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## Neem (*Azadirachta indica* A. Juss), A Potent Biopesticide and Medicinal Plant: A Review

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**Abstract:** Neem, *Azadirachta indica* A. Juss, “the wonder tree”, has the multiple pesticidal and medicinal properties, which is ecofriendly. Since time immemorial it has been extensively used in Ayurveda, Unani and Homeopathic medicines. Recently in modern science also, considerable progress has been achieved regarding the pesticidal and medicinal applications of about 135 different types of compounds found in every part of the tree. This review highlights the progresses on various research-based approaches on Neem in past and present and also focuses on the future prospects with safety application towards mankind.

**Key words:** Neem, pesticide, medicine, products

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### INTRODUCTION

Pests and diseases are the two great menaces for human civilization on the planet earth. Earlier men used to apply various biological (plant or animal based) raw products to get rid of their problems. The tribal people are still solely dependent on biological resources for their medicine and other needs (Jain, 2004). Even the modern pharmaceutical companies also dependent on biological (chiefly plants) resources to prepare various medicinal formulae. After industrial revolution in Europe, it became a common trend to use the chemical pesticides as an easy mean to eradicate the pest from agricultural fields. Recently, it has been noticed that chemical pesticides are not at all the safe mean (Gupta, 2004; Sara *et al.*, 2004). They are not biodegradable and prove as health hazards. Besides they kill not only the harmful, but also the beneficial as well as other organisms present in the field, thus affecting the natural balance. Now it is again realized that pesticides of biological origin can only solve the problem, which are eco-friendly (ICAR, World Neem Conference, 1993).

Neem, an evergreen, tall, fast growing tree of Meliaceae family, has pesticidal and medicinal properties that have been exploited for at least 2500 years ago. For centuries, millions have cleaned their teeth with neem twigs, smeared skin disorders with neem leaf juice, taken neem tea as a tonic and placed neem leaves in their beds, books, grain bins, cupboards, closets to keep away troublesome bugs. The tree has relieved so many different pains, fevers, infections and other complaints that it has been called the village pharmacy (Schmutterer, 1995, Singh *et al.*, 1996). The botanical name of neem i.e., *Azadirachta indica* derived from Farsi azad darakht I hindi literally means the free or noble tree of India suggesting that it is intrinsically free from pest and disease problems and is benign to the environment (Schmutterer, 1995; Tran and Perry, 2003). According to ad hoc panel of the Board of Science and Technology for International Development this plant may usher in new era in pest control, provide millions with inexpensive medicines cut down the rate of human population growth and even reduce erosion, deforestation and the excessive temperature of an overheated globe. Neem's other descriptions such as Nature's gift to mankind, the tree for many an occasion, the tree that purifies, the wonder tree, the tree of the 21st century, a tree for solving global problems, the divine tree etc. are recognition of its versatility (Puri, 1999, Schmutterer, 1995, Suri and Mehrotra, 1996).

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Viewing the tremendous potentiality and possibility of neem tree in the field of medicine and pesticide and the products are natural, nontoxic, 100% biodegradable and environment friendly (Sara *et al.*, 2004; Rao and Rao, 1977), it has been justified to create a review on neem research, so that diverse traditional and documented knowledge and modern scientific research approaches on neem can be brought under a single heading. It is expected that this review will help in thinking about the future prospects on neem research for the better benefit and well being of the globe.

### MEDICINAL ASPECTS OF NEEM

Sanskrit texts dating back to sixth century BC documented the microbiocidal prophylactic effects of neem extracts. Charaka, in the sixth century BC recommended the oral consumption of neem extracts toward off pimples, leprosy and edema. Sushruta, in the fifth century BC recommended the use of neem leaf smoke for fumigation and maintenance of general hygiene. He also recommended it as a krimihara, an agent effective against insect, grubs and maggots and detailed the ability of neem leaves to cure gangrenous and otherwise difficult to cure wounds (Schmutterer, 1995; Singh *et al.*, 1996). The medicinal use of neem as mentioned in Ayurveda are shown in the Table 1.

Kirtikar and Basu (1935) described that neem oil, bark and leaf extracts have been therapeutically used as folk medicine to control leprosy, intestinal helminthiasis, respiratory disorders, constipation and also as a general health promoter. He also mentioned that bark, leaf, root, flower and fruit of neem together cure blood morbidity, biliary afflictions, itching skin ulcers, burning sensation and pthysis. Biswas *et al.* (2002) have recently reviewed the biological activity of some neem compounds (Sastri *et al.*, 2006), pharmacological actions of the neem extracts, clinical study and plausible medicinal applications of neem along with their safety evaluation. They mentioned that the tree is still regarded as a village dispensary in India. They have also reviewed that more than 135 compounds have been isolated from different parts of neem, which have tremendous biological activity as Antiarthritic, Antipyretic, Hypoglycaemic, Antigastric ulcer, Spermicidal, Antifungal, Antibacterial, Diuretic, Antimalarial, Antitumour, Anti-inflammatory, Immunomodulatory etc (Govindachari, 1992). Some bioactive compounds from neem and its sources are shown in the Table 2.

At this context anti-fertility effect of neem is an interesting point to be emphasized (Khillare and Shrivastav, 2003). Biswas *et al.* (2002) mentioned that it could be a novel method of contraception, as intra-vaginal application of neem oil, prior to coitus could prevent pregnancy. Another point to be emphasized is the anti-malarial activity of neem seed and leaf extracts (Udeinya, 1993). They are effective against both choroquin-resistant and sensitive strain of malarial parasites (Agrawal, 2005). Further research especially in these two fields are needed and should be encouraged since population explosion and malaria are the two burning problems in the third world countries in present time.

Agrawal (2005) in his online article, reported anticancer activity of neem leaf and flower aqueous extract (Tepsuwan *et al.*, 2002) that effectively suppressed oral squamous cell carcinoma, induced by 7,12-dimethylbenz (a) anthracene (DMBA), as revealed by reduced incidence of neoplasm. Neem may

Table 1: Some medicinal uses of neem as mentioned in Ayurveda (Biswas *et al.*, 2002)

Part	Medicinal use
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 disorder, epistaxis, phlegm, eye problem wounds and leprosy
Twig	Relieves cough, asthma, piles, phantomb tumour, intestinal worms, spermatorrhoea, urinary discover and dibetes
Gum	Effective against skin diseases like ringworms, scabies, wounds and ulcers.
Seed pulp	Leprosy and intestinal worms.
Oil	Leprosy and intestinal worms.
Root, bark, leaf, flower and fruit together	Blood morbidity, biliary afflictions, itching, skin ulces, burning sensation and leprosy.

Table 2: Some neem compounds and their biological activity (Biswas *et al.*, 2002)

Neem compounds	Source	Biological activity	References
Nimbidin	Seed oil	Anti-inflammatory	Bhargava <i>et al.</i> (1970) Chattopadhyay (1998)
		Antiarthritic	Pillai and Santhakumari (1981)
		Antipyretic	David (1969)
		Hypo glycaemic	Chattopadhyay <i>et al.</i> (1993)
		Antigastric ulcer	Garg <i>et al.</i> (1992)
		Spermicidal	Khillare and Shrivastav (2003)
		Antifungal	Bhattacharyya <i>et al.</i> (2005)
		Antibacterial	Chary <i>et al.</i> (1984)
		Diuretic	Murthy and Sirsi. (1958) Bhide <i>et al.</i> (1958)
		Sodium nimbidate	
Nimbin	Seed oil	Spermicidal	Chattopadhyay (1998) Khillare and Shrivastav (2003)
Nimbolide	Seed oil	Antibacterial	Chopra <i>et al.</i> (1952)
		Antimalarial	Udeinya (1993)
Gedunin	Seed oil	Antifungal	Rochanakji <i>et al.</i> (1985)
		Antimalarial	Rao and Rao (1977)
Azadirachtin	Seed	Antimalarial	Sengottayan <i>et al.</i> (2005)
Mahmoodin	Seed oil	Antibacterial	Khalid <i>et al.</i> (1989) Jones <i>et al.</i> (1994)
			Devakumar and Dev (1996) Van der Nat <i>et al.</i> (1991)
Gallic acid, epicatechin and catchin	Bark	Anti-inflammatory and Immunomodulatory	Ara <i>et al.</i> (1989)
Margolone, margolonone and isomargolonone	Bark	Antibacterial	
Cyclic trisulphide and cyclic tetraulphide	Leaf	Antifungal	Kakai and Koho (1984)
		Anti-inflammatory	Pant <i>et al.</i> (1986)
Polysaccharides	Bark	Antitumour	Fujiwara <i>et al.</i> (1982)
Polysaccharides GIa, Gib	Bark	Anti-inflammatory	Fujiwara <i>et al.</i> (1984)
Polysaccharides GIHa, GIHa	Bark	Immunomodulatory	Vander Nat <i>et al.</i> (1987, 1989)

exert its chemo-preventive effect in the oral mucosa by modulation of glutathione and its metabolizing enzymes. Kumar *et al.* (2006) described that treatment with neem extract showed decreased level of Bcl-2, which is anti-apoptotic protein and increased the level of Bax protein that could be potentially effective against prostate cancer treatment. Baral *et al.* (2005) suggested that neem leaf preparation might be a potential immune adjuvant for inducing active immunity towards tumor antigens. Agrawal also reported the antioxidant activity of neem seed extracts. Extracts from leaf, flower and stem bark of neem tree have strong antioxidant potential which supports the ethnomedical use of young leaves and flowers of neem as a vegetable bitter tonic to promote good health (Sithisarn *et al.*, 2005). Shafeek *et al.* (2004) observed varying degrees of Central Nervous System (CNS) depressant activity in mice with the fractions of acetone extract of neem leaf. Another important finding is the antiviral activity of aqueous leaf extracts (Subapriya *et al.*, 2006; Haque and Baral, 2006) against vaccinia virus, chikungemya and measles virus. The antiviral activity of neem against AIDS virus is now becoming prominent field of R and D works and the research may come out with great success (NACO, 2004). Joshi *et al.* (2005) found that Praneem polyherbal formulations containing purified extracts of neem have activity against HIV and sexually transmitted disease pathogens. Extensive research in this field has become necessary, since AIDS (Stein, 1990) has become a potent threat to the human civilization, recently.

### NEEM: A POTENTIAL BIOPESTICIDE

Khan and Wassilew (1987) reports that *A. indica* is a potent botanical pesticide of choice for organic agriculture and it is widely used in several countries around the world today either singly in Integrated Pest Management (IPM) or in conjunction with Synthetic pesticides. He also cites that neem based pesticide is superior to other botanical pesticides (Charleston *et al.*, 2005) such as Rotenone and Pyrethrins. It belongs to the category of medium to broad- spectrum pesticides. In

Egypt, huge amount of information showing that botanical extract based pesticides especially neem, are very active against number of different pest species under laboratory, green house, semi field and field conditions and in different environments. They showed influence on wide range of pest insects, mites, nematodes, snails, crustaceans and parasitic species of human being, domestic animals and household pest as well as plant diseases (Charleston *et al.*, 2006; Nathan *et al.*, 2006; Peveling and Ely, 2006; Seljasen and Meadow, 2006; Rembold, 2005; Khan and Wassilew, 1987).

### **BENEFITS OF NEEM PESTICIDES**

Sara *et al.* (2004) and Rao and Rao (1977) reports that neem based pesticide is suited for mixing with other synthetic pesticides and infact enhances their action. None or lesser quantity of synthetic pesticides need to be used thereby reducing the pollution load. They also cited that several synthetic pesticides being single chemical compounds cause easy development of resistance in species of pests. Neem consists of several compounds hence development of resistance is impossible. Neem doesn't destroy natural predators and parasites of pest (Xuan *et al.*, 2004) thereby allowing these natural enemies to keep a check on the pest population (Sara *et al.*, 2004). Neem also has systemic action and seedlings can absorb and accumulate the neem compounds to make the whole plant pest resistant. Neem has a broad spectrum of action active on more than 200 species of pest. Neem is harmless to non-target organisms like pollinators, honeybees, mammals and other vegetables (Rao and Rao, 1977). Charleston *et al.* (2006) described that botanical extracts had adverse effects on survival, fecundity, development, oviposition and feeding of *Plutella xylostella*, but no direct negative effects on the survival and foraging of the parasitoids.

Randhawa and Parmar (1996) found that when neem compounds, especially Azadirachtin entered in the body of insect larvae, the activity of ecdyson (i.e., juvenile hormone) was suppressed and the larvae failed to moult and remained in the larval stage and ultimately died (Seljasen and Meadow, 2006; Naumann and Isman, 1995) (Oviposition Deterrent Insect Growth Regulation). The neem compound produces something similar to vomiting sensation; because of this sensation the insect does not feed on the neem treated surface (23, Arnason *et al.*, 1985; Isman *et al.*, 1990; Prijono and Hassan, 1993; Villanueva-Jimenez *et al.*, 2000) (Feeding deterrent). The neem oil also reduces pest not by allowing the female to deposit eggs on stored grains and after treatment the insect will not feed on them (Oviposition Deterrent). They also mentioned that neem had other pesticidal activities that include formation of chitin (exoskeleton) is inhibited, mating as well as sexual communication is disrupted, larvae and adults get repelled and also poisoned, adults get sterilized etc.

A Neem pesticide is a natural product, absolutely non-toxic, 100% biodegradable and environment friendly. M Lehmann of Germany described the guidelines to the use of neem pesticides towards leaf destroying insects on ornamental plants and tree of public green areas. Test applications under use of Neem Azal T/Sor its active substances have been carried out under employment of ground based machines, trunk painting and infusions in to the trunk and by helicopter. The efficacy was satisfactory and nearly as high as compared to chemical insecticides. He also mentioned that the neem extracts could be applied in many ways including sophisticated methods. They may be employed as sprays, powders drenches or diluents in irrigation water- even through trickle or sub surface irrigation systems. Sara *et al.* (2004) reviewed on safety evaluation of neem pesticide and safety assessments for the various neem- derived preparations that were made compared to the ingestion of residues on food treated with neem preparations as insecticides. He concludes that, if applied with care, use of neem derived pesticide, as an insecticide is an eco- friendly one. In addition, they may be applied to plants through injection or tropical application, either as dust or as sprays. The possible application of neem based pesticides with target pests are shown in the Table 3 (Singh and Sing, 2000; Vijayalakshmi *et al.*, 1985).

Table 3: Methods of application of neem based pesticide

Materials	Methods of preparation	How to use	Target pests
<p>Neem leaf extract: 1-2 kg of neem leaves Mortar and pestle Used cotton cloth Pot, Soap, Strainer and String .10-12 kg of neem leaves are needed for 0.4 ha (Sridhar <i>et al.</i>, 2002)</p>	<p>Pound neem leaves gently. Place in a pot. Add 2-4 liters of water. Cover the mouth of the pot securely with the cloth and leave it as such for 3 days. Strain to get clear extract</p>	<p>Dilute 1 liter of neem leaf extract with 9 liters of water. Add 100 ml of soap. Stir well. Spray on the infested plants</p>	<p>Aphids, Colorado, beetles, Grasshoppers, Grubs, Japanese, beetles, Leafhoppers, Locusts, Planthoppers, Scales, Snails, Thrips, Weevils, Whiteflies</p>
<p>Neem seed extract: 3-5 kg of neem seeds Mortar and pestle Used cotton cloth Earthen pot Soap, Strainer, String (Sridhar <i>et al.</i>, 2002)</p>	<p>Remove the shells. Pound seeds gently. Place in a pot. Add 10 liters of water. Cover the mouth of the pot securely with the cloth and leave it as such for 3 days. Strain to get clear extract.</p>	<p>Dilute 1 L of this extract with 9 liters of water. Add 100 mL of soap. Stir well. Spray on the infested plants.</p>	<p>Aphids, Beetles, Bugs, Grasshoppers, Grubs, Flies, Leafhoppers, Locusts, Moths, Nematodes, Planthoppers, Scales, Snails, Thrips, Weevils, Whiteflies</p>
<p>Neem seed powder extract: Matured, dried neem seeds, Mortar and pestle, Basin, pail Muslin pouch Strainer Soap (5 ml/10 l of water) and Water (Singh <i>et al.</i>, 2000)</p>	<p>Remove shells and pulps from seeds in the desired amount. Then pound seeds gently in such a way that no oil comes out. Once done, put the desired amount of powder in a pail of water. Stir well for about 10 min and steep for at least 6 h but not more than 16 h. Stir it again for another 10 min. Strain. Add soap. Stir well.</p>	<p>Spray on the infested plants thoroughly. Spray early in the morning or late afternoon.</p>	<p>Cotton bollworm, Aphids, Colorado beetles, Cotton leaf roller, Cutworm, Diamondback moth, Fall armyworm, Grasshopper, Japanese beetles, Leafminer, Leaf hopper, Locust, Mexican bean beetle, Whiteflies</p>
<p>*Neem seed oil suspension in water: 5 kg of finely ground neem seeds ½L of hot water Soap, Basin (Singh <i>et al.</i>, 2000)</p>	<p>Put the finely ground seeds into a basin. Add hot water little by little until it is possible to knead the mixture. Knead and press the mixture to get the oil. Approximately 650-750 mL oil is extracted from this mixture.</p>	<p>Take desired amount of neem oil and mix with soap before adding water. Stir thoroughly to prevent oil separation. Fill-in the knapsack sprayer. Spray thoroughly on infested plants.</p>	<p>Aphids, Brown plant hopper, Flea beetle, Leafhopper, Potato tuber moth, Psyllid, Scale insects, Whitefly, Whorlmaggot</p>

\*Precaution: Oil maybe phytotoxic at a ratio of 10 mL oil L<sup>-1</sup> of water on sensitive plants. Wait for 2 days for the effects (symptoms) to appear before going into large scale application

National Research Council (1992) found that the azadirachtin was relatively harmless to butterflies, bees, ladybugs and wasps since these beneficial feed on nectar and pollen. Azadirachtin must be ingested to be effective so that pests which feed on plants are affected by its content. However, constant spraying of flowering plants with highly concentrated neem products affect bees since they carry contaminated pollen and nectar to the hives. Rossner and Zebitz (1986) conducted a study on neem products and their effects on mortality, growth and reproduction of 7 species of earthworms. Various neem products were incorporated in the upper 10 cm soil layer of tomato plots. None of the materials had negative side effects on earthworms. Positive effects on weight and survival were found in soil treated with ground neem leaves and ground seed kernels under greenhouse conditions. Reproduction was slightly favored over a period of 13 weeks in a neem-enriched substrate in rearing cages.

At this point further research approaches can be made to identify the specific compound responsible for enhancing survival and reproduction of earthworms in agricultural fields since many of them are going to be extinct causing biological imbalance. Again one can approach for the effect of

neem products on harmful rats in agricultural fields. Martineau (1994) explained that azadirachtin had no side effects on birds and other animals. There is no toxic residue left to contaminate the environment and insects do not develop resistance to neem (Sara *et al.*, 2004). These above mentioned findings of NRC (1992), Rossner and Zebitz (1986) and Martineau (1994) clearly reveal the ecofriendly and superior quality of neem based pesticides, through which we can overcome the ecological and health threats imposed by chemical pesticides.

For last few years, there has been a little increasing trend and awareness in neem research. We hope that the traditional knowledge, ancient documents and modern findings, mentioned in this review will encourage new thoughts towards extensive research to solve the ever increasing challenging problems of the human civilization in the globe.

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