

NEEM: A REVIEW ON ITS MEDICINAL PROPERTIES

Prashant Gupta, Shantala R. Naik*, L. Ashok, Anjani Kumar Shukla and Tanya Khaitan

¹Associate Professor Dept. of Oral Medicine and Radiology Dental Institute – Rajendra Institute of Medical Sciences Ranchi – 834001.

²Assistant Professor Dept. of Oral Medicine and Radiology Dental Institute – Rajendra Institute of Medical Sciences Ranchi – 834001.

³Professor and Head Dept. of Oral Medicine and Radiology Bapuji Dental College and Hospital Davangere Karnataka.

^{4,5}Tutor Dept. of Oral Medicine and Radiology Dental Institute – Rajendra Institute of Medical Sciences Ranchi– 834001.

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***Corresponding Author**

Shantala R. Naik

Assistant Professor Dept of
Oral Medicine and
Radiology Dental Institute –
Rajendra Institute of
Medical Sciences Ranchi –
834001.

ABSTRACT

Aim: this review lists all the information about neem since in this era of modern medicine we need to know more about this wonder plant which can be the best alternative medicine **Background:** neem is rightly termed as wonder plant. It has wide spectrum of pharmacologically useful actions. Its widespread everywhere in India and hence readily available **Review results:** review articles and original research articles related to use of neem and history of neem as available on EBSCO host and pubmed were included in the study. Keywords such as “medicinal” “Values” “neem” “folk medicine” were used for search **Conclusion:** neem is a very useful tree and every part of it is useful. Neem extract obtained from leaves, flowers, seeds, bark have multiple pharmacological actions and can be the best alternative

medicine for many medical conditions. **Clinical significance:** neem can be the best alternative medicine and it is promising to be a boon in this era of modern medicine. Let us warmly accept neem based natural products to treat medical conditions.

KEYWORDS: Neem, Anti Inflammatory, Anti malarial, Village pharmacy, Herbal medicine.

Introduction and History of neem

Medicinal herbs have been a part of all of us since the dawn of history. Plant products used as an alternative medicine plays a very important role in disease prevention and treatment, because of their antioxidant, antibacterial and gene protector properties.^[1] One such plant is *Azadirachta Indica*. This tree has two named species, Indian Lilac/ margosa tree/Indian neem and the other is Persian lilac.^[2] Neem is used as a herbal medicine in ayurveda, Unani and homeopathy. Neem belongs to *Meliaceae* family and is found in abundance in tropical and semitropical countries like India, Pakistan, Bangladesh, Nepal. It is a fast growing tree.

US national academy of science has entitled "Neem- as a tree for solving global problems"^[2] Neem deserves to be called as a wonder plant.^[3] Neem is the native tree of India and was called as "tree of 21st century" by United nations.^[4,5] This tree is also called by several other names like, sacred tree, divine tree, life giving tree, nature's drug store, village pharmacy and panacea for all diseases.^[5,6,7]

The word neem is derived from Sanskrit word "nimba" which means "bestower of good health". It is also called as "Ravisamba" that means "sun ray like effect in providing health". Around 75% of all ayurvedic preparations has neem in it.^[8]

Ayurvedic texts describe neem as "sarva roga nivarini" that means "the universal healer or cure of all ailments", the other names are "Aristha" which means "perfect, complete and imperishable", "Nimba nimbaty syarthamdadati" that means "to give good health".^[8]

It is also called as "Pinchumada" that means destroyer of leprosy and healer of skin infections. Kautilya "Arthashastra" written in 4th century BC mentions about neem and its uses. Charaka samhita and Sushruta samhita also mentions about neem. It has been used as a medicine in ayurveda since 4000 years. "Upavanavinod" that is a Sanskrit treatise says neem is a cure for ailing soils, plants and livestock. Unani medicine scholars called neem as "Shajar-e-munarak" or the blessed tree. Persian scholars called neem as "azad dirakth-I-hind" that means noble or free tree of India.^[8]

In Andhra Pradesh neem is called as "vepa" that means purifier of air. It is considered as a prophylactic measure to plant a neem tree in and around human habitat to protect from malaria and cholera. In Uttar Pradesh there is proverbial explanation of village surrounded by neem tree to be free from fever and those without neem tree around to be severely affected by

fever. Patients with chicken pox and small pox in south India are made to lay down on a bed of neem leaves and also fanned with neem branch. This is done to limit the spread of virus. The khasi and Jaintia tribe of north eastern India use neem to treat diarrhoea, dysentery, tuberculosis and cardiac diseases. Neem has secured a place in “Indian Pharmacopea”.

Hindu mythology considers neem as a divine tree. It is said that few drops of amrita (ambrosia) was dropped on neem tree while being carried by garuda.^[8] Neem in Kenya’s Kiswahili language is called as “Mwarunaini” that means reliever of human diseases.^[8]

Neem for indian villages^[8]

Neem has been the legendary medicinal tree of India. It is considered as a village dispensary. It has been an integral part of Indian way of life for centuries. It is the protector and friend for Indian villages. It has been used to fortify health and treat various diseases. It is still being used to protect food and store grains through out the year. It is used as natural fertilizer and also as a pesticide. It is used as medicinal potion for cattle and livestock. It is said that the breeze that blew through the boughs of tree kept their home free of bacteria and viruses. “Kaajal” that is used to beautify ones eyes by ladies is prepared from lampblack of neem kernel. This has been an age old tradition that when an Indian village family is about to welcome newborn child into family, the family makes lampblack in advance for application onto babies eyes.

Villagers believe that goddess “Sithala” lives in the neem tree. They also believe that planting a neem tree in the front yard helps in purifying the air. The new born babies are made to lay down on leaves after neem oil massage. The child is given small doses of neem oil, when it falls ill and bathed with neem soaked water to treat minor cuts, rashes and the lesions of chicken pox.³⁰ One of our Indian festival named “Ugadi” gives crushed neem leaves and Jaggery mixture as prasada to people on that auspicious day which is celebrated as new year on Konkan belt in Karnataka. Neem leaves are tied onto the main entrance of houses to restrain from evil spirits.

Chemistry and uses of neem

About 400 constituents of neem have been identified.^[9] All the parts of neem is useful in one or the other way as an alternative medicine. The young twigs are used for oral hygiene, infusion of neem is used as drink to cure diseases, salad of tender leaves, lozenges for dryness of throat, sweet pulp of fruit is sucked in summers.^[8] The constituents of neem are classified

into two types such as isoprenoids and non isoprenoids.^[10,11] Isoprenoids include: diterpenoids, triterpenoids (containing protomelaicins, limonoids, azadirons and its derivatives), gedunin and its derivatives (vilasinin, C-secomeliacins such as nimbin, salannin, azadirachtin). Non isoprenoids include proteins (amino acids) and their glycosides dihydrochalcone, coumarin and tannins, aliphatic compounds. Terpenoids are the important constituents. Around 70 different terpenoids are present in different parts of neem.^[12] Azadirachtin is a very important terpenoid. Several types of azadirachtins are known A-K but the most active is Azadirachtin A.^[12]

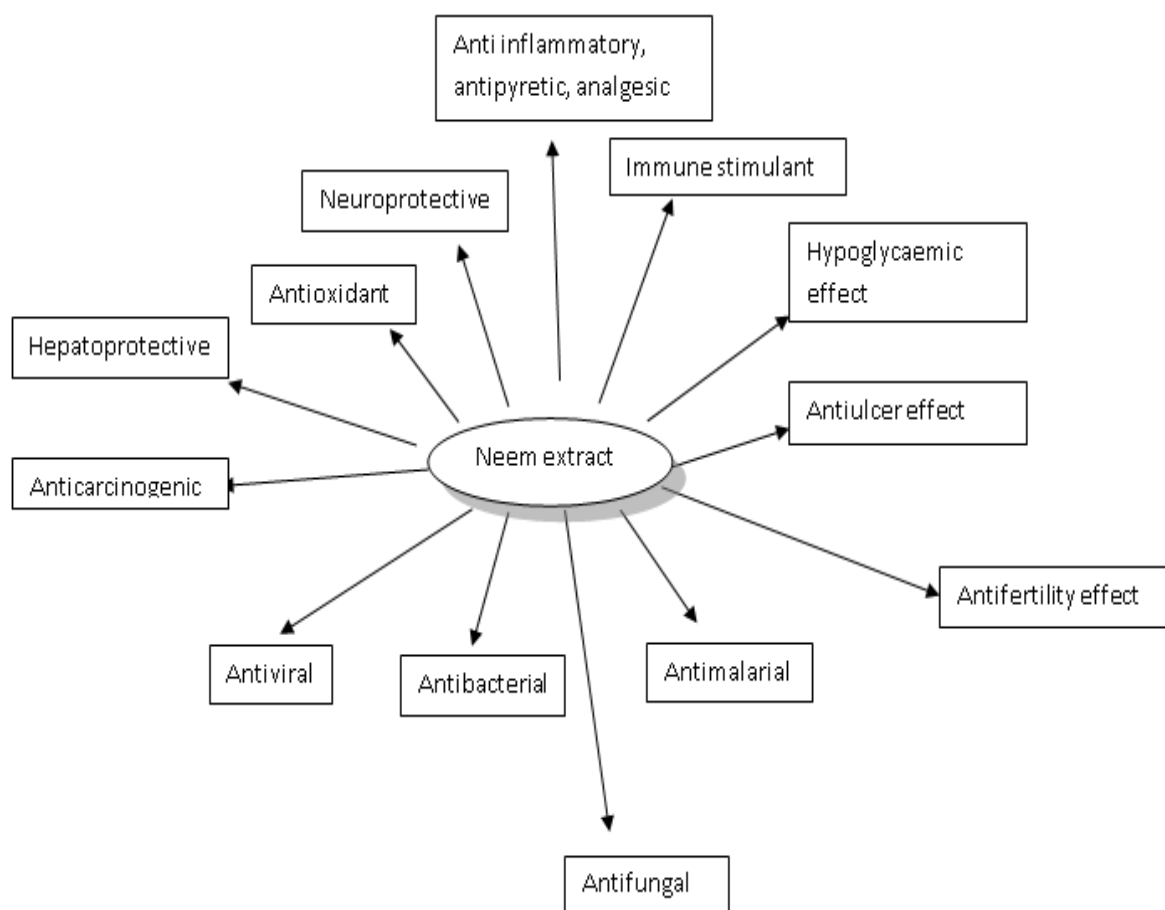
Neem oil is a rich source of fatty acids. It is very bitter and has sulphur or garlic like odour. It has vitamin E and essential fatty acids like oleic acid, stearic acid, palmitic acid and linoleic acid. Others like condensed tannins like gallic acid, galocatechin, epicatechin, catechin and epigallocatechi. Epicatechin and catechin inhibit oxidative burst of PMNs. Sulphur containing compounds such as cyclic trisulphides and tetrasulphides isolated from matured neem leaves has antifungal activity. Polysaccharides have anti tumor effect.^[2]

Azadirachtins are the most important constituents and others being nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbidate, gedunin, salamin, quercitin. The neem leaves also contain nimbin, nimbanine, 6-desacetyl nimbinine, nimbandiol, nimbolids, ascorbic acid, n-hexacoranol and amino acids.^[1]

Pharmacological actions of neem extract

The most analysed compounds of neem and their pharmacological actions so far are:^[13]

Nimbin	Anti-inflammatory, antipyretic, antihistamine, antifungal
Nimbidin	Antibacterial, antiulcer, analgesic, antiarrhythmic, antifungal
Nimbidol	Antitubercular, antiprotozoan, antipyretic
Gedunin	Vasodilator, antimalaria, antifungal
sodium nimbidate	Diuretic, spermicidal, antiarthritic
Quercitin	Anti protozoal
Salannin	Repellent
Azadirachtin	Repellent, antihormonal, antifeedent



Neem leaf, bark, root, seed and oil extract have been used for the medicinal purpose. All its extracts are of medicinal value. Its therapeutic implications is because of its anti oxidant effect exerted by the various chemical constituents like azadirachtin, nimbolinin, nimbin, nimbidin, nimbidol, salannin and quercetin. The antimicrobial effect is because of inhibitory effect on microbial growth and breakdown of cellwall. It acts as a free radical scavenger because of the high concentration of antioxidants in neem. The anticancer effect is exerted by regulation of cell signalling pathways. It modulates the activity of tumor suppressor genes such as p53, pTEN, VEGF, transcription factors (NF- κ B) and apoptosis (bcl2, bax). It also regulates proinflammatory enzyme activities, cyclooxygenase and lipoxygenase enzymes and thus exerts anti inflammatory effect.

Anti-inflammatory, antipyretic and analgesic effect: it is an effective anti inflammatory agent. Nimbidin of neem suppresses the function of macrophages and neutrophils relevant to inflammation.^[14] It acts as an immunomodulator, anti inflammatory and analgesic.^[14,15,16] The anti inflammatory effect is mediated by epoxy azadiradione against macrophage migration inhibitory factor.^[17]

Immunostimulant activity: neem possesses anti complement activity. It is an immune stimulant. It selectively activates the cell mediated immunity to enhance response to an antigenic challenge.^[2]

Hypoglycemic Effect/Antidiabetic: neem reduces blood sugar levels significantly. It reduces hyperglycemia secondary to adrenaline and glucose.^[1] “Jamu” / “Loloh” is a drink used to treat high sugar levels. It is a decoction or infusion of neem. It is practised since thousand of years in Bali. For commercial purposes, the same preparation is sold as packaged tea like bags containing dried powdered leaves that are ready for use.^[9,18]

Anti ulcer effect: the glycoside in neem has a potent antacid and antiulcer activity. Neem oil has active ingredients that deals directly with wound healing. It has high fatty acid that plays an important role in adding moisture and a soft texture to skin during wound healing. The antibacterial property of neem helps prevents secondary infection during wound healing.

Antifertility effect: neem is spermicidal. It is considered as a potent contraceptive for females. Oral administration of neem could be used to terminate pregnancy. This action is said to be cell mediated and non hormonal and hence has less side effects.

Antimalarial effect: It is an excellent antimalarial agent. Neem trees around human habitat could make that area free of malaria. This was used as folk medicine too.

Antibacterial effect: Neem seed oil, leaves and bark of neem is a broad spectrum antibacterial agent that acts against various gram positive and negative bacteria. It is a potent immune stimulant that activates both humoral and cell mediated immunity. 5 / 10 % neem acts as a potent antibacterial for both gram positive and negative bacteria.^[19]

Antiviral effect: polysaccharides in neem has the antiviral property.^[20]

Anti carcinogenic effect: Neem has chemopreventive effect by modulating glutathione and its metabolising enzymes. The anticancer activity is by their effect on cellular proliferation, apoptosis, tumor suppressor gene that is responsible for the growth of malignant cell.^[21] Neem oil has limonoids that prevent the mutation process.^[13] Azadirachtin and nimboloids inhibit the activation of procarcinogen and oxidative DNA damage, upregulation of enzymes that act as anti oxidants and detoxify the carcinogen, inhibits tumor invasion and angiogenesis.^[22]

It activates the tumor suppressor genes and deactivates the cancer promoting genes like VEGF, NF- κ B and p13k/Akt. p53 inhibits proliferation of abnormal / mutated cell thereby inhibits development and progression of cancer. Neem upregulates the proapoptotic genes and proteins like p53, Bcl-2 associated x-protein (bax), bad (bcl-2) and tensin homolog gene (TEN) and c-jun-N-terminal kinase (JNK), caspase 8 and caspase 3.^[23,24,25]

Nimbolids in neem has the cytotoxic property that down regulates various cell survival proteins and upregulates proapoptotic proteins.^[26] Neem extracts play a vital role in induction of apoptotic cell death in cancer.^[27,28] It is said to inhibit expression of proangiogenic genes, VEGF-A, angiopoietin.^[29] It suppresses expression of c-myc oncogene.^[30] Neem extracts inhibits PBK/Akt pathways thereby inducing apoptosis and inhibiting cell proliferation.^[31] Neem inhibits NF- κ B transcription factor that plays an important role in cancer development and progression.^[32]

Hepatoprotective effect: Oral administration of neem reduces elevated serum aspartate aminotransferase and gamma glutamyl transpeptidase.^[2]

Antioxidant activity: we all know about the main culprits in the genesis of various diseases and they are the free radicals or reactive oxygen species. Hence neutralization of these radicals or reactive oxygen species helps prevent disease. Neem as an antioxidant helps stabilize free radicals and also help activate the antioxidant enzyme system.^[33] Leaves, flowers and bark extracts of neem has significant antioxidant activity.^[34,35,36] Other functions of neem are anti arthritic, anti nephrotoxic.^[1]

Neem as folk medicine^[8]

Neem extracts has been used as folk medicine since ages and to list a few of mentioned folk medicinal values.

- **Building immunity:** chewing of neem leaves (around 8-10 leaves) in the morning for twenty four days protects the body from diabetes and hypertension. It also protects our skin from various skin diseases.
- Mixture of neem seed powder (10gms), rock salt (10gms), alum (10gms) mixed well can be used for teeth cleaning. It maintains healthy teeth and gums.
- **Hair care:** decoction of neem is used as hair wash in case of premature graying, hair loss, lice, dandruff

- **Conjunctivitis:** 5-10ml of fresh juice of neem leaves (obtained by crushing leaves and filtered with double folded cotton cloth) is warmed slightly and used as eye drops.
- **Ear drops:** 5ml of fresh neem leaf juice with equal amount of honey is mixed well and used as drops in oozing ears that reduces oozing and inflammation too. If discharge and foul smell persists, experts advice has to be taken.
- **Jaundice:** 15-30 ml of neem juice and half the quantity of honey is taken on an empty stomach for seven days.
- **Stomatitis:** in case of infantile stomatitits, 10-15 dry neem leaves, 5 gm of pipili (long pepper) and honey should be grounded on a stone and applied onto tongue dorsum.
- **Worms:** 10 ml of neem leaf juice, honey, 5gm of asafoetida is used to cure intestinal worms in children.
- **Stomach problems:** 5 gms of dried neem flowers, mixed and fried with 5 gm each of rock salt, tamarind, chillies and curry leaves is made into a chutney and eaten to get rid of vomiting, anorexia, sour belching and worms.
- **Urinary stones:** khsara or ash prepared by burning the neem leaves in an earthen pot is powdered and mixed well with water and allowed to sediment. The sediment is used as khsara after filtering the water out. 50gms of khsara taken with warm water every day in the morning is used to cure urinary stones. However when there is complete retention of urine an expert advice is obtained.
- **Urticaria:** a decoction of neem bark, sandal and guduchi (*tinospora cordifolius*) is taken orally
- **Piles:** powdered neem seed mixed with water taken as a drink for a week stops bleeding in piles. Neem seed fried with copper sulphate and mixed with coconut oil is used an ointment in piles.
- **Pruritis:** juice of neem leaves applied along the groin and anal region cure pruritis in children.
- **Dysmenorrhoea:** 15ml of neem leaf juice and 15 ml of ginger juice is mixed and taken orally cures painful menstruation.
- **Post delivery care:** 30 ml of neem leaf juice taken on an empty stomach in the morning for 27 days help to reshape the uterus post delivery
- **Skin care:** 1tsp of dried neem leaf powder, ghee, dry goose berry powder each mixed with sufficient quantity of honey cures allergic skin reactions. Boil 50 mg of neem bark in 400ml of water and boil it till it become 100ml, to this add 400ml of ghee and boil in a

wide mouthed container till frothing. Frothing is suggestive of ghee preparation and this ghee is used internally and externally for herpes, lymphadenitis and skin problems.

- **Psoriasis:** ash of dried neem leaves mixed with oil, ghee is beneficial
- **Sweating/burning:** 10 drops of neem oil with milk at bed times helps reduce sweating and burning
- **Chicken pox:** neem soaked water is used to bathe the patient to prevent further spread of the virus and to soothe the patient
- **Measles:** 20 gms each of tender neem leaves and yasti (liquorice) pill taken with warm water is beneficial in measles.

CONCLUSION AND CLINICAL SIGNIFICANCE

Neem is termed as wonder plant. It is readily available and most importantly inexpensive. It is called as village pharmacy since neem has been used as folk medicine. It is used as antimalarial since ages. Even till date dried neem leaves are kept in containers that stores grain to prevent worm infestation. It is used to cure many skin ailments. Most of the face massage or facial scrub creams available in market are based on neem formula. Toothpaste, mouth washes too are neem based. It is a very potent anti inflammatory agent. Making neem a part of our livelihood can be very useful. It is of great help to new born babies where one would be worried to try allopathic drugs. Hence we say that neem can be a best alternative medicine for many illnesses.

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