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MEDICINAL BENEFITS OF NEEM: A REVIEW

Zeeshan Haider Rizvi, Mohd Tariq, Jamal Akhtar*, Mohd Naime, Maqbool Ahmad Khan

Central Research Institute of Unani Medicine, Lucknow.
*Central Council for Research in Unani Medicine, New Delhi.

***Corresponding Author: Jamal Akhtar**
Central Council for Research in Unani Medicine, New Delhi.

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ABSTRACT

Herbal medicines are also known as herbal products, herbal remedies, phyto-medicines, herbal medicinal products, phyto-therapeutic agents and phyto-pharmaceutical agents. Neem consists of dried root bark *of Azadirachta indica* A. Juss. syn. Meliaazadirachta Linn. (Fam. Meliaceae), a medium to large evergreen tree attaining a height of 15 to 20 m or more under favourable conditions and found throughout the plains of India upto an altitude of 900 m. It is having antimicrobial, antifungal, anthelmintic, insecticidal, antiviral, antipyretic, anti- malarial, antiperiodic, mosquito larvicidal, anti-inflammatory, antifertility, spermicidal, hypoglycaemic activities and recommended in inflammation of gums, gingivitis, periodonitis, sores, boils, enlargement of spleen, malarial fever, fever during childbirth, measles, smallpox, head scald and cutaneous affections. Oil—used (CPK) as a contraceptive for intravaginal use, for the treatment of vaginal infections, and as a mosquito repellent. In this review an attempt has been made to give a detailed description of this medicinal plant and the scientific data on it.

KEYWORDS: Neem, Unani, *musaffi khoon.*

INTRODUCTION

Herbal medicines are also known as herbal products, herbal remedies, phyto-medicines, herbal medicinal products, phyto-therapeutic agents and phyto-pharmaceutical agents. The use of herbal medicines in an evidence based advance for the management and avoidance of disease is known as phytotherapy. vegetations have been in use for antiquity by civilization all over the world. In the history there has been improved awareness and curiosity in the use of traditional medication worldwide.[1]

In China, traditional medication reports for approximately 40% of all health care services. In Chile 71% of the population, and in Colombia 40% of the population, have used such medicine. In India, 65% of the population in rural areas use medicinal plants to help meet their primary health care needs. In developed countries, traditional, complementary and alternative medicines are becoming more popular. For example, the percentage of the population that has used such medicines at least once is 48% in Australia, 31% in Belgium, 70% in Canada, 49% in France and 42% in the United States of America.[1,2]

Neem consists of dried root bark *of Azadirachta indica* A. Juss. syn. Meliaazadirachta Linn. (Fam. Meliaceae), a

medium to large evergreen tree attaining a height of 15 to 20 m or more under favourable conditions and found throughout the plains of India upto an altitude of 900 m.

Synonym *Meliaazadirachta* Linn. CPK
Family *Meliaceae*.
Habitat Native to Burma; found all over India.
English Neem tree, Margosa tree.
Ayurvedic Nimba, Nimbaka, Arishta, Arishtaphala, Pichumarda, Pichumanda, Pichumandaka, Tiktaka, Sutiktak, Paaribhadra.
Unani Aazaad-Darakht-e-Hindi., Neem
Siddha/Tamil Vemmu, Veppu, Veppan, Arulundi.
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Unani Aazaad-Darakht-e-Hindi.
Siddha/Tamil Vemmu, Veppu, 3.

Root bark available in quilled or curved pieces of varying sizes with a thickness of 0.25 to 0.50 cm; outer surface irregular, rough, scaly, fissured, reddish-brown or greyish- brown; inner surface, yellowish-brown with parallel striations; fracture, splintery and fibrous; odour like that of saw dust; taste, bitter.

Root bark shows cork, cortex and phloem; cork generally 6 or 7 layers of polygonal and thin walled cells with reddish-brown contents; outer cortex of tangentially elongated large rectangular cells with tangentially elongated sclereids, singly or in groups in isolated patches; sclereids vary in size and wall thickness, distinctly striated, pitted and often associated with cells containing crystal; inner cortex of polygonal parenchymatous cells with bundles of sclerenchymatousfibres, thick walled with irregular lumen; secondary phloem composed of alternating tangential bands of bast fibres and parenchymatous tissues intercepted by uni to biseriate phloem rays; abundant starch grains present in parenchymatous cells of cortex and phloem; starch grains simple, or more usually, compound with 2 or 3 components, hilum cleft or radiate, individual grain 5 to 20 μ; abundant prismatic crystals of calcium oxalate in cortex, of 10 to 15 μ, also associated with phloem fibres; idioblasts with reddish-brown contents seen in cortex; cells with fat droplets seen in inner cortex and phloem.

Powder - Reddish-brown; shows cork cells; numerous prismatic crystals of calcium oxalate both isolated, and in association with phloem fibres; individual fibres with narrow lumen and elongated tapering ends; pitted macrosclereids with wide lumen and distinct striations; simple, and compound starch grains with 2 or 3 components, of 5 to 20 μ in size; parenchymatous cells large and occasionally filled with brown contents.

Morphology

Dried flowers are brown to deep brown; individual flower 5 to 6 mm long and 6 to 11 mm wide, pentamerous, bisexual, regular and hypogynous; calyx 5, short, united at base; corolla 5, free, spathulate, spreading, 4.5 to 5.5 mm long 2 mm wide; stamens 10, monoadelphous, staminal tube inserted at base of corolla; gynoecium tricarpellary, syncarpous, superior, trilocular, two ovules in each locule, style 1, stigma 3-lobed; taste, mildly bitter: odour, indistinct.

Calyx - Sepal shows thin walled polygonal papillose epidermis; elongated thin walled unicellular conical trichomes of varying lengths; rosette crystals in cells of epidermis.

140 Petals - Petal shows epidermis of rectangular cells papillose at margins, non-glandular unicellular trichomes, over 150 µ long, tubular and hyaline; glandular trichomes of about 20 µ, numerous rosette crystals in epidermal cells.

Androecium - Epidermis of staminal tube composed of thick walled rectangular parenchymatous cells and the endothecium of the anther walls.

Gynoecium - Stigma sticky, parenchymatous epidermal cells, elongated into extensive papillae, style thin walled, rectangular, ovary superior, trilocular.

Pollen Grain - Porous, 4-colporate, spherical 105 to161µ in dia., with a smooth exine.

Powder - Yellowish-brown, fragments of parenchymatouspapillose epidermal cells, trichomes, numerous vessels, rosette calcium oxalate crystals, and yellowish-brown pollen grains.

Seed- Brownish, dorsally convex; upto 1.5 cm long and 0.6 cm wide; seed coat thin, brownish, shell-like, cracks to touch, inside of cracked pieces golden yellow; seed kernel, light brown, oily; odour, strong; taste, bitter.

Fruit - Glabrous, dark reddish-brown, ovoid to ellipsoid drupes. 0.5 to 2 cm long, over one cm wide; indehiscent, deeply wrinkled, enclosing a single seed in a brownish leathery pulp; odour strong; taste, bitter.

Fruit - Pericarp well differentiated into epicarp, mesocarp and endocarp; epidermis more than one layered; squarish to rectangular cells containing yellowish- brown contents and oil droplets; mesocarp, many layered of loosely packed cells with large elongated sclereids scattered in outer layers; endocarp of two distinct layers, outer of closely packed lignified stone cells, inner fibrous, loosely packed, lignified.

Seed - Seed kernel shows a thin brown testa, of isodiametric stone cells overlying integument of loosely packed parenchymatous cells; cotyledon consisting of parenchy- matous cells containing abundant oil droplets.

Powder - Dark brown; shows abundant brachysclereids, columnar sclereids and pitted stone cells with wide lumen and distinct wall striations; groups of lignified fibres, thin- walled, arranged in network of loose strands; parenchymatous cells of cotyledon containing aleurone grains and oil globules; fragments of testa showing distinctly striated isodiametric stone cells; a few scattered rosette crystals of calcium oxalate.[4]

Action Leaf, bark—antimicrobial, antifungal, anthelmintic, insecticidal, antiviral, antipyretic, anti-malarial, antiperiodic, mosquito larvicidal, anti-inflammatory, antifertility, spermicidal, hypoglycaemic; used in inflammation of gums, gingivitis, periodonitis, sores, boils, enlargement of spleen, malarial fever, fever during childbirth, measles, smallpox, head scald and cutaneous affections. Oil—used (CPK) as a contraceptive for intravaginal use, for the treatment of vaginal infections, and as a mosquito repellent.

Plant tetranortriterpenoids have been examined extensively for their an- tibiotic, antitumour, insecticidal, antibacterial and antifungal activities.

The methanolic extract of the bark shows antimalarial activity against *Plasmodium falciparum*.

The aqueous extract of leaves exhibited antiulcer and anti-inflammatory activity.

The water-soluble portion of alcoholic extract of leaves reduces blood sugar in glucose-fed and adrenaline-induced hyperglycaemic rats (but not in normal and streptozotocin-induced diabetic rats).

A volatile fraction of the Neem oil is reported to be responsible for spermicidal activity at a dose of mg/ml for human sperm. The oil has been found to retard the growth of human immunodeficiency virus.

Neem oil has caused mitochondrial injury in mice; poisonous in high doses. (Sharon M. Herr.).[3]

Women with abnormal vaginal discharge who presented to a gynecological clinic in India were randomized to receive either a cream containing Azadirachtaindica(neem) seed oil, Sapindusmukerossi(reetha) saponin extract and quinine or placebo. They applied the cream intravaginally at bedtime for 14 days. The results were quite impressive. Symptomatic and microbial assessment revealed that 10 of 12 women with Chalmydia trachomatis vaginitis recovered within 1 week, and 10 of 17 with bacterial vaginosis recovered within 2 weeks. There was no benefit found in women with candidal or trichomonal infections and none of the women using the placebo recovered from any of the infections.[5]

Activities (Neem) — Alterative; Amebicide, Analgesic. Anorectic, Antiarrhythmic, Antibacterial, Antidiabetic, Antifeedant, Antiinflammatory, Antiperiodic, Antiplaque, Antipyretic, Antiseptic, Antiviral, Aphrodisiac, Astringent, Bitter, Carminative, Contraceptive, Demulcent, Deobstruent, Diuretic, Emmenagogue, Emollient, Expectorant, Fungicide, Insectifuge, Larvicide, Laxative, Parasiticide, Pectoral, Pesticide, Stimulant, Stomachic, Tonic, Uterocontractant, Vulnerary.

Indications (Neem) — Adenopathy; Allergy; Alopecia; Amenorrhea, Arrhythmia, Asthma, Biliousness; Bite; Boil; Bruise; Burn; Cancer; Cancer colon, Cancer, skin Carbuncle; Cardiopathy; Catarrh; Cholera; Constipation; Debility Dermatosis; Diabetes, Diarrhea, Dusgeusia; Dysentery; Dyspepsia; Dysuria; Earache; Eczema; Enterosis; Fatigue; Fever; Fungal Infection; Furunculosis; Gingivosis; Gray Hair; Heat Rash; Hemorrhoid; Hepatosis; Hernia; Herpes; Infections; Inflammation; Insomnia; Itching; Jaundice; Leprosy; Leukoderma; Malaria; Measles; Metrosis; Mycosis; Nausea; Nervousness; Pain; Parotosis; Pediculosis; Plaque; Pyorrhea; Rheumatism; Rhinosis; Ringwor; Salmonella; Scabies; Scald; Scrofula; Seborrhea; Smallpox; Snakebite; Sore; Splenosis; Sprain; Sting; Stomatosis, Syphilis; Toothache; Toxemia, Tuberculosis; Ulcer; Worm; Wound.

Dosages (Neem) — 2–4 (500 mg) leaf-powder capsules with meals (trade recommendation); 100 g bark soaked in 1 liter water daily for one month as male contraceptive (SKJ).

Contraindications, Interactions, and Side Effects (Neem) — Not covered (AHP). No health hazards known at proper dosage levels (PHR). Excessive doses can cause convulsions, dyspnea, stupor, even death (APA). The oil seems to be more toxic to children because of an as yet undefined toxin that is particularly significant to younger people.[6]

1. Anticancer Activity

Finding confirmed that neem and its constituents play role in the scavenging of free radical generation and prevention of disease pathogenesis. In a study based on animal model established that neem and its chief constituents play pivotal role in anticancer management

through the modulation of various molecular pathways including p53, pTEN, NF-*κ*B, PI3K/Akt, Bcl-2, and VEGF. It is considered as safe medicinal plants and modulates the numerous biological processes without any adverse effect.[7]

2. Antifungal activity

Antifungal activity of different neem leaf extracts and the nimonol against some important human pathogens was reported by Mahmoud et al. The study was conducted to evaluate the effect of aqueous, ethanolic and ethyl acetate extracts from neem leaves on growth of some human pathogens (*Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger*, *Aspergillus terreus*, *Candida albicans* and *Microsporum gypseum*) *in vitro*. Different concentrations (5, 10, 15 and 20%) prepared from these extracts inhibited the growth of the test pathogens and the effect gradually increased with concentration. The 20% ethyl acetate extract gave the strongest inhibition compared with the activity obtained by the same concentration of the other extracts. High Performance Liquid Chromatography (HPLC) analysis of ethyl acetate extract showed the presence of a main component (nimonol) which was purified and chemically confirmed by Nuclear Magnetic Resonance (NMR) spectroscopic analysis. The study proved antifungal activity of neem.[8]

3. Antimicrobial Activities

The antimicrobial activity of neem extract at different concentrations was evaluated by Sherein et al using agar-well diffusion method against 13 microbial pathogens strains of animal origin. Results revealed that the neem extract has great bactericidal activities at lower concentrations 10 and 50% than at concentrations above 75 to 100%. Diluted neem extract showed bactericidal activities against Gram negative bacteria but did not against Gram positive bacteria. Zone of inhibition reached 14 and 12 mm against Citrobacter, 19 and 18 mm against Klebsiella, 18 and 17 mm against S. bodyi, 18 and 15 mm against S. sonnei, 13 and 12mm against S. flexeneri, 14 and 12 mm against E. coli O157, 17 and 15 mm against E. coli O78, 14 and 13 mm against E. coli O26 and 16 and 14 mm against Salmonella at conc. 10 and 50%, respectively. Neem extract has no antibacterial activities against tested Gram positive bacteria; S. aureus and MRSA. Against mycotic isolates only 10% of Neem extract showed fungicidal effect with zone of inhibition 25 and 20 mm against C. albicans and Asp. flavus, respectively. Neem extract was evaluated for its capability for hindrance of bacterial count in ground beef as well as monitoring of its capability for hindrance of E. coli O157 ATCC 700728 inoculated in ground meat. Neem extract significantly decreases bacterial count Mean± SD from 1.90±0.35 to 0.0064±0.0002cfu/ml before and after addition of neem, respectively. Inoculated of ground meat with E. coli in relation to addition of 10% neem extract, showed significant decline of aerobic bacterial count Mean± SD from 78.00±2.31cfu/ml to 0.0310±0.0015cfu/ml and E. coli count from 0.60±0.23 to 0.0012±0.0002, respectively. Results concluded that, diluted neem extract showed great antimicrobial properties at low concentration (10%) with significant decrease of bacterial count after addition of 10% neem extract.[9]

4. Spermicidal activity

Khillare B present study was carried out to evaluate the effective concentration of aqueous extract of old and tender Azadirachta indica (neem) leaves to immobilize and kill 100% human spermatozoa within 20 s. Sander-Cramer test was used to study the spermicidal activity of neem leaf extract. Under the test conditions, minimum effective spermicidal concentrations for tender and old leaf extracts were 2.91 +/- 0.669 mg/million sperm and 2.75 +/- 0.754 mg/million sperm, respectively. The effect of extracts on morphology and viability of sperm was also studied and no change was observed in morphology of head, mid-piece and tail and no viable sperm seen. The leaf extracts were found to be water soluble and carbohydrate in nature. The effect of different concentrations of extracts (old and tender) on percentage motility of the sperm was also studied. With an increase in concentration, there is a linear decrease in percentage motility, becoming zero at a 3-mg dose within 20 s.[10]

5. Antidermatophytic Activity

The antidermatophytic activity of the aqueous and ethanolic extracts of Neem (Azadirachta indica) leaves was investigated by Pankajalakshmi V against 88 clinical isolates of dermatophytes by agar dilution. The isolates included Microsporumcanis (50), M.audouinii (5), Trichophytonrubrum (6), Tmentagrophytes (5), T.violaceum (12), T.simii (5) T.verrucosum (1) T.soudanense (l), T.erinacei(1) and Epidermophytonfloccosum (2). The results were compared with the minimal inhibitory concentrations of ketoconazole. The ethanolic extract was found to be more active inhibiting 90% (MIC 90) of the isolates at a concentration of 100 ug/ml. The MIC 50s and MIC 90s of the aqueous extract were 500 and > 500 ug/ml whereas the values for ketoconazole were1and2.5ug/ml ‘respectively.[11]

6. Antibacterial Activity of Neem (*Azadirachtaindica*) Leaves on *Vibrio* spp. Isolated from Cultured Shrimp

The use of antibiotics in aquaculture to treat infections has resulted in the development of resistant strains which have rendered antibiotic treatment ineffective. Therefore, alternative antibacterial materials must be found. Extracts of neem tree (*Azadirachtaindica*) leaves were tested against *Vibrio parahaemolyticus* and *Vibrio alginolyticus* isolated from cultured shrimp. Aqueous extract of neem leaves did not produce any inhibitory zone while the neem juice produced inhibitory zone that showed linear relationship to the concentration of neem juice on both bacteria. The Minimum Inhibitory Concentration (MIC) for *V. parahaemolyticus* and *V. alginolyticus* was 3.13 and 6.25%, respectively. The Minimum Bactericidal Concentration (MBC) for *V.*

parahaemolyticus and *V. alginolyticus* was 12.50 and 25.00%, respectively. It is concluded that neem juice is an antibacterial agent and is useful for inhibition of vibrios in shrimp.[12]

7. Anthelmintic activity of Azadirachta Indica Leaves

The aqueous extract of Azadirachta Indica Leaves was investigated by Haque rabiu for anthelmintic activity using earthworms (Pheretimaposthuma), tapeworms (Raillietinaspiralis) and roundworms (Ascaridiagalli). Various concentrations (10-70 mg/ml) of plant extract were tested in the bioassay. Piperazine citrate (10 mg/ml) was used as reference standard drug whereas distilled water as control. Determination of paralysis time and death time of the worms were recorded. Extract exhibited significant anthelmintic activity at the concentration of 40 mg/ml. The result shows that aqueous extract possesses vermicidal activity and found to be effective as an anthelmintic. Therefore, the anthelmintic activity of the aqueous extract of Azadirachta Indica Leaves has been reported.[13]

8. Hypoglycemic Activity

In a study, Rats were used as animal models to study the anti-diabetic effects of neem. Diabetes was induced in rats by alloxan monohydrate. The assessment was done by fasting blood glucose levels and oral glucose tolerance test. The results of the study indicate that neem oil has got the potential to reduce blood glucose levels within a short period of time and also it has potential to improve the glucose tolerance after a treatment period of 4 weeks. Azadirachta Indica may have beneficial effects in diabetes mellitus and holds the scope of new generation of antidiabetic drug.[14]

In a similar study In vivo Antidiabetic evaluation of Neem leaf extract in alloxan induced rats was evaluated by Shravan Kumar Dholi et al. *Azadirachta indica* After treatment for 24 hrs, *Azadirachta indica* 250 mg/kg (single dose study) reduced glucose (18%), cholesterol (15%), triglycerides (32%), urea (13%), creatinine (23%), and lipids (15%). Multiple dose study for 15 days also reduced creatinine, urea, lipids, triglycerides and glucose. In a glucose tolerance test in diabetic rats with neem extract 250 mg/kg demonstrated glucose levels were significantly less compared to the control group., *Azadirachta indica* significantly reduce glucose levels at 15th day in diabetic rats. *Azadirachta indica* serves as an important alternative source in the management of diabetes mellitus involved in reducing increased blood glucose during diabetes which should be examined further by oral hypoglycemic therapy.[15]

9. Anti Inflammatory Activity

In the study Albino rats were used; they were divided into three groups. Control group treated with normal saline, standard treated with Indomethacin and test drug used was neem oil. For acute inflammation; Carregennan induced rat paw edema inhibition method and for sub acute inflammation: cotton pellet granulation method. Ulcer index of Indomethacin and test compound were also studied. It is found that neem oil showed significant anti-inflammatory effect in both acute as well as chronic inflammation, it was also found to have low ulcerogenic potential compared to Indomethacin, hence can be safely used as a potent anti-inflammatory agent.[16]

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