



An Overview of Pharmacognostical, Phytochemical and Pharmacological Activities of *Azadirachta indica* Juss

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Abstract

Neem (*Azadirachta indica*) belonging to the Meliaceae family is popular tree. In Traditional System of Medicine, bark, leaf, flower, seed, oil and other parts are used for number of ailments. Number of patents has been filed for neem for pharmacological uses. This review provides a detailed view on Pharmacognosy, phytochemistry and pharmacological activity reported so far.

Keywords: Neem, *Azadirachta indica*, Pharmacognosy, phytochemistry, Pharmacological activity, Review

Introduction

Azadirachta indica is an adaptable medicinal tree belonging to Meliaceae family. Every part of neem has some beneficial effects on human ailments and hence it has gained worldwide importance. 4000 years existence plant in India is *Azadirachta indica*.

A. indica also known as Margosa tree, as 'arista' or 'nimba' and 'nimbatī swasthyamdadati in Sanskrit meaning 'to give good health'. The biological benefits of neem are enlisted in 'Charak-Samhita' and 'Susruta-Samhita', which forms the basis of Ayurvedic system of treatment. 'Azad- Darakth- E- Hind' means 'Free tree of India' in Persian. Neem is considered genetic diverse plant. In India, Neem was used for chicken pox and small pox from antiquity. It has been used for environment protection such as soil erosion, soil fertility, insecticide, pesticide etc. [1].

Habitat

Although the exact native region of Neem tree is not known, it is thought to be originating naturally in south Asia and it grows in natural forests with drier-climatic condition of southern India and Burma. For many millennia, neem has been cultivated in India, Pakistan, Sri Lanka, Bangladesh, Myanmar, Thailand, Southern Ma-

laysia, and the drier Indonesian islands from Java eastward. Neem was introduced to Fiji and Mauritius during early 19th century.

Climate

It is a drought resistant tree and the mean annual temperature ranges from 21 to 32°C for its growth. In India, neem grows at temperatures between 0 to 49°C and annual rainfall of less than 600 mm. The plant is also used in afforestation programmes in arid and semi-arid regions.

Propagation and cultivation

It is a hard tree, grows well in saline soils and drought conditions. Growth is slow in water-logged conditions. Propagated from seeds, which should be sown immediately after ripening, as their viability is very short. Seeds germinate within three weeks time. Root suckers and stem cuttings are also used for planting. It can be grown in all types of soil, but black-loam soil is more suitable. Within one year, the seedlings grow up to a height of 120 cm. Rapid multiplication through leaf culture has been found successful. Tissue culture techniques have been reported for the production of azadirachtin from cultures of leaves and flowers. 20 weeks old callus of leaves is reported to yield maximum concentration of azadi-

rachtin up to 2.68% and the 12 weeks old flower callus 2.46 % of azadirachtin on dry weight basis [2,3].

Scientific classification of neem

- Kingdom: Plantae
- Division: Magnoliophyte
- Class: Magnoliopsida
- Order: Sapindales
- Family: Meliaceae
- Genus: *Azadirachta*
- Species: *indica*
- Scientific name: *Azadirachta indica*

Vernacular names

- Hindi - Nim, Nimb
- English - Margosa, Neem, Indian Lilac
- Konkani - Beva-rooku
- Bengali - Nim, Nimgach
- Marathi - Kadunimb
- Gujarathi - Limba
- Tamil - Veppamaram, Vempu, Veppam
- Punjabi - Nimb
- Malayalam - Veepu, Aryaveppu, Aruveppu, Kaippan, Veppu, Vepa
- Oriya - Nimo
- Telugu - Vepa, Yapachettu
- Kannada - Bevinmar, Kahibeve [4].

Botanical description

Macroscopical characteristics

A large evergreen tree, 12 to 18 m high with bitter in taste.

- **Bark:** Dark brown to grayish, thick hard woody, external rough surface, scaly, oblique furrows, bitter taste, characteristic odor, straight trunk.
- **Leaves:** Leaves are dark green coloured, compound, ovate-lanceolate, attenuate, opposite, imparipinnate (5-15 leaflets), serrated edges, short petioles, 3-8 cm long, with typical odor.
- **Fruits:** Glabrous, olive like drupe, oval to roundish, green, edible and thin skinned.
- **Flowers:** Flowers are white, fragrant, arranged in axillary panicles, protandrous, bisexual flowering.
- **Seed:** One seeded only, dirty brown in color, with gritty touch and oily.

Microscopical characteristics

The transverse section showed outer dark reddish brown rhytidoma consisting of 10 to 15 rows of outer most dark brown colored cells of cork, and a narrow band of stone cells lying underneath this followed by outer few rows of parenchyma and inner wide 20 to 25 rows of dark orange brown colored phloem tissue; very narrow band of phelloderm with tangentially running tannin cells and very wide phloem with discontinuous groups of crystal fibers alternating with medullary rays. Prismatic crystals of calcium oxalate traversed throughout the parenchymatous cells.

Powder characteristics

It shows abundant fragments of rhytidoma embedded with stone cells, isolated or groups of fibres; few oval to rectangular sclerides associated with idioblast containing prismatic crystals of calcium oxalate, few simple, oval to spherical starch grains and parenchymatous cell filled tannin contents [5].

Traditional actions and uses

- **Bark:** It is urinary astringent, acrid, pectoral, tonic, hyperdipsia, leprosy, skin diseases, eczema, leucoderma, pruritis, malaria, burning sensation, tumor, dyspepsia, intestinal worms, hepatopathy, cough, bronchitis, urine incontinence, diabetes, inflammation, wound healing, ulcer, amenorrhoea, lumbago, hemorrhoids, otalgia, syphilis and fatigue.
- **Leaves:** It is anthelmintic, insecticidal, demulcent, refrigerant, skin diseases, leucoderma, in burning sensation, leprosy, pruritus, antiseptic, ophthalmic, ophthalmopathy, intestinal worms, dyspepsia, ulcer, tuberculosis, boils, eczema, malarial and intermittent fevers.
- **Flowers:** It is used as a refrigerant, ophthalmic, stomachic, anthelmintic, tonic, burning sensation, ophthalmopathy, colic, dyspepsia, intestinal worms and general debility.
- **Seeds:** It is used as acrid, thermogenic, purgative, emollient, anodyne, anthelmintic, depurative, vulnerary, uterine stimulant, urinary astringent, tumors, leprosy, skin diseases, odontalgia, intestinal worms, wounds, ulcers and diabetes.
- **Oil:** It is anthelmintic, anodyne, depurative, chronic skin diseases, syphilitic sores, ulcer, ringworm, scabies, worms, fever and leprosy [1,4].

Ayurvedic properties

- Rasa: Tikta, Kashaya
- Guna: Laghu
- Veerya: Sheeta
- Vipaka: Katu
- Doshaghna: Kaphapitashamaka
- Rogaghna: Vidradhi, Granthi, Amavata, Vamana, Kaphapaitika etc.
- Karma: Vranapachana, Vranashodhana, Ampachana, Juaraghna, Vishamapwara pratibandhaka, Chakshushya etc.

Doses

- Bark powder: 2 to 4 gm
- Leaf juice: 10 to 20 ml;
- Powder: 2-4 g.
- Oil- 5 to 10 drops [6].

Chemical constituents

More than 100 compounds, mostly triterpenoids of protomonoids (proto-meliacin). Limonoids (or meliacins or tetranortriterpenoids) tetranortriterpenoid- γ hydroxy butenolides, pentanortriterpenoids. Hexanortriterpenoid apart from a few non-triterpenoid constituents have been reported from various parts as detailed below.

- **Leaves:** Azadirachtin, azadirachtol, azadirachnol, deacetylazadirachtinol (-3- tigloylazadirachtol), azadiradione, an isomer of epoxyszadiradione, 17 epi and 17-B-hydroxyazadiradione, gedunin, 7-hydroxygedunin, melianone, bol nimboeinol (7-acetoxy-7-hydroxy azadiradione), nimocin, 7-deacetoxy-nimolicin, nimolinone, nimbochalcin and nimocetin, 21,23 24,25- diepoxytirucall-7-en-21-ol salannin, azadirachtin, azadirachtanin, azadirone, azadiradione, epoxyazadiradione, isoazadirolide, nimbandiol nimbinene desacetylnimbinene, nimbin, nimboicinolide, isonimboicinolide, nimbolide nimocinolide, isonimocinolide, nimocinone, 2,3'-dehydrosalannol kaempferol-3-0-8-glucoside, myricetin and 3-L-arabinoside (mellictrin), 3-0-L-ehanmonide and 3-0-rutinoside, quercetin, its 3-galactoside, 3-0-L- thanoside and 3-0-runinoside, nimbaflavones, scopoletin, β -sitosterol and its β -D-glucoside, amino acids, β -carotene, carbohydrates, n-hexacosanol, nomacommol, protein and vitamins.
- **Fruits and Seeds:** Kernels yield about 400-48.9% of the oil and contain high amount of tocopherol, arachidic, linoleic, margosic, myristic, oleic, palmitic and stearic acids, azadirone azadiradione, epoxyazadiradione (nimbinin), gedunin, meldonin, meliatriol, nimbine, mbinene 6-desacetyl nimbinene, nimbidin, nimbidiol, 6-O-acetylnimbandiol, nimbidic acid, salannin, 3-desacetylsalannin, salannol and its acetate, salannolide, vepinine, vilasinin 1,3-diacetylvilasinin, 1-tigloyl-3-acetyl-vilasinin, and tiglic acid (seed oil), in addition, azadirachtin, 22,23-dihydro-23-8-methorey- azadirachtin (vepaol) and its C-23 epimer (isovepaol), 7-desacetyl-7-benzoyl derivatives of azadirone, azadiradione, epoxyazadiradione, 2-dihydro- epoxyazadiradione, 18,28-diepoxyazadiradione, 7-desacetyl-7-benzoyl-geduni acetylneotrichilenone, nimbidin, nimbidinin, salannic (nimbidic) acid (seeds),
- **Flowers:** Benzyl alcohol, β -sitosterol, thioamyl alcohol, arachidic, behenic, colec, oleic, palmitic and stearic acids, kaempferol and its 3-glucoside, quercetin -3- galactoside and myricetin-3-L-arabinoside, azadirachtin and margosene. flowerine, flowerone, O- methylazadirone and diepoxyazadirol. Other known constituents present in flowers are triterpenoid (trichilenone acetate), flavanones, nimbaflavone, 3'-prenyl-naringenin and 4-(2-hydroxyethyl) phenol.
- **Heartwood:** Tannin, β -sitosterol and its glucoside, 24-methylene-cycloartenol, 4,14, α -dimethyl-3- α -ergosta-8, 24(28)-d-38-ol 4-methyl-Sa-ergosta-8, 24(28)-dien-38-ol, nimatone, nimbinene, 6-desacetyl nimbinene, nimbolins A and B.
- **Stem bark:** Vanilic acid, catechol, campesterol stigmaterol, sitosterol, β -amyrin, lupeol, nimbin, nimbidin, nimbinin sumpiol kulinone, kulactone, kulolactone methyl kulonate, 60-hydroxy-4-stigmasten-3-one and 68-hydroxy-4-campesten-3-one.
- **Wood:** Gedunin 7-deacetoxy-7-axogedunin, fraxinellone, nimbolin A and gydoeucalmon, melanin A and B.
- **Twigs:** Margosinolide, isomargosinolide, desacetyl nimbinolide and desacetyl isonimbinolide
- **Wood Oil:** Cycloeucaenol, 24- methylene cycloartenol and β -sitosterol
- **Trunk bark:** Nimbiol, sugiol and bosterol nimbolins A and B (trunk wood),

- **Root:** 24-methylene- cycloartenol, 24-methylene-cycloartanone, cycloeucalenol, cycloeucalenone, 4- campesten-3-one, 4-stigmasten-3-one, trans-cinnamic and vanillic acids. nimbin and nimbidin.
- Besides aesculetin, campesterol, 6-hydroxy- 7-methoxy-coumarin, 4 α , 6 α -dihydroxy-A-homoazadirone, isomeldenin, meldenindiol, 17-acetoxy-meliacin, 6-O-acetylnimbandiol, de-sacetylnimbin, nimocinol, isonimolicinolide and nimolinolic acid have been isolated from various parts of tree [7-9].

Identification by TLC

- Stationery phase: Silica Gel GF254 precoated plates
- Mobile phase: Toluene: ethyl acetate: glacial acetic acid: 5:5:1
- Standard preparation: 10 mg of epicatechin is dissolved in 5 ml of methanol
- Sample preparation: Reflux 5 g of drug with methanol for 8 hrs [2 times]. Filter and remove the solvent. Dissolve in 10 ml of methanol.
- Spray reagent: Spray with 10% ethanol potassium hydroxide solution and observe under UV 365 nm.
- Detection: Rf 0.29 corresponding to epicatechin is seen in both standard and test.

Estimation by HPTLC

- Method is followed as per identification method except plate after drying is scanned at 424 nm.
- Content present in the sample is determined from the peak area under the curve.

Quantitative standards

Foreign matter: not more than 0.3 % w/w
 Ash: not more than 3.0 % w/w
 Acid insoluble ash: Not more than 0.25 % w/w
 Alcohol soluble extractive: Not less than 4.5 % w/w
 Water soluble extractive: Not less than 5.0 % w/w [6,10]

Therapeutic properties

The pharmacological activities of phytoconstituents reported so far from this plant is given below in the Table.

Chemical constituents	Biological activity
Nimbidin	Anti-inflammatory Antiarthritic Antipyretic Hypoglycaemic Antigastric ulcer Spermicidal Antifungal Antibacterial Diuretic
Sodium nimbidate	Anti-inflammatory
Nimbin	Spermicidal
Nimbolide	Antibacterial Antimalarial
Gedunin	Antifungal Antimalarial
Azadirachtin	Antimalarial
Mahmoodin	Antibacterial
Gallic acid, (-)epicatechin and catechin	Anti-inflammatory and Immunomodulatory
Margolone, margolonone and isomargolonone	Antibacterial
Cyclic trisulphide, cyclic tetrasulphide	Antifungal
Polysaccharides	Anti-inflammatory
Polysaccharides GIa, GIb	Antitumour
Polysaccharides GIIa, GIIIa	Anti-inflammatory
NB-II peptidoglycan	Immunomodulatory [7-9]
Glycoprotein	Immunomodulatory [10]
Proline	Alzheimer’s and Parkinson’s disease [11]
Epoxyazadiradione	human cervical cancer [12]

Table 1

Pharmacological activities

To understand the pharmacological activity it is given in form of Table below.

Sl No	Activity	Part of plant	Extract	Observation	Reference
1	Antioxidant activity	Leaf, flower, stem bark	Different extracts	High activity in ethanol extract in all parts	[13]
		Flower and seed oil	Ethanol extract	High scavenging activity in both	[14]
		Bark and leaves	Ethanol extract	Bark had high antioxidant activity then leaves	[15]
		Roots	Methanol extract	High scavenging activity	[16]
		Leaves	Methanol and chloroform extract	Methanol extract had better antioxidant activity	[17]
2	Wound healing activity	Oil	-	50% wound healing activity in non healing wound in 44% patients	[18]
		Leaves	Aqueous extract	Significant reduction in wound size	[19]
3	Anti-inflammatory activity	Neem fruit skin	Alcohol extract	Significant anti-inflammatory activity in rats treated with 100mg/kg dose	[20]
		Seed	Oil	Increased inhibition of edema in dose of 0.05-2 ml/kg	[21]
4	Hepatoprotective activity	Leaf	Aqueous extract	Reduced elevated levels of AST and ALT; liver necrosis was reduced	[22]
		Leaf	Aqueous extract	Prevented and reversed the hepatotoxic effect caused by antitubercular drugs	[23]
5	Neuroprotective activity	Neem	Standardized extract	Significantly decreased allodynia, hyperalgesia, motor coordination and motor nerve conduction velocity and reduced oxidative stress and inflammatory markers	[24]
		Leaf	Ethanol extract	Reversed effects of cisplatin and proved neuroprotective activity	[25]
6	Nephroprotective activity	Leaves	Methanol extract	Significant protective effect	[26]
7	Immunomodulatory activity	Oil	-	Activation of cell mediated immune mechanism against mitogens.	[27]
		Leaves	Infusion	Improved antibody titer growth when mixed in drinking water	[28]
8	Antifertility activity	Flower	Alcohol extract	It caused prolongation of diesterus phase with reduction in esterus phase and also reduced numbers of ova	[29]
		Neem	Oil	Reduced spermatogenesis and testosterone level is not affected	[30]
9	Dental health	Neem	Extracts and neem sticks	Decreased the plaque formation and gingival scores reduction	[31]
		Leaves	Petroleum and chloroform extract	Chloroform extract had strong antimicrobial activity against <i>Streptococcus mutans</i>	[32]
10	Antidiabetic activity	Leaves	Ethanol extract	Glucose level is reduced at 250mg/kg dose	[33]
		Root bark	Ethanol extract	Glucose level is reduced at dose of 200,400 and 800mg/kg by 54%	[34]

		Kernel powder	-	Alone and along with glibenclamide was capable of reducing blood glucose level and serum enzymes also	[35]
11	Cardioprotective activity	Leaves	Alcohol extract	Restored biochemical and hemodynamic parameters and had similar effect as cardioprotective as compared to Vitamin E	[36]
12	Antimicrobial activity	Leaves	Ethanol extract	Controls food borne pathogens and other spoilage organism	[37]
		Leaves	Ethanol extract	Zone of inhibition is greater when compared to standard	[38]
		Leaves and seed	Ethanol extract	MIC was found to be 31ug/ml for dermatophytes	[39]
13	Antiviral activity	Bark	Ethanol extract	Blocked HSV-1 virus entry into cells	[40]
14	Anticancer activity	Leaves	Ethanol extract	Increased death of 4T1 breast cancer cells	[41]
		Leaves	Ethanol extract	Decreased lymphocytic leukemia cell survival and increased death	[42]
		Leaves	Ethanol extract	Inhibited mammary tumor including growth and occurrence	[43]
		Leaves	Ethanol extract	suppressed prostate cancer cell lines	[44]
		Leaves	Ethanol extract	Suppressed MCF-2, HeLa, skin, lung, liver cancers	[45]
		Leaves	Ethanol extract	Tumor size decreased in buccal carcinoma in hamster	[46]
		Leaves	-	Reduction in tumor size in murine solid Ehrlich carcinoma	[47]
15	Pesticide activity	Seeds	Oil	Natural pesticide	[48,49]
16	Intestinal ischemic-reperfusion injury	Leaves	Methanol extract	Reduced myeloperoxidase levels	[50]
17	Colitis activity	Leaves	Methanol extract	Inhibited inflammation and colon mucosal damage; increased GSH level	[51]
18	Antipyretic activity	Leaves	Ethanol extract	Reduced body temperature	[52]

Table 2

List of few marketed products and their use.

Sr.	Marketed Product	Uses
1.	Nature neem oil	Making Shampoo, Tooth Paste, Soaps, Cosmetics, Mosquito repellent, Insecticidal,
2.	Total care	Pest Control
3.	Biocare	Animal Skin Care, Healing Aid For Skin Irritation, Minor Cuts, Broken Skin, Pesticidal, Insecticidal
4.	Neem guard	Urea Coating Agent
5.	Nature neem seed cake and seed powder	Organic Plant Food which increase productivity & Soil Fertility, Antifungal

Table 3

Formulations and preparations

Shankhapushpi taila, Jwarasamhara rasa, Mahamarichyadi taila, Pathyadi kvatha, Mahamanjishthadyarishta, Punarnavadi kvatha, Mahasudarshana churna, Raktashodhaka vati, Nimbaharidra khanda, Nimbarishta, Mahagandhaka vati, Nimbadi churna, Panchaguna taila, Madhyam narayana taila, Guduchyadihana kvatha [6].

Safety aspects

The drug used traditionally in prescribed doses may be considered safe.

Conclusion

We can say neem as one plant for treatment of number of ailments. Scientifically it has been proven to be antioxidant, wound healing, antipyretic, antiallergic, antiasthmatic, anti-inflammatory, hepatoprotective, neuroprotective, nephroprotective, immunomodulatory, antifertility, dental hygiene, antidiabetic, cardioprotective, antimicrobial, anticancer, pesticide etc. This review gives the details of chemicals isolated and pharmacological activity of the isolated compounds as well as extract. An extensive research and development work should be undertaken on neem and its products for their better economic and therapeutic utilization.

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Conflicts of Interest

There are no conflicts of interest.

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