

Neem: A Comprehensive Review of Its Therapeutic and Agricultural Applications

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ABSTRACT

Extract of plant are being used as mosquito repellent from generation to generation, in Traditional lifestyle. Neem is commonly known most popular mosquito repellent, having Latin name “AZADIRACHTA INDICA” or “Indian LILAC” or “MARGOSA” belongs to family Meliaceae and sub family of Meloideae , Neem is undoubtedly a potential tree, donating its each and every part either wooden or non wooden (Leaves, bark, Flowers, Fruits, Seed, Gum, Oil) in versatile usages. Its non wooden products are used as Antidermatic, Anti Fungal, Anti allergic, anti-inflammatory, Anti pyorrhoeic, insecticidal, larvicidal, spermicidal, antiscabic, nematocidal, cardiac and alot more biological usage. Because of all such virtues make this green treasure as richest donator of nature.

Keywords: *Azadirachta indica*; *Neem products*, *neem oil*.

I. INTRODUCTION

The neem tree (*Azadirachta indica* A.Juss.) is a tropical evergreen tree (deciduous in drier areas) native to Indian sub-continent. It has been used in Ayurvedic medicine for more than 4000 years due to its medicinal properties. Neem is called ‘arista’ in Sanskrit a word that means ‘perfect, complete and imperishable’. Today is science returning towards their roots and herbal medicines are formulated and preferred for most of the disease. NEEM works as the base of diseases developed in tropical and sub tropicals geography. In traditional indian societies, Neem was used as a natural antinode for a, most of diseases, but recently market has been captured by chemical based products. Many chemicals which directly affect the human organs, and so far affect the environment [1 & 2].

Neem is about 25 m in height with semi-straight to straight trunk, 3 m in girth and spreading branches forming a broad crown. A neem tree normally starts fruiting after 3-5 years. In about 10 years it becomes fully productive. From the tenth year onwards it can produce up to 50 Kg of fruits (niboli) annually [3]. Age of the neem plant become about 200 year. The tree has adaptability to a wide range of climatic, topographic and edaphic factors. It thrives well in dry, stony shallow soils and even on soils having hard calcareous or clay pan, at a shallow depth. Neem tree requires little water and plenty of sunlight [4 & 5] The tree grows naturally in areas where the rainfall is in the range of 450 to 1200 mm. However, it has been introduced successfully even in areas where the rainfall is as low as 150 to 250 mm. Neem grows on altitudes up to 1500 m [6 - 8]. It can grow well in wide temperature range of 00C 49oC. The pH range for the growth of neem tree lies in between 4 to 10. It grows on almost all types of soil including clayey, saline and alkaline soil, but does well on black cotton soils and deep well drained soil with good sub-soil water. Neem trees have the ability to neutralize acidic soils by a unique property of calcium mining [9]. In india 4,42,300 tons of neem seeds , 88,400 tons of neem oil and 3,53,800 tons of neem cake [10] are produced annually.

There are an estimated 25 million trees growing all over India neem tree is found Andhra Pradesh, Assam, Bihar, Delhi, Gujarat, Haryana, Himachal Pradesh, Kerala, Madhya Pradesh, Maharashtra, Meghalaya, Orissa, Punjab, Rajasthan [11].

Neem is well-known for its durable wood. In addition, the non-wood products of neem like flowers, fruits, seeds (oil, cake), leaves bark and gum also find various uses. The antifungal, antibacterial, insecticidal and other versatile biological activities of these products are well established [9], because of which they find multipurpose use in daily

life of humans. The most useful and valuable product of the tree are the seeds which yield 40% of a deep yellow oil, the wellknown 'Margosa oil' [12].

Neem is a member of the Mahogany family. Taxonomic position of neem

Order	- <i>Rutales</i>
Suborder	- <i>Rutinae</i>
Family	- <i>Meliaceae</i>
Subfamily	- <i>Melioideae</i>
Tribe	- <i>Melieae</i>
Genus	- <i>Azadirachta</i>
Species	- <i>indica</i>

II. NEEM PRODUCTS AND THEIR USES

Seeds: Seed give neem oil and neem cake.

1. **Neem oil** is use as Analgesic, Anticholinergic, Anthelmintic, Antihistaminic, Antiprotozoal, Antipyretic, Antiviral, Bactericidal, Contraceptives, Fungicides, Insecticides, Insect repellents, Veterinary medicines. Technical: Cosmetics, Hair oils, Lubricants, Propellants, Shampoos, Soaps, Tooth pastes.
2. **Neem cake** is use as Animal feed, Soil fertilizer, Soil moisturizer, Soil neutralizer, Soil protectant.

Leaves: Neem leaves use as Antidermatic, Antifungal, Anticlotting agent, Anthelmintic, Antituberculosis, Antitumour, Antiseptic, Antiviral, Contraceptive, Cosmetics, Fertilizers, Insecticides, Nematicides, Insect repellents.

Twigs: Twigs use as Oral deodorant, Toothache reliever, Tooth cleaners.

Bark: Antiallergenic, Antidermatic, Antifungal, Antiprotozoal, Antitumor, Deodorant.

Wood: Agricultural implements, Carts, Boats, Building articles, Furniture, Idols, Tools and wood use as fuel.

Flowers: Flowers are use as Analgesic, Curries, Nectaries, Soaps, Stimulant.

Others parts: Neem also give glue which is use as Adhesives, and Food from fruits, it gives honey, Pulp biogas, Resin, Tannin, Wind breaker, Wood preservatives [13]. The different parts of the Neem can be seen in Figure 1.





Figure 1. Different parts of Neem Tree.

More than 135 compounds have been isolated from different parts of neem. These compounds are classified into two major groups- isoprenoids and others. The isoprenoids include diterpenoids and triterpenoids containing protomeliacins, liminoids, azadirone and its derivatives, genudin and its derivatives, vilarin type of compounds and csecomeliacins such as nimbin, salannin and azadirachtin. The first compound to be studied was nimbin. The non-isoprenoids include proteins (amino acids) and carbohydrates (polysaccharides), sulphurous compounds, polyphenolics such as flavonoids and their glycosides, dihydrochalcone, coumarin and tannins, aliphatic compounds, phenolic acids, etc. Bioactivities of only few compounds have been studied. Some bioactive compounds from neem can be seen in Table 1 [14 - 19].

Table 1 : Biological activities of different compounds of Neem

Source	Neem compound	Biological activity
Seed	Nimbidin	Anti-inflammatory, Antiarthritic, Antipyretic, Hypoglycaemic Antigastric ulcer, Spermicidal Antifungal, Antibacterial Diuretic
Seed	Sodium nimbidate	Anti-inflammatory
Seed oil	Nimbin Seed oil Spermicidal	Spermicidal
Seed oil	Nimbolide	Antibacterial Antimalarial
Seed oil	Gedunin	Antifungal Antimalarial
Seed	Azadirachtin	Antimalarial
Seed oil	Mahmoodin	Antibacterial
Bark	Gallic acid, (–) epicatechin and catechin	Anti-inflammatory immunomodulatory
Leaf	Cyclic trisulphide and cyclic tetrasulphide	Antifungal
Leaf	Polysaccharides	Anti-inflammatory
Bark	Polysaccharides Gia, GIb	Antitumour
Bark	Polysaccharides GIIa, GIIa	Anti-inflammatory
Bark	NB-II peptidoglycan	Immunomodulatory

III. ENVIRONMENT AND NEEM

Neem compared to other species is well adapted to stress conditions. It is also known to increase soil fertility and water holding capacity. Thus the large scale plantation of neem trees help to combat desertification, deforestation, soil erosion and to reduce excessive global temperature. Today, modern societies, finding themselves confounded in the web of their creation, are willing to revert to nature for remedies and neem tree provides a promising means in this matter. Neem has high rate of photosynthesis and liberates more oxygen than many other tree species, thus purifying the atmosphere. The temperature under the neem has been found to be ~10°C less than the surrounding temperature, during hot summer months in the northern parts of India [20 & 21]. Over 10 kms on the plains of Arafat, about 50,000 neem trees were planted to provide shade for Muslim pilgrims during Hajj. A marked impact on the areas microclimate, microflora, microfauna and sand soil properties was noticed. The plantation when fullgrown is expected to provide shade to about two million pilgrims. In areas of low rainfall and high wind speed neem is useful as wind breaks. In the Maijia valley in Niger, 20% increase in grain yield was observed in millet crops protected by double rows of neem trees providing 500 km of wind break. Large scale planting of neem has been initiated in the Kwimba afforestation scheme in Tanzania. Neem plantations have been used for halting the spread of Sahara desert in the countries from Somalia to Mauritania [22]. Completely grown neem tree yields about 10- 100 tons of dried biomass/ha, comprised of leaves (50%) and fruits and wood (25% each). Neem wood is durable and termite resistant and thus used in making poles for house construction, furniture etc. In rural India, neem is a good source of firewood and fuel. Its charcoal has high calorific value]. Neem has the ability to resprout after cutting and to regrow its canopy after pollarding. Thus it is highly suited for pole production. Neem products have water purifying activity. Neem leaf powder could be used as biosorbent for the removal of dyes like Congo red from water [23 & 24].

IV. NEEM AND AGRICULTURE

More than 20000 Species and pests destroys the 1/3 rd food production of the world. In India we lose approx. Rs. 5000 crores worth of agricultural produced every year. Because of pests intrusion in yields. To prevent this loss, synthetic pesticides are applied in large scale, 0.1 % of prevention methods works and more than 99 % contaminates the ecosystem. Because of use of such large scale of synthetic pesticides, pests has started to develop the resistance against them example is DDT, obsolete from market because Mosquito has strongly developed antigen against its usage. Inexpensive, nontoxic, eco-friendly, Biodegradable and botanical are the need of present day agriculture as an Non Toxic Pesticides are alternative for hazardous and avoidable synthetic pesticides. Among the list of 2400 plant species, Neem is on top of the list of reported to have pesticidal properties and bio pesticidal properties, these are most reliable pesticide source of eco-friendly. Neem is also used as a biocontrol agent to control many plant diseases [25 & 26]. The neem insecticides are non-phytotoxic with good shelf life and effective against a wide range of insects and pests. More than 350 species of arthropods, 12 species of nematodes, 15 species of fungi, three viruses, two species of snails and one crustacean species are effectively affected from Neem products. Two tetracyclic triterpenoids - meliantetraolone and odorone isolated from neem shows insecticidal activity against *Anopheles stephensi* [27-31]. More than 195 types of insects are affected by neem extracts and those insects which have developed resistance to synthetic pesticides are also controlled with the help of these extracts. The assumptions that bulk usage of neem based insecticides may lead to develop resistance among pests, as happening with synthetic pesticides, has been not seen yet. Because the neem based insecticides have relatively weak contact effect seen on insects and also insecticides have unique mode of action on insect's life cycle and physiology. According to World Health Organization (WHO) reports, Due to acute poisoning annually 2,20,000 deaths occurs, caused by synthetic pesticides]. This can be avoided by usage of biopesticides. Neem based pesticides are much safer in this regard [32]. Today, neem has gained importance internationally because all communities have inclined towards green technology. Neem products have no ill effects on humans and animals, and on agricultural produce. This makes neem the best, reliable substitute to hazardous pesticides. The demand for chemical pesticides will be reduced by large scale use of neem based pesticides that will in turn reduce the load of synthetic chemicals in environment. Treatment of mice with neem leaf extract (aqueous) caused adverse effects on motility, morphology and number of spermatozoa. Neem seed extracts inhibited folliculogenesis in albino rats. Thus Neem extracts could be used as bio-rodenticides instead of toxic synthetic rodenticides. All the treatments resulted in higher seed germination and higher mean dry biomass than in untreated control. Therefore neem can be used against phytopathogenic fungi as a means of biological control [33 & 34].

Neem based pesticides are easy to prepare, cheap and highly effective and thus constitute an important source of pesticide for economically poor developing country's farmers. Neem bio-pesticides are systemic in nature and provide long term protection to plants against pests. Pollinator insects, bees and other useful organisms are not affected by neem based pesticides. Neem cake is a cheap and useful fertilizer. The plant debris are potential source of organic manure. Neem cake-coated urea has been produced, which when used increases nitrogen assimilation compared to untreated urea. Neem leaves could be used as a source for the preparation of vermicompost having both fertilizer and pesticidal potential [35-38]

V. VETERINARY USES

In India, neem has been used for centuries to provide health cover to live stock in various forms. It has also been very widely used as animal feed. The epic of Mahabharata (3000 B.C.) refers to two pandava brothers Nakul and Sahadeva, who used to treat wounded horses and elephants with neem oil and leaves' preparations. Neem extracts having antiulcer, antibacterial, antiviral properties are used successfully to treat cases of stomach worms, ulcers, cutaneous diseases, intestinal helminthiasis. All parts of neem viz., gum, bark, leaves, fruits, seeds are used to treat animals. Neem leaves have been mainly used as antiviral agents against vaccinia, variola, fowl pox and newcastle disease viruses. The hot infusion of leaves is used to treat swollen glands, bruises and sprains. Bark is effective against cutaneous diseases. Seed and kernel oil are used as antiseptic, antifungal and antibacterial agents. Neem oil has antihyperglycaemic effect. Alcohol and aqueous extracts of flowers of neem exhibits lethal effect against cattle filarial parasite *Setaria cervi*. Livestock insects such as maggots, horn flies, blow flies and biting flies are controlled traditionally using neem. Neem leaves, neem oil and de-oiled neem seed cake are used as animal feed. Neem leaves contain appreciable amount of proteins, minerals, carotene and adequate amount of trace minerals except zinc. They also have appreciable amount of digestible crude proteins (DCP) and total digestible nutrients (TDN). Thus cattle, buffaloes, goat, sheep, camel are fed with neem leaves. Neem oil which is rich in eBio Electronic Journal of Biology, 2008, Vol. 4(3):102-111 ISSN 1860-3122 - 107 - long chain fatty acids is used in poultry feed. Deoiled neem seed cake is rich in essential amino acids, crude proteins, fiber contents, sulphur and nitrogen. The processed cake has good appetizer and wormicidal activity and can be used as an excellent poultry feed. In the poultry industry, aflatoxicosis caused by *Aspergillus flavus* which originates from contaminated poultry feed is prevented using neem leaves. Neem leaf extract inhibits the production of aflatoxin by *Aspergillus parasiticus* and Patulin production by *Penicillium expansum* [39 & 40].

VI. MEDICINAL USES

Since time immemorial, Indians are aware of medicinal properties of neem. Neem has been extensively used in Ayurveda, Unani and Homeopathic medicine. Traditionally, many disorders like inflammation, infections, fever, skin diseases, dental disorders and others have been treated with different parts of neem tree such as leaves, flowers, seeds, fruits, roots and bark. Neem leaf exhibits a wide range of pharmacological activities viz., anti-inflammatory, antihyperglycaemic, antiulcer, antimalarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic anticarcinogenic and immunomodulatory [41]. Ayurvedic literature lists various medicinal uses of neem. It describes neem bark to be cool, bitter, astringent, acrid and refrigerant and useful in tiredness, cough, fever, loss of appetite, worm infestation. The bark is reported to heal wounds and vitiate conditions of kapha, vomiting, skin diseases, excessive thirst and diabetes. Neem leaves are reported to be beneficial for eye disorders and insect poisons and to treat vatic disorder. It is reported to be antileprotic. Neem fruits are bitter, purgative, antihemorrhoid and antihelminthic. Neem is called 'Sarvaroga nivarini' meaning 'the curer of all ailments'. In rural India, delivery chambers are fumigated with burning bark of neem. Dried margosa leaves are burnt to repel mosquitoes. In India several viral diseases are treated with neem. Neem leaf paste has been used to treat small pox, chicken pox and warts. Neem twigs are used as tooth brushes in rural India and Africa. Dental gel containing neem leaf extract reduces the oral plaque index and bacterial count. Methanolic extract fraction of neem leaves when tried against Coxsackie 'B' group viruses, produced in vitro antiviral and virucidal effect. Neem is used to treat malarial fever in ayurvedic medicine system. Neem oil treated mosquito nets and mosquito-repellent tablets are now available in the North-east India. Gedunin (a liminoid) obtained from neem has activity similar to quinine against malarial pathogen [42 & 43]. The neem liminoids (Azadirachtin, salannin, deacetylgedunin) exhibited high larvicidal, pupicidal and antiovipositional bioactivity against malarial vector – *Anopheles stephensi*. Tablet suspension of the bark and leaf of neem showed moderate effect against malarial pathogen, *Plasmodium*. Currently, studies on effect of administration of neem solutions on cancer, diabetes, heart disease and AIDS are being carried out. Anticarcinogenic activity of neem leaf extract was observed in murine system]. Injection of neem leaf preparation to tumor in mice reduced

tumour growth, exhibiting anticarcinogenic activity. Induction of apoptosis in rat oocytes was seen when treated with neem leaf extract. Buccal pouch carcinogenesis in hamsters was inhibited by ethanolic leaf extract of neem. The ethanolic leaf extract of neem also caused cell death of prostate cancer cells (PC-3) by inducing apoptosis. Good antioxidant activity was observed with neem leaf aqueous extract, flower and stem bark ethanolic extracts. Administration of aqueous extract of neem along with DOCA salt prevented the development of hypertension in rats. Neem leaf extracts are antimutagenic. The ethanolic extract of neem leaves exhibited strong antimutagenic activity in *Channa punctatus*, a fresh water fish model. Aqueous extract of neem root and leaves reduced blood sugar level in rats exhibiting antidiabetic activity [44 & 45]. The bark extract completely healed the duodenal ulcers when administered at the dose of 30-60 mg twice daily for 10 weeks. Neem bark extract had potential of controlling gastric hypersecretion, and gastroesophageal and gastroduodenal ulcers. Acetone-water neem leaf extract showed antiretroviral activity through inhibition of cytoadhesion. The extract increased haemoglobin concentration, mean CD4⁺ cell count and erythrocyte sedimentation rate in HIV/AIDS patients [46]. Enhancement of antibody production and cellular mediated response by neem components helps in the treatment of AIDS. Neem leaf and seed extracts exhibited antidermatophytic activity against dermatophytes viz., *Trichophyton rubrum*, *Mentagrophytes*, *Trichophyton violaceum*, *Microsporum nanum* and *Epidermophyton floccosum* under in vitro conditions. Neem seed oil showed bactericidal activity against 14 strains of pathogenic bacteria. Crude aqueous and solvent extracts of neem were tried against 20 strains of pathogenic bacteria wherein crude extract produced better results. The contraceptive property of neem oil has been reported. Neem leaf extract has spermatotoxic effect. The leaf extracts of neem showed 100% immobilization and mortality of human spermatozoa at a 3 mg dose within 20 seconds [47]. Several industries including pharmaceuticals, cosmetics, disinfectants, rubber, bio-pesticide and textile industries use neem oil. Many such neem-based commercial preparations are currently available. In India neem is highly exploited by many Ayurvedic drug industries. Neem oil and powdered neem leaves are employed in various cosmetic preparations such as face creams, nail polish, nail oils, shampoos, conditioners. A new shampoo, based on seed extract of neem was highly effective, more than permethrin-based product, against head lice under in vitro conditions. Neem cake a byproduct of neem oil industry is used as livestock feed, fertilizer and natural pesticide. Neem oil is commonly used in soap production. Medicated neem soaps are gaining popularity. Neem based toothpaste is widely used in India and European countries. Neem is a source for many oral-hygiene preparations and dental care products [48]. Neem bark yields gum and tannins which are used in tanning, dyeing etc. Neem seed pulp is used as a rich source of carbohydrate in fermentation industries and for methane gas production. Cultivation of neem and processing of neem products provides employment and income generation opportunities. Collection of neem seeds to be supplied to the industries provides important means of supplementary employment and income for the poor households, especially the rural women. India stands first in neem production and about 5,40,000 tons of seeds are produced annually yielding 1,07,000 tons of neem oil and 4,25,000 tons of neem cake (Anonymous, 1995). The amount of azadirachtin available is estimated to be about 1600 tons per annum, providing enormous amount of raw material for pesticide industry. In the product sector, annual estimated turnover is about Rs. 1000-1200 crores. Small scale industries have a major role to play in harnessing the potential. Therefore, in India it is the time to take right steps in promoting neem, both for the benefit of farmers and industries [49 & 50].

VII. CONCLUSION

Owing to its versatile characteristics neem is rightly called the 'Village pharmacy' or 'Doctor tree' or 'Wonder tree of India' or 'The bitter gem'. National Research Council (NRC), Washington, USA considers the neem, "One of the most promising of all plants and the fact is that it may eventually benefit every person on this planet. Probably no other plant yields as many strange and varied products or has as many exploitable byproducts."

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