-) epicatechin and catechin	Bark	Anti-inflammatory
9.	Margolone, mergolonone and isomargolonone	Bark	Antibacterial
10.	Cyclic trisulphide and cyclic tetrasulphide	Leaf	Antifungal
11.	Polysaccharides		Anti-inflammatory
12.	Polysaccharides G1A, G1B	Bark	Antitumor
13.	Polysaccharides G2A, G3A	Bark	Anti-inflammatory
14.	NB-2 peptidoglycan	Bark	Immunomodulatory

Table 2: Medicinal Uses of Neem [43-45]

Part	Medicinal uses
Leaf	Leprosy, eye problem, epistaxis, intestinal worms, anorexia, biliousness, skin ulcers
Bark	Analgesic, alternative and curative of fever
Flower	Bile suppression elimination of intestinal worms and phlegm
Fruit	Relieves piles, intestinal worms, urinary disorders, epistaxis, phlegm, eye problem,

	diabetes, wounds and leprosy
Twig	Relieves cough, asthma, piles, phantom tumor, intestinal worms, spermatorrhea, obstinate urinary disorders, diabetes
Gum	Effective against skin diseases like ring worms, scabies, wounds and ulcers
Seed pulp	Leprosy and intestinal worms
Oil	Leprosy and intestinal worms
Root, bark, leaf, flower and fruit together	Blood morbidity, ulcers, burning, biliary afflictions, leprosy, skin sensation and itching

Conclusion

Azadirachta indica (Neem) plant acts as a medicinal plant have been found effective in the treatment of bacterial, fungal, viral and other diseases and revealed the antibacterial, antifungal, antiviral, antimalarial, antiulcer and other biological activities.

Due to increasing antibiotic resistance in microorganisms and side effects of synthetic antibiotics neem plant are now growing popularity in the treatment of many infections. Neem plant is considered as clinically effective and safer alternatives to the synthetic antibiotics. Extensive research in the area of isolation and characterization of the active principles of neemplant is essential so that better, safer and cost effective drugs for curing various diseases and infection.

References

- Pingale Shirish S. Hepatoprotection study of leaves of *Azadirachta indica* A. Juss, International Journal of Pharmaceutical sciences, review and research. 2010;3(2):37-42.
- Girish K, Bhat S, Shankara. neem-A green treasure, Electronic Journal of Biology. 2008;4(3):102-111.
- Biswas Kausik, Chattopadhyay Ishita, Banerjee K Ranjiit and Bandyopadhyay Uday, biological activities and medicinal properties of neem (*Azadirachta Indica*) current science. 2002;82(10):1336-1345.
- Faiza Aslam, Khalil-Ur-rehman, Muhammad Asghar, Muhammad Sarwar. Pak. J Agri. Sci, 2009, 46(3).
- Thakurta P, Bhowmik P, Mukharjee S, Hajra TK, Patra A, Bag PK. antibacterial, anti-secretory and anti-hemorrhagic activity of *Azadirachta indica* used to treat cholera and diarrhea in India. J Ethnopharmacol. 2007;111(3):607-612.
- Koona S, Budida S. / not Sci boil. 2011;3(1):65-69.
- Winee Surabhilal, Amit Alexander Charan, Abhilesh Bind, International Journal of Medicine and Pharmaceutical Sciences (IJMPS) ISSN 250-0049. 2013;3(2):79-86.
- Irshad S. / Intl R. J of pharmaceuticals. 2011;01(01):9-14. ISSN 2048-4143
- Baswa M, Rath CC, Dash Sk. *et al* Antibacterial activity of karanj (*Pongamia pinnata*) and neem (*Azadirachta indica*) seed oil; a preliminary report, *microbios*. 2001;105:183-189.
- Srinivasan D, Nathan S, Suresh *et al*. antibacterial activity of neem (*Azadirachta Indica*) and Tamarind (*Tamarindus indica*) leaves. Asian J microbial bio technol Environ Sci. 2001;3:67-73.
- Siswomihardjo, *et al*. Int chin J dent. 2007;7:27-29.
- Venugopal PV, Venugopal TV. anti-dermatophytic activity of neem (*Azadirachta indica*) leaves *In vitro* Indian J Pharmacol. 1994;26:141-3
- Ranganathan S Menon Thangam Balajee AM, Raja SM. Antidermatophytic activities of *Azadirachta indica*: An *in vitro* and *in vivo* studies Indian Journal of dermatology. 1996;41(4):113-117.
- Mahmood DA, Hassanein NM, Youssef KA, Abou Zeid MA. Antifungal activity of different neem leaf extracts and the nimonal against some important human pathogens. Braz J microbial, 2011, 42(3). sao Paulo July/sept
- Rao BS, Nazma, Rao MJ. Antifungal activity of gedunin, cur. Sci. 1977;46:714-716.
- Pant N, Garg HS, Madhusudanan KP, Bhakuni DS. Fitoterapia, sulfurous compounds from *Azadirachta indica* leaves. 1986;57:302-304.
- Dua VK, Nagpal BN, Sharma VR. Repellant action of neem cream against mosquitoes. Indian J malarial. 1995;32:47-53.
- Rojanapo W, Suwanno S, Somaree R, Glinsukon T, Thebtaranonth Y. screening of antioxidants from some thia vegetables and herbs, JSci Thailand,1985:11:177-188.
- Khalid SA, Duddeck H, Gonzalez-Sierra M. isolation and characterization of antimalarial agent of the neem tree, *Azadirachta indica*, Journal of natural product. 1989;52:922-927.
- kabeh Jd, MGDSS jalingo. Mini review exploiting neem for improved life / Int J agrbiol. 2007;9:3.
- Hassan Amer, Wafaa A, Helmy, Hanan AA. Taie *In vitro* antitumor and antiviral activities of seeds and leaves from neem (*Azadirachta indica*) extracts; International journal of Academic research. 2010;2:2.
- Pillai NR, Seshadri DS, Santhakumari G. Indian Journal of Medical Research. 1978;68:169-175.
- Pillai NR, Santhakumari G. effects of nimbidin on acute and chronic gastro-duodenal ulcer models in experimental animals, *plantamedica*. 1984;50:143-146.
- Dharmani P, Palit G. exploring Indian Medicinal plants for antiulcer activity, indian J pharmaceutical. 2006;38(2)95-99.
- Bhargava KP, Gupta M B, Gupta G P, Mitra C R, anti-inflammatory activity of saponins and other natural products. Indian J Med res. 1970;58(6):724-730.
- Pillai NR, Santhakumari G. antiarthritic and anti-inflammatory actions of nimbidin *planta medica*. 1981;43:59-63.
- David SN. Mediscope, antipyretic of neem oil and its constituents. 1969;12:25-27.
- Pillai NR, Santhakumari G. Hypoglycemic activity of *Milia Azadirachta linn* (neem), Indian journal of medical research. 1981;74:931-933.
- Sharma VN, Saxena KP. Spermicidal action of sodium nimbinat Indian journal of medical research. 1959;47:322-324.
- Murthy SP, Sirsi M. Pharmacological studies on melia *Azadirachta indica*. Indian journal of physiology and pharmacology. 1958;2:387-396.

31. Bhide NK, Mehta DJ, Lewis RA. Diuretic action of sodium nimbinate. Indian Journal of Medical Sciences. 1958;12:141- 145.
32. Jones I, Ley SV, Denholm AA, Lovell H, Wood A, Sinden RE. Sexual development of malaria parasites is inhibited *in vitro* by the neem extract azadirachtin and its semi-synthetic analogus, FEMS microbial let. 1994;120(3):267-273.
33. Sharma VN, Saksena KP. Sodium nimbinate-*in vitro* study of its spermicidal action. Indian journal of medical research; c1959. 13 Dec p. 1038-1042.
34. Rachanakij S, Thebtarananth Y, Yenjal CH, Yuthavong Y. nimbolide a constitute of *Azadirachta indica* inhibits Plasmodium falciparum in culture Southeast Asian J trop med public health. 1985;16:66-72.
35. Deva kumar C. Sukh Dev in neem (eds Randhawa and parmar B S). 1996;2:77-110.
36. Van der Nat JM, Van Der Sluis WG, T Hart LA, Van disk H silva KTD, Labadie RP. Planta med. 1991;57:65-68.
37. Ara I, Siddiqui BS faizi S, siddiqui S. structurally novel diterpenoid constituents from the stem bark of *Azadirachta indica* (Meliaceae) J chemsocperkin trans. 1989;2:343-345.
38. Kakai T, Koha JP, anti-inflammatory polysaccharides from *Melia Azadirachta*, chem. Abst. 1984;100:91350.
39. Fujiwara T, Takeda T, Ogihara Y, Shimizu M, Nomura T, Tomita Y. studies on the structure of polysaccharides from the bark of *Melia Azadirachta*, chem pharm bull. 1982;30:4025-4030.
40. Fujiwara T, Takeda T, Ogihara Y, Sugishita E, Shimizu M, Nomura T *et al.* further studies on the structure of polysaccharides from bark of *Malia Azadirachta* chem pharm bull *ibid.* 1984;32:1385-1391.
41. Vander Nat JM, Kierx JPAM, Van Dijk H, De Silva KTD, Labadie RPS. Ethnopharmacol. 1987;19:125-131.
42. Vander Nat JM, Hart LAT, Vander Sluis WG, Van Dijk H, Vander Berg, A JJ De Silva, *et al.* *ibid.* 1989;27:15-24.
43. Ranjit R, Raut Ajit R, Sawant, Bhagyashree B. Jamge. Antimicrobial activity of *Azadirachta indica* (Neem) Against Pathogenic Microorganisms. Journal of Academia and Industrial Research (JAIR) ISSN:2278-5213. 2014;3(7):327-329.
44. Sudhir Kumar P. Debasis Mishra, Goutam Ghosh, Chandra S. Panda. Biological action and medicinal properties of various constituent of *Azadirachta indica* (Meliaceae) an Overview, Annals of Biological Research ISSN 0976-1233. 2010;1(3):24-34.
45. Sharma Pankaj, Tomar Lokeshwar, Bachwani Mukesh, Bansal Vishnu. Review on Neem (*Azadirachta indica*): Thousand problems one solution, International Research Journal of Pharmacy, ISSN 2230-8407. 2011;(12):97-102.