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Pharmacological review on natural products (*Azadirachta indica* Linn)

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Abstract

Neem is a tree in the mahogany family Meliaceae. It is native to India, Myanmar, Bangladesh, Sri Lanka, Malaysia and Pakistan. It grows in tropical and semi-tropical regions. It was also the state tree of Andhra Pradesh. Neem is a fast-growing tree that can reach up to 15–20 m (about 50–65 feet) tall, and sometimes even to 35–40 m (115–131 feet). It is evergreen. This Plant is used folk medicine to cure burns, fever, diarrhea and skin disease and syphilis, *Azadirachta Indica* have a rich source of tannin, Flavonoides, Glycosides, terpenoid. *Azadirachta indica* have been known to possess a wide range of pharmacological properties included anti malaria, anti-oxidant, wound healing activity, anticancer, antiulcer, anti fertility, antimicrobial activity. The present paper reviews the Pharmacological activity aspects of Neem.

Keywords: Pharmacological activity, flavonoides. skin disease antimalaria, antioxidant

Introduction

The neem tree is noted for its drought resistance. Normally it thrives in areas with sub-arid to sub-humid conditions, with an annual rainfall of 400–1,200 millimetres (16–47 in). It can grow in regions with an annual rainfall below 400 mm, but in such cases it depends largely on ground water levels. Neem can grow in many different types of soil, but it thrives best on well drained deep and sandy soils. It is a typical tropical to subtropical tree and exists at annual mean temperatures of 21–32 °C (70–90 °F). It can tolerate high to very high temperatures and does not tolerate temperature below 4 °C (39 °F). Neem is one of a very few shade-giving trees that thrive in drought-prone areas e.g. the dry coastal, southern districts of India and Pakistan. The trees are not at all delicate about water quality and thrive on the merest trickle of water, whatever the quality. In India and tropical countries where the Indian diaspora has reached, it is very common to see neem trees used for shade lining streets, around temples, schools and other such public buildings or in most people's back yards. In very dry areas the trees are planted on large tracts of land.

Weed status

Neem is considered a weed in many areas, including some parts of the Middle East, most of Sub-Saharan Africa including West Africa and Indian Ocean states, and some parts of Australia. Ecologically, it survives well in similar environments to its own, but its weed potential has not been fully assessed [7].

In April 2015, *A. indica* was declared a class B and C weed in the Northern Territory, Australia, meaning its growth and spread must be controlled and plants or propagules are not allowed to be brought into the NT. It is illegal to buy, sell, or transport the plants or seeds. Its declaration as a weed came in response to its invasion of waterways in the "Top End" of the territory [8].

After being introduced into Australia, possibly in the 1940s, *A. indica* was originally planted in the Northern Territory to provide shade for cattle. Trial plantations were established between the 1960s and 1980s in Darwin, Queensland, and Western Australia, but the Australian neem industry did not prove viable. The tree has now spread into the savanna, particularly around waterways, and naturalised populations exist in several areas [9].

Uses

Neem leaves are dried in India and placed in cupboards to prevent insects eating the clothes, and also in tins where rice is stored [1]. Neem leaves are dried and burnt in the tropical regions to keep away mosquitoes. (*Citation needed*) These flowers are also used in many Indian

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festivals like Ugadi. See below: #Association with Hindu festivals in India. As an ayurvedic herb, neem is also used in baths.

As a vegetable

Tender neem leaves used as medicine, Karnataka, India, the tender shoots and flowers of the neem tree are eaten as a vegetable in India. A souplike dish called *Veppampoo charu* (Tamil) (translated as "neem flower rasam") made of the flower of neem is prepared in Tamil Nadu. In West Bengal, young neem leaves are fried in oil with tiny pieces of eggplant (brinjal). The dish is called *nim begun* and is the first item during a Bengali meal that acts as an appetizer. It is eaten with rice [2].

Neem is used in parts of mainland Southeast Asia, particularly in Cambodia aka sdom—^{វៀត}, [3] Laos (where it is called *kadao*), Thailand (where it is known as sadao or sdao), Myanmar (where it is known as *tamar*) and Vietnam (where it is known as *sâu đầu* and is used to cook the salad *gỏi sàu đầu*). Even lightly cooked, the flavour is quite bitter and the food is not enjoyed by all inhabitants of these nations, though it is believed to be good for one's health. Neem gum is a rich source of protein. In Myanmar, young neem leaves and flower buds are boiled with tamarind fruit to soften its bitterness and eaten as a vegetable. Pickled neem leaves are also eaten with tomato and fish paste sauce in Myanmar.

Traditional medicinal use

Products made from neem trees have been used in India for over two millennia for their medicinal properties [1]. Neem products are believed by Siddha and Ayurvedic practitioners to be Anthelmintic, antifungal, antidiabetic, antibacterial, antiviral, contraceptive and sedative [4]. It is considered a major component in siddha medicine and Ayurvedic and Unani medicine and is particularly prescribed for skin diseases [5]. Neem oil is also used for healthy hair, to improve liver function, detoxify the blood, and balance blood sugar levels [6]. Neem leaves have also been used to treat skin diseases like eczema, psoriasis, etc. [1].

However, insufficient research has been done to assess the purported benefits of neem [7]. In adults, short-term use of neem is safe, while long-term use may harm the kidneys or liver; in small children, neem oil is toxic and can lead to death [7]. Neem may also cause miscarriages, infertility, and low blood sugar [7].

Safety issues

Neem oil can cause some forms of toxic encephalopathy and ophthalmopathy if consumed in large quantities [8].

Pest and disease control

Neem is a key ingredient in non-pesticidal management (NPM), providing a natural alternative to synthetic pesticides. Neem seeds are ground into a powder that is soaked overnight in water and sprayed onto the crop. To be effective, it must be applied repeatedly, at least every ten days. Neem does not directly kill insects on the crop. It acts as an anti-feedant, repellent, and egg-laying deterrent, protecting the crop from damage. The insects starve and die within a few days. Neem also suppresses the hatching of pest insects from their eggs. Neem cake is often sold as a fertilizer [9].

Neem oil has been shown to avert termite attack as an ecofriendly and economical agent [10].

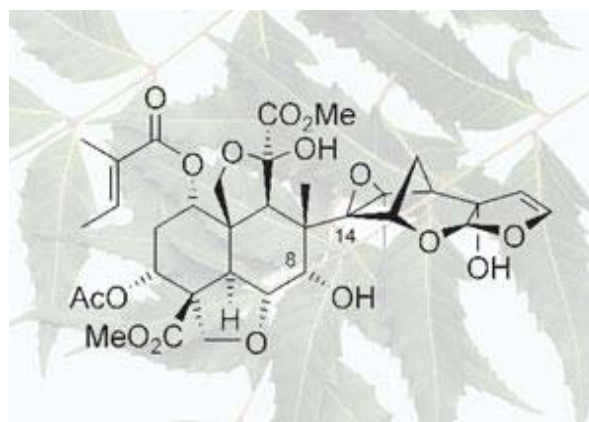
Neem oil for polymeric resins

Applications of neem oil in the preparation of polymeric resins have been documented in the recent reports. The synthesis of various alkyd resins from neem oil is reported using a monoglyceride (MG) route and their utilization for the preparation of PU coatings [11]. The alkyds are prepared from reaction of conventional divalent acid materials like phthalic and maleic anhydrides with MG of neem oil. In other reports, different routes for preparation of polymeric resins from neem oil are also reported [12].

Classification	
Common Name	Neem
Botanical Name	<i>Azadirachta indica</i>
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Sapindales
Genus	<i>Azadirachta</i>
Species	<i>A. indica</i>
Family	Meliaceae



Neem tree



Chemical structure of *Azadirachta Indica* Linn

Description

Azadirachta indica is a tree in the mahogany family Mellaceae. It is one of two species in the genus *Azadirachta*, and is native to India, Burma, Bangladesh, Sri Lanka, Malaysia and Pakistan, growing in tropical and semi-tropical regions. Neem is a fast-growing tree that can reach a height of 15–20 m, rarely to 35–40 m. It is evergreen, but in severe drought it may shed most or nearly all of its leaves. The branches are wide spread.

It blossoms in spring with the small white flowers. It has a straight trunk. Its bark is hard rough and scaly, fissured even in small trees. The color of the bark is brown grayish. The leaves are alternate and consist of several leaflets with serrated edges. Its flowers are small and white in color. The olive like edible fruit is oval, round and thin skinned.

The Neem tree is noted for its drought resistance. Normally it thrives in areas with sub-arid to sub-humid conditions. Neem is a life-giving tree. It is one of the very few shade-giving trees that thrive in the drought-prone areas. The trees are not at all delicate about the water quality and thrive on the merest trickle of water, whatever the quality.

Medicinal Uses

Azadirachta indica is variously known as Sacred Tree, Heal all, Village Pharmacy and Panacea for all diseases. Products made from Neem tree have been used in India for over two millennia for their medicinal properties. All parts of Neem tree used as anthelmintic, anti-fungal, anti-diabetic, antibacterial, antiviral, contraceptive and sedative. Neem tree is used in many medicinal treatment like skin diseases, healthy hair, improve liver function, detoxify the blood, Pest and disease control, fever reduction, dental treatments, cough, asthma, ulcers, piles, intestinal worms, urinary diseases etc. oil of Neem used in soap, shampoo, balms and creams as well as toothpaste. Small branches of Neem used as toothbrush. Neem oil also useful for skin care such as acne treatment, and keeping skin elasticity. Neem oil has been found to be an effective mosquito repellent. All parts of this tree also used in pharmacy companies for making different types of drugs.

Neem gum is used as a bulking agent and for the preparation of special purpose food (for diabetics). Aqueous extracts of Neem leaves have demonstrated significant anti-diabetic potential. Neem leaf paste is applied to the skin to treat acne, and in a similar vein is used for measles and chicken sufferers. Practitioners of traditional Indian medicine recommend that patients suffering from chicken pox sleep on Neem leaves. A decoction prepared from Neem roots is ingested to relieve fever in traditional Indian medicine.

Pharmacological Study

Wound healing activity

The effect of traditional herbal formulation was screened on excision and incision wound models with the control (simple ointment base B.P) and reference standard (framycetin sulfate cream 1% w/w). The measurements of the progress of the wound healing induced by the control (simple ointment base B.P), reference standard (framycetin sulfate cream 1% w/w). It is observed that the wound contraction ability of the test formulation was significantly greater than that of the control and reference standard ($p < 0.001$)

In the incision wound model, there was a significant increase in tensile strength of the 10 d old wound due to treatment with test formulation (592 ± 12.2). Measurements of the tensile strength [13].

Anti oxidant activity

DPPH free radical scavenging assay The free radical scavenging activity (antioxidant capacity) of AILE on stable radical 1,1-diphenyl -2-picrylhydrazyl (DPPH) was estimated by method mentioned by Brand-Williams *et al.*, Briefly, 2ml of AALE at varying concentrations (50 μ g/ml to 250 μ g/ml) was mixed with 2.0 ml of DPPH solution in methanol (0.004% w/v). The mixture was allowed to stand at room temperature in dark for 20 min. Then the mixture was

vortexed and absorbance was recorded at 517nm using spectrophotometer. Ascorbic acid was used as a reference standard and control consisted of DPPH solution without extract. The test was performed in triplicate and percentage scavenging of DPPH free radical by extract was calculated using the equation: $(A_{\text{control}} - A_{\text{test}}) / A_{\text{control}} \times 100$, where A control is the absorbance of control and Atest is the absorbance in presence of extract or standard [14].

Antimicrobial activity

The minimum inhibitory concentration was defined as the lowest concentration of the compound to inhibit the growth of microorganisms (Kumar, G.S. *et al.*, 2007) The minimum inhibitory concentration values were determined by broth dilution assay of microdilution assay. Varying concentrations of the extracts (200mg/ml, 150mg/ml, 100mg/ml, 50mg/ml, and 25mg/ml) were prepared. 0.1ml of standardized test organism of Controls was equally set up by using solvents and test organisms without extract. The tube with least concentration of extract without growth after incubation was taken and recorded as the minimum inhibitory concentration [15-16].

Antimalaria activity

Malaria Culture Media RPMI 1640 medium containing L-glutamine (High Media), 25 mM HEPES (CDH), 10 μ g ml⁻¹ gentamicin (CDH), 0.225% NaHCO₃ (CDH). Medium is adjusted to a pH of 7.3 to 7.4. Once media was prepared media was filtered through 0.22 μ m syringe filters then stored in air tight plastic bottles, at 4-8 °C till further use. During culture maintenance media was supplemented with 5% fresh human serum (O+ blood group) [17].

Herpes simplex virus type 1 (HSV-1 local isolate) was used as a model of DNA virus for antiviral screening. The virus was isolated, propagated and identified by Prof. Mohamed Ali, Virology Laboratory of the Department of Water Pollution, National Research Center. African green monkey cells (Vero) were used as virus host. Cells grew in minimum essential medium with Hank's buffer (HMEM) supplemented by 1% antibiotic-

Antiviral screening

Antimycotic mixture (GIBCO-BRL), 8% fetal bovine serum and the pH adjusted to 7.2-7.4 by 7.5% sodium bicarbonate solution. Cells grew as monolayer sheets dissociated by trypsin-versine solution (0.15% trypsin and 0.04% ethylene diamine tetraacetic acid, EDTA 2Na). The dissociated cells subcultured in a 96-well plate to measure the cytotoxicity of the extract by incubation with the cells at 37 °C for 24 h. Cytotoxicity was measured microscopically and by viable cell counting. The optimal concentration of extract was estimated; compared with acyclovir as standard (>95%-4669) Sigma. Control virus and cells were treated identically without the extract or standard. Virus plaques were counted and the percentage reduction was calculated [27]. Also, the concentration range of the oil was determined. The virucidal activity was determined by plaque reduction method [18-19].

Conclusion

The extensive literature survey revealed that *Azadirachta indica* is an important medicinal plant. This plant is used by traditional medical practitioners for the treatment of various diseases. Pharmacological reviews on plants will give valuable information which will assist the scientists in getting more advanced knowledge about a plant species.

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