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Tree of the 21st century - Neem and its 5 parts

Kaur R[1*], Ankita[2]

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[1*] Ramandeep Kaur, Second Year Post Graduate Scholar, Department of Dravyaguna UG and PG Studies, Government Ayurvedic College, Patiala, Punjab, India.

[2] Ankita, Lecturer, Department of Dravyaguna UG and PG Studies, Government Ayurvedic College, Patiala, Punjab, India.

In traditional medicine, most of the diseases have been treated by plant or plant product administration. Nimba (also known as Margosa tree) is one of the most commonly used plants in Ayurveda to manage many ailments. It is a member of the Meliaceae family, found commonly in India, Africa and America. Different parts of the Nimba have been used since so many centuries for various ailments. Each part of the Neem tree has some medicinal properties. All the plants' parts have been used to prepare therapeutic formulations. Nimba contains various bioactive compounds like Azadirachtin, Nimbinin and Nimbidin. Present paper focuses on the therapeutic use of five parts of the nimb which is also called Panchnimb.

Keywords: Panchnimba, Azadirachta indica, Traditional uses, Ayurvedic drugs

Corresponding Author

Ramandeep Kaur, Second Year Post Graduate Scholar, Department of Dravyaguna UG and PG Studies, Government Ayurvedic College, Patiala, Punjab, India.

Email: ramanbanwait024@gmail.com

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Introduction

The plant products or natural products show an important role in disease prevention and treatment through the enhancement of antioxidant activity, inhibition of bacterial growth, and with modification of genetic pathways. Neem is one of the indigenous medicinal plants of India which possesses medicinal properties in every part viz., roots, seeds, flowers, bark, leaves, fruit pulp, etc. Each of the plant part has been used in the Indian *Ayurvedic* and Unani systems of medicine and has become a cynosure of modern medicine. Indians have long valued the *Nimba* tree; for centuries, millions have cleaned their teeth with *Nimba* twigs, smeared skin disorders with *Nimba*-leaf juice, taken *Nimba* tea as a tonic, and placed *Nimba* leaves in their beds, books, grain bins, cupboard, and closets to keep away troublesome bugs.

In *Ayurvedic* literature Neem is well known for its medicinal properties viz., Neem bark is cool, bitter, astringent, and acrid. In addition to this, it is used to cure tiredness, cough, fever, loss of appetite, worm infestation etc. It also heals wounds and vitiated conditions of *Kapha*, vomiting, skin diseases, excessive thirst and diabetes. Its fruits are bitter, purgative, anti-haemorrhoids and anthelminthic.**[1]**

This tree is an incredible plant that has been declared the "Tree of the 21st century" by the United Nations. The importance of the *Nimba* tree has also been recognised by the US National Academy of Sciences, which published a report in 1992 entitled 'Neem-a tree for solving global problem.**[2]**

This review summarises the role of Neem and its 5 parts along with their active constituents in disease prevention and treatment.

History

The earliest authentic record of the curative properties of Neem and its use in the indigenous system of medicine in India is found in Kautilya's "*Arthashastra*" around the 4th century BC. *Ayurvedic* texts in Sanskrit describe neem as *'Sarva Roga Nivarini'* - (the universal healer or curer of all ailments), *'Arishtha'* (perfect, complete, and imperishable), and *'Nimba'* from the term *'Nimbati Syasthyamdadati'* which means 'to give good health'.

However, in India, it is famous with many other names like 'Divine Tree', "Heal All", "Nature's Drugstore", and "Village Dispensary".**[3]**

The Latinized name of *Nimba* (*Azadirachta indica*), is derived from the Persian. Azad means "free", Dirakht means "tree"; Hind meaning is "of Indian origin". Hence, it means "the free tree of India".**[4]**

Distribution and Botanical Description

Neem tree belongs to the family Meliaceae which is found in abundance in tropical and semitropical regions like India, Bangladesh, Pakistan, and Nepal. **[5]**

The neem tree is a native tree of East India and Burma. Its taxonomical classification is shown in table 1. It is a fast-growing tree with 20–23m tall and the trunk is straight and has a diameter of around 4-5ft. It has rough dark brown bark with wide longitudinal fissures separated by flat ridges. The leaves are compound, and imparipinnate, each comprising 5-15 leaflets.

The compound leaves are themselves alternating with one another. It bears many flowered panicles, mostly in the leaf axils. It produces yellow drupes that are ellipsoid and glabrous, 12-20 mm long. Fruits are green, turning yellow on ripening, aromatic with garlic like odour. Fruit is single seeded. seed is ellipsoid. Fresh leaves and flowers come in March-April. Fruits mature between April and August depending upon locality. Fig no. 1-A,B,C**[6]**

Figure 1A: Leaf

Figure 1B: Bark

Figure 1C: Fruits of Neem

Table 1: Taxonomic classification of *Azadirachta indica* (Neem)

Kingdom	Plantae
Division	Magnoliophyte
Class	Dipsacales
Order	Rutales
Sub-order	Rutinae
Family	Meliaceae
Genus	Azadirachta
Species	Indica

Classification of *Nimba* in Classical Texts

In *Ayurveda*, *Nimba* has been classified based on *Doshkarma*, properties, morphological characters, therapeutic values, etc. *Nimba* is classified in various *Gana* in *Brihattrayi* and *Nighantus*. *Panchnimba* has been mentioned in *Paryaya Ratnamala*, *Dhanvantri Nighantu, Abhidhan Ratanmala, Madanpal Nighantu,* and *Kaidev Nighantu* and it has been described in as below:

Table 2: Classical Classification of Neem

SN	Samhita/ Nighantu	Gana/ Mahakashaya/ Skandha	Verse
1.	Charak Samhita[7]	Kandughna Mahakashaya	CS.Su. 4.14
		Tikta Skandha	CS.Vi. 8.143
		Anuvasan Dravya Kalpa Sangrah	CS.Vi. 8.150
		Sirovirechana Dravya Kalpa Sangrah	CS.Vi. 8.151
2.	Sushrut Samhita[8]	Aragvadhadi Gana	SS.Su.38.6
		Guduchyadi Gana	SS.Su.38.50
		Lakshaadi Gana	SS.Su.38.64
3.	Ashtanga Hridaya[9]	Vaman Gana	AH.Su.15.1
		Pittashamak Gana	AH.Su.15.6
		Aragvadhadi Gana	AH.Su.15.17
4.	Soushrutha Nighnatu[10]	Aragwadhadi Gana	43
5.	Ashtang Nighantu[11]	Aragwadhadi Gana	
6.	Paryayaratnamala[12]	-	1702
7.	Madanadi Nighantu[13]	Pratham Gana	8-9
8.	Dravyaguna Sangraha[14]	Shaka Varga	21
9.	Dhanvantari Nighantu[15]	Guduchyadi Varga	28
10.	Shabadchandrika[16]	Vrikshadi Varga	84
11.	Nighantu Shesh[17]	Vrikshkanda	136
12.	Shodal Nighantu[18]	Guduchayadi Varga	127
13.	Madhav Dravyaguna[19]	Vividhaoushdhi Varga	19
14.	Abhidhan Ratnamala[20]	Tiktasakanda	144
15.	Sidhamantra[21]	Tridoshahara Dravya	137
16.	Madanpala Nighnatu[22]	Abhyadi Varga	138-140
17.	Kaiyadev Nighnatu[23]	Mishrak Varga	9
18.	Bhavprakash[24]	Guduchayadi Varga	81-84
19.	Raja Nighnatu[25]	Mishrakadi Varga	33
20.	Rajavallabh Nighantu[26]	Aoushdhaparicedha	63
21.	Laghu Nighnatu[27]	-	140
22.	Shaligram Nighantu[28]	Guduchyadi Varga	
23.	Nighantu Adarsha[29]	Nimbadi Varga	
24.	Priya Nighantu[30]	Haritakyadi Varga	180

The *Ayurvedic* pharmacodynamics**[31]** and chemical composition **[32]** of Panchnimba are mentioned below in Fig. no. 2, Table No 3,4:

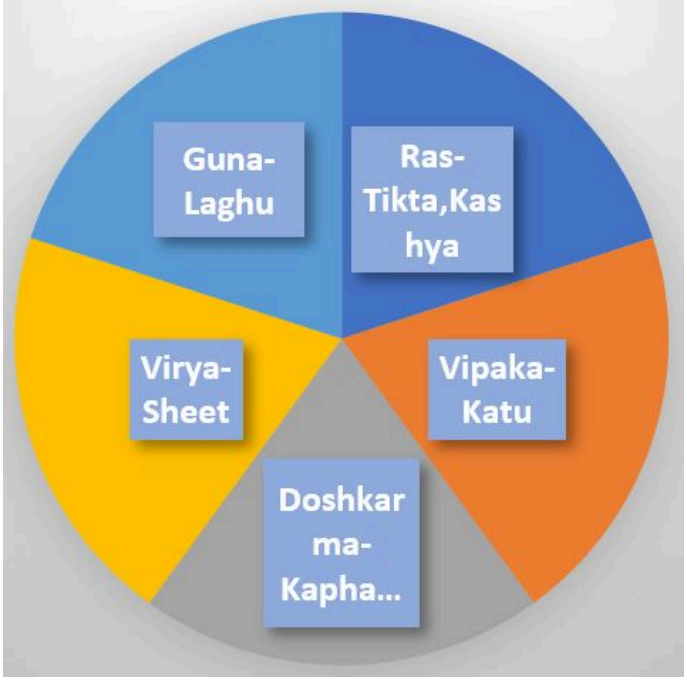

Figure 2: Ayurvedic pharmacodynamics of Neem

Table 3: Chemical composition of *Panchnimba*

Part	Chemical composition
Leaves	1. Vitamin C and Carotene 2. Quercetin and β-sitosterol 3. Isoprenylated flavanone, Nimbaflavone 4. Limonoid Azadirachtin A. 5. Amino acids like Glutamic acid, Tyrosine, Aspartic acid, Alanine, Proline, Glutamine, Cysteine 6. Saponins, Mucilage, Essential oils 7. Steroids, Saponins, Flavonoid
Flowers	1. Nimbosterol, Glycoside- Nimbosterin, Flavon- Nimbecitin, Hydrocarbon- nonacosane, Pungent essential oil 2. Myricetin glycoside -Melicitrin 3. Tetranortriterpenoid Neeflon 4. Essential oil from flowers contained Thio-amyl alcohol (7.6%), Benzyl alcohol (9.67%), Benzyl acetate (8.2%), Sesquiterpenes viz azadirachtin, Margosene.
Fruits/ seeds	1. HPLC yielded Azadirachtins i.e., Azadirachtin A, Azadirachtin B, Azadirachtin D 2. Azadirachtin H and 11β-H epimer 3. Azadirachtin I 4. Arabinogalactan isolated from fruit pulp contained D-galactose, L-arabinose, L-rhamnose, D-glucuronic acid 5. Amino acids obtained are Aspartic acid, Isoleucine, Lysine 6. Seed oil contained Azadirone, Azadiradione, Epoxyazadiradione, Gedunin
Stem bark	1. Nimbin (0.04%), Nimbinin (0.001%), Nimbidin (0.4%), Nimbosterol (0.03%) 2. Desacetyl Nimbin, Sugiol or 7-ketoferruginol, Nimbiol 3. Limonids gedunin, 7-desacteylgedunin 4. Tannin (15.76%) 5. Steroids/terpenoids, Alkaloids, Flavonoids, Tannins, Phenolics and Saponins 6. Proteins, Alkaloids and minerals, Amino acids like Arginine, Aspartic acid, Cysteine, Glutamic acid, Isoleucine, Methionine, Norleucin, Phenylalanine, Proline, Threonine, and Tryptophan
Root Bark	Nimbin, Nimbidin, Nimbosterol, Nimbidiol

Table 4: The Ayurvedic pharmacodynamics and classical use of *Panchnimba* as per different *Nighatus*.

Raspanchak	DhanwantriNighantu[33]	Madanpala Nighantu [34]			Kaiyadev Nighantu[35]			Bhavprakash Nighantu [36]		
		Patra	Phala	Pakwa Phala	Pushpa	Phala	Pakwa Phala	Patra	Phala	Pushpa
Ras	-	-	-	-		Tikta	Madhur, Tikta		Tikta	
Guna	-	-	Snigdha, Laghu	-		Aruskha	Snigdha, Guru, Pichalla		Snigdha, Laghu	
Virya	-	-	Ushna			Ushana			Ushna	
Vipaka	-	-	-		Katu	Katu		Katu	Katu	Katu
Dosha-karma	-	Pitt Shamak	-		Vata Kara, Pitta Hara		Kapha-Hara	Vata Kara, Pitta Hara		Vata Kara, Pitta Hara
Karma	Kushthahara, Varnanashana	Krimi Hara, Visha Ghana, Netraya	Kustha-Hara, Bhedhana	Pari-Shoshan	Chak-Shuya, Krimi-Visha Hara, Ruchi-Kara	Bhedhana, Kushta Ghana, Gulma, Arsh, Krimi Hara, Meha-Nashak	Rakta-Pitthara, Aam Pachak, Kshata-Kshaya	Krimi Hara, Visha Ghana, Netraya, Ruchi Kara	Bhedhana, Kushta Ghana, Gulma, Arsh, Krimi Hara, Meha-Nashak	

Therapeutic uses of *Panchnimba*

1. Neem leaves

Leaves are applied as poultices to relieve boils, ringworms, eczema, ulcers, itching, and other skin diseases. Paste of the leaves is used in case of acne vulgaris. Their infusion is used as an antiseptic wash to promote the healing of wound and ulcers. Leaves are useful for chickenpox, reduce fever caused by malaria, treat various foot fungi, and cure neuromuscular pains.**[37]** Leaf juice is given in gonorrhoea and leucorrhoea. The leaf's fresh juice is administered with salt to treat intestinal worms. The aqueous extract of leaf shows potent immuno-stimulant activity as evidenced by both humeral and cell-mediated responses. The wound-healing property of leaf extract is also validated in animal models of rats with excisional and incisional wounds. Early research recommends that applying a gel containing neem leaf concentrate to the teeth and gums twice day by day for about a month and a half may lessen measure of plaque on teeth.**[38]**

2. Neem bark

The bark is used as a bitter tonic, astringent, antipyretic, against nausea and vomiting. It controls fleas and ticks on pets, fights against skin infections such as acne, psoriasis, scabies, eczema, etc, treats diabetes, AIDS, cancer, heart disease, herpes, allergies, ulcers, hepatitis and several other diseases.**[39]**

Steam inhalation of bark is useful in inflammation of the throat. Inflammatory stomatitis in children is cured by the bark. Neem bark has an anti-bacterial property, it is quite useful in dentistry for curing gingival problems and maintaining oral health.

3. Neem flower

Infusion of flower is given in dyspepsia and general debility. The dried flower is taken orally for diabetes and are stomachic.

4. Neem fruit

Hot water extract of dried fruit is used externally for skin disease and ulcers. The fruits work as a purgative and an emollient, and are useful in the control of intestinal worms, urinary tract diseases, and piles.

5. Neem root

Root of the neem is used in case of diabetes.

Extrapharmacopiel uses

1. Neem leaves

- Neem leaves are used as green leaf manure and also in the preparation of litter compost.**[40]**
- Neem leaves are also used in the storage of grains.
- Leaves due to insecticidal properties are kept with woollen and other clothes for a long time.

2. Neem seed cake

Neem seed cake performs the dual function of both fertilizer and, pesticide, acts as a soil enricher, reduces the growth of soil pest and bacteria, provides macronutrients essential for all plant growth, and helps to increase the yield of plants in the long run, biodegradable, Eco friendly and excellent soil conditioner.**[41]**

3. Neem bark and roots

Bark & roots in powdered form are also used to control fleas & sucking pests in rice cultivation.

Pharmacological profiling on *Panchnimba*

1. Neem leaves

Hepatoprotective effect

Aqueous neem leaf extract (ANLE) showed hepatoprotection against anti-tubercular drug-induced damage in rats as indicated by minimized alteration of bilirubin, Alanine aminotransferase, Aspartate aminotransferase, and Alkaline phosphatase in serum. Azadirachtin-A, and, Nimbolide the major components of neem, showed a hepatoprotective effect against carbon tetrachloride (CCl4)-induced liver injury in rat models with efficacy similar to that of Silymarine standards.**[42]**

Anti diabetic effect

Neem leaf extracts showed promising results in decreasing blood sugar level and prevents adrenaline as well as glucose induced hyperglycaemia. Recently, hypoglycaemic effect was observed with leaf extract and seed oil in normal as well as alloxan-induced diabetic rabbits.**[43]**

Immunostimulant effect

The aqueous extract of leaf also possesses potent immune-stimulant activity as evidenced by both humoral and cell-mediated responses.

Leaf extract at 100 mg/kg after three weeks of oral administration causes higher IgM and IgG levels along with increased titter of ant ovalbumin antibody.**[44]**

2. Neem flower

Anti-cancerous activity

Dietary neem flowers, at level of 10% in diet, reduced both incidence and multiplicity (number of tumours per rat) of mammary gland tumours in female Sprague Dawley rats induced by DMBA (Dimethylbenz[a]Anthracene) when given 1 week prior to carcinogen administration. Dietary neem flowers, at the level of 12.5% in the diet, could also suppress the development of liver tumour in male Wistar rats induced by AFB1 (Aflatoxin B1).**[45]**

Antifertility potential

An alcoholic extract of neem flowers is used to observe its effects on oestrous cycle, ovulation, fertility, and the foetal morphology on rat models. The results of this study clearly confirmed that oestrous cycle of 80% of the rats was altered with a marked prolongation of the dioestrus phase.**[46]**

Antioxidant activity

Ethanolic extracts of flowers and seed oil were also found to have better free radical-scavenging action. **[47]**

3. Neem fruit

Anti-ulcer activity

Some active ingredients (Phytosterols) were isolated from lipophilic fraction of neem fruit, exhibit antiulcer activity in stress induced gastric lesion. **[49]**

Anti-inflammatory activity

The anti-inflammatory activities of neem fruit skin and its specific ingredient, azadiradione, have also been evaluated. The results have concluded that the animals treated with 100 mg/kg dose of this fruit skin extract and azadiradione exhibited significant anti-inflammatory activities.**[50]**

4. Neem stem

Anti-microbicidal activity

Neem bark extract at the concentration of 50 to 100µg/ml have shown ability to stop the entry of HSV-1 into cells.

Also, three tricyclic Diterpenoids, Margolone, Margolonone and Isomargolonone isolated from stem bark of *Nimba* were found to be active against Serratia species, Klebsiella, and Staphylococcus which shows its antimicrobial property.

Immuno-stimulant activity

The aqueous extract of bark of *Azadirachta indica* showed anti complimentary activity, acting on both classical pathway activation and alternative pathway activation.**[51]**

Antiulcer

Neem bark extract reduced human gastric acid hypersecretion, and gastro-oesophageal and gastroduodenal ulcers. After 10 weeks, the duodenal ulcers were nearly fully healed; after 6 weeks one case of oesophageal ulcer and gastric ulcer were fully healed.**[52]**

Anti-microbial activity

The bark extract exhibited significant antimicrobial activity on Pseudomonas aeruginosa, Proteus mirabilis and Enterococcus faecalis at all the concentrations tested, whereas its antimicrobial activity on Staphylococcus aureus, Aspergillus fumigates and Candida albicans was observed at higher concentrations (>500µg/ml).**[53]**

5. Neem root

Antidiabetic activity

A study was undertaken to evaluate the 70% alcoholic neem root bark extract (NRE) in diabetes and results showed that neem root bark extract showed statistically significant results in 800mg/kg dose.**[54]**

Free radical scavenging activity

Qualitative chemical analysis of root bark extract showed the presence of saponins, flavonoids, and terpenoids. The root bark hydro alcoholic extract of Azadirachta indica exhibited significant free radical scavenging activity as determined by DPPH (2, 2 Diphenly 1 picryl hydrazyl solution (DPPH) assay and total antioxidant activity.**[55]**

Important Preparation

There are various preparations from parts of the neem such as Fruits, Leaves, Roots, Bark, flower,

- *Panchtikta Ghrita Guggul*
- *Panchnimbadi Churna*
- *Panchnimbadi Vati*
- *Nimba - Haridra Khand*
- *Aarogya Vardhini Ras (Bhawna Dravya).*
- *Nimbadi Churnam*
- *Nimbaristam*
- *Nimbadi Tailam*
- *Nimbadi Churnam*
- *Nimbadi Lepa*
- *Nimbadi Kashaya*
- *Laghu Shivagutika*
- *Baladi Ghrit*

Different varieties of Neem

In the Ayurvedic literature there are 3 different varieties of *Neem* has been found.

- Neem or *Nimba* - Azadirachta indica
- Maha nimb - Melia azaderachta (Kaidev Nighantu)
- Parvata Nimba - Aralu (Ailanthus exelsa)

Dosage

- Fresh juice of neem can be taken 10-20 ml
- Seed oil can be used 5-10 drops
- The bark powder can be used 2-4 gm.

Discussion

The above-collected information regarding the *Azadirachta indica* indicates that this is the most versatile medicinal plant. It is seen that how Neem has led to the preparation of numerous medicinally and industrially useful formulations with potent medicinal applications in the development of novel drugs to treat various acute and chronic diseases. Although the neem tree is a native tree of East India and Burma but the use of this plant is seen in the whole world. The importance of neem is seen when united nation has declared the "Tree of the 21st century". Neem and its derivatives show an important role in disease prevention and treatment. It is done by the enhancement of antioxidant activity, inhibition of bacterial growth and by modulate the numerous biological processes without any adverse effect. The active constituents like Nimbin, Nimbinin, Nimbidine, Azadirachatin etc.

Are responsible for its anti-inflammatory, anti-microbial activity, anti-diabetic and anti-cancerous property. It also possess hepatoprotective, anti-fertility, immunostimulant, anti-ulcer, & antimicrocidal activity. The use of neem is not just limited to its single part but each part has been used extensively since time immemorial. In *Ayurveda*, many *Nighantus* have mentioned the *Panchnimba* or its five useful parts along with their *Ayurvedic* pharmacodynamics. Leaves having *Katu Vipaka* it pacifies the *Pitta Dosha* and it possess *Krimi-Vishahra* property, *Netraya* and *Ruchikara*. Unriped fruit showed *Kushth-Krimihara* actions due to its *Tikta Rasa, Ushna Virya* and *Katu Vipaka*. It cures *Gulma* and *Arsh* because of its *Laghu Guna, Tikta Rasa* and *Ushana Virya*. Whereas riped fruit possess *Raktapitthara* property because of its *Tikta Rasa* which purifies blood, it has bitter taste, it improves the digestive fire. Due to *Katu Vipaka*, Flower of the neem alleviates *Pitta Doshas* and vitiate *Vata Doshas*.

Ayurvedic Pharmacodynamics reveals that although neem itself is *Sheet Virya* but its fruits in *Apakwa Awastha* and *Pakwa Awastha* are *Ushna Veerya*. Also, the fruit has *Madhur* and *Tikta Rasa* whereas neem has *Tikta* and *Kashaya Rasa.*

Conclusion

Neem and its active bio constituents have therapeutics implications and have been traditionally used worldwide especially in Indian subcontinent since ancient times. People used neem at home as remedy they apply the leaves paste on their face and bark of the stem on any kind of wound or on skin disorders. It can be easily available and not as much expensive as comparison to other modern medicine. Neem has commercial and high economic importance used as a bioavailability enhancer can be explored in various formulations. All parts of the neem are useful for various body ailments. Also, it is helpful to relieve excessive thirst, it is helpful in relieve cough, it is useful in fever. It is very helpful in relieve from anorexia. Neem is useful in intestinal and other worms, also helpful to heal wounds and cleans the wounds. It is very useful in vomiting and nausea, also helpful in various skin disease also helpful in diabetes and urinary tract related infection. So, it can be concluded that neem heals the various ailments of the body. From Samhita time to modern era neem is an important, always available, economical, Environment friendly ancient drug which is very helpful to cure diff. ailment in body. Recent research has supported drug efficacy with evidences.

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