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THE NATURE'S GIFT TO MANKIND: NEEM

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ABSTRACT
Neem (*Azadirachta indica*) is popularly known as the miracle tree. It is known as 'Nimba' in India. The Sanskrit name of neem is 'Arishtha' meaning the reliever of the sickness. Neem also holds medicinal value. Each and every part of neem is used in the medicines. It has been used in Ayurvedic medicines for more than 4000 years. Its important phytoconstituents are nimbin, nimbinene acetylnimbinase, nimbandial, nimbolide and quercentin. Medicinal uses are purgative, antihemorrhoidal, antihelminthic, antileprotic and antipoisonous in nature. Neem bark is cool, astringent, acrid and refrigerant. It is useful in tiredness, cough, fever, loss of appetite, worm infestation. Nimibidin present in used as antipyretic and non-irritant, and it has found to be effective in the treatment of skin diseases such as eczema, furunculosis, arsenical dermatitis, burn ulcers, herpes labialis, scabies and seborrheic dermatitis. Nimbidin and sodium nimbidmate contained in bark are reported to possess spermicidal and anti-inflammatory activity. So it is a tree that has a long history of use by humans. It is said to have medicinal, cosmetic and insecticidal potential.

KEYWORDS: *Azadirachta indica*, Ayurvedic medicines, Nimbidin, Antihelminthic, Insecticidal.

INTRODUCTION

Neem; botanically known as *Azadirachta indica* Juss (*syn. Melia indica* and *Melia azadirachta*) belongs to the Family Meliaceae. Many other name are likely Bengali: Nim, Nimgachh; Burma: Bawtamaka, Kamaka, Tamabia, Thamaka; English: Indian Lilac, Margosa tree, Neem tree; Gujrati: Danujhada, Kohumba, Libado, Limba, Limbado, Limbra; Hindi: Balnimb, Nim, Nimb, Ninb; Punjab: Bakam, Bukhain, Drekh, Mahanim, Nim; Sanskrit: Arishta, Arkapadapa, Chhardana, Hingu, Kaitarya, Neta, Nimba, Nimbaka; Marathi: Balantanimba Limba, Nimbay, Limba chajhada[1]. Neem is one of the most valuable and yet least exploited of all tropical trees. It grows in arid regions, even nutrient-deficient soil of India and Africa and is a fast growing source of fuel-wood. In addition, it has many commercially exploitable and beneficial attributes. It can survive high temperatures at altitudes between 50 and 1000 meters, as little rainfall as 130 mm per year and long stretches of drought. The Neem tree is undemanding and grows well on moist, dry, stony, clay or shallow soils. The roots seem to have an unusually great ability to extract nutrients and moisture even from highly leached, sandy soils. Although Neem grows well at pH 5, it brings surface soil to neutral by its leaf litter. It propagates easily by seed, without pre-treatment. Nine to twelve months old seedlings are good for transplanting. Fruiting begins after five years. In India, the neem tree flowers from the beginning of January to May and the fruit matures from May to August[2]. Neem is a large glabrous tree, 10-20 m high with a straight trunk and long spreading branches. Leaves are imparipinnate, alternate, existipulate, 3-6 cm long on long slender petioles; leaflets 7-17; altenuate or opposite, very shortly stalked 1-15 cm long ovate-lanceolate, attenuate at the apex, unequal at the base, the upper half much longer than the lower and the leaflet in consequence more or less falcate, coarsely and bluntly serrate, smooth and dark green. Odor is typical and taste is bitter. The fruit is an ovoid bluntly pointed, smooth drupe, green when young and unripe, yellow to brown when mature and ripe, with a very scanty pulp and a hard bony endocarp. The seed is solitary with a thick testa and embryo with foliaceous cotyledons in the axis of scanty endosperm. The seed contain fixed acrid bitter oil (23-31 %), deep greenish-yellow to brown in colour, extracted from the seeds by pressure; specific gravity 0.91; soluble in ether, chloroform; practically insoluble in alcohol and water, odor of garlic, bitter taste. The picture of neem is described in Figure 1.

Uses

Root, bark and young fruit are astringent, tonic and antiperiodic. Bark is bitter, tonic, astringent, antiperiodic and also vermifuge, cures ulcers and inflammation; good for leprosy, blood complaints, urinary discharges; recommended for children. Leaves are anthelmintic, insectisidal, good in ophthalmic, biliousness and skin diseases. The tender young leaves are astringent; cause "Vata" good for eye and skin diseases and in leprosy. Oil from nuts and leaves is local stimulant, insecticide and antiseptic. Flowers are stimulant, tonic and stomachic. In Ayurveda the juice of the leaves is useful in biliousness and cures snake bite. In Unani the bark and the leaves are anthelmintic aphrodisiac, maturant, useful in Leucoderma, Piles, and Earache; cure all wounds, reduce all inflammation. The flowers are stimulant and stomachic. The seeds are good for treatment of Leprosy[3].

Phytochemical Investigation

The total bitter principles isolated from fresh neem seed oil by column chromatography over silica gel (C_6H_6-EtoAc 2:3) yielded a new meliacin (80 mg/kg seed oil) named Salannolide[4]. A new tetranortriterpenoid nimocinol has been isolated from undried winter leaves of neem[5]. Amino acid compositions are presented for the proteinaceous components of the gum exudated from *Albizia glaberrima*, *A. sericoephala*, *Aralia elata*, *Azadirachta indica*, *Entada Africana*, *Grevillea robusta*, *Lannea humilis* and *Moringa oleifera*. The gum from four of these genera *Albizia*, *Azadirachta*, *Grevillea* and *Moringa* contain low proportions, all the other contain high proportions of hydroxyproline. Tetracyclic triterpenoid and their derivatives have been isolated from neem. The headspace volatile constituents from freshly crushed neem seeds were purged with nitrogen, trapped onto amberlite XAD-4 resin, concentrated into diethyl ether and analyzed by means of gas chromatography, capillary gas chromatography, mass spectroscopy and high resolution mass spectroscopy. The volatile constituents were found to consist principally of derivatives of di-n-propyl and n-propyl-1-propenyl, di, tri and tetrasulfides. A total of 25 compounds were identified[6]. Spectroscopic and biological investigation of nimbolide and 28-deoxonimbolide from neem was carried out. The unambiguous ^{1}H and ^{13}C-NMR assignments of compounds nimbolide and 28-deoxonimbolide are presented, as well as *in vitro* cytotoxic activity against human tumor cell lines was investigated or reported[7]. Mahmoodin, a new limonoid has been isolated from neem

oil along with seven known tetranortriterpenoids, azadirone, epoxyazadiradione, nimbin, gedunin, azadiradione, deacetylnimbin, and 17-hydroxyazadiradione. A new protolimonoid, naheedin, has been obtained from the neem fruits along with azadirachtol. Mahmoodin showed significant antibacterial activity against various Gram positive and Gram negative organisms. Four hydrocarbons icosane, decosane, 2-methyltricosane and docosane have also been identified by gas chromatography and mass spectroscopy of the ethanol extracts of the fruit coats. Only docosane has earlier been reported from neem, while the remaining three are unreported from this plant. Studies on the acidic fraction of the fresh uncrushed twigs of neem have resulted in the isolation and structure elucidation of one new and three unreported isocoumarins along with two unreported coumarins. The petroleum ether extract of the fresh leaves yielded a hydrocarbon fraction, the Gas chromatography-Mass spectroscopy of which lead to the identification of eight saturated hydrocarbons, fatty acid compositions of leaves, twigs and fruits of neem have also been determined. Two novel compounds, the first 29-oxymethylene azadirachtin analogue, 29-oxymethylene-11-demethoxy-carbonyl-11 α -hydroxya-zadirachtin and 22, 23-dihydro-23α-hydroxy-3-tigloyl-11-deoxyazadirachtinin together with known compound 11-epi azadirachtin were isolated from a methanolic extract of seed kernels of neem[8]. Two new triterpenoids 22, 23-dihydronimocinol and desfurano-6α-hydroxyazadiradione were isolated from a methanolic extract of the fresh leaves of neem along with a known meliacin, 7α-senecioyl-(7-deacetyl)-23-O-methylnimocinolide[9].

PHARMACOLOGICAL ACTIVITY

Abortifacient Activity

The dried fixed oil when administered intraperitoneally to rat was 100% effective. Ethanol/water (1:1) extract of the dried seed, administered orally to pregnant rats at a dose of 100 mg/kg was inactive. The seed oil, administered intra vaginally to pregnant rat at doses of 0.25 ml/animal and 12.5 µl/animal was active[10].

Analgesic Activity

Ethanol (95%) extract of the dried leaf administered intragastrically to female mice at a dose of 100 mg/kg was active versus acetic acid-induced writhing. A dose of 1.0 gm/kg was inactive in the male versus tail clip method. At a dose of 300 mg/kg the extract was active versus subcutaneous injection of brewer's yeast[11].

Anhelmintic Activity

A mixture of equal parts of *Butea frondosa*, *Moringa pterygosperma*, *Piper nigrum*, *Azadirachtia indica* and *Embelia ribes* was taken orally by adults of both sexes, at a dose of 1-2 gm/person with dosing 3 times daily for 4-8 weeks. The results indicated that the treatment was positive on 11 cases of ascariasis, 9 cases of ancylostomiasis, 9 cases of enterobiasis and 7 cases of hymenolipis nana. Stool specimens were found negative at the end of the treatment period[12].

Antibacterial Studies

Acetone extract of the oven-dried leaf, on agar plate was active on *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Staphylococcus aureus*, *Streptococcus faecalis* and *Vibrio cholera*. Ethanol (95 %) extract of the dried seed and seed oil, on agar plate was active on several gram+ve and gram-ve organisms. The microbial study of the alcoholic extract of the bark and leaves was carried out by Cup-plate method using gram+ve, gram-ve organisms and fungi. It was found that the bark is more active than leaves against gram+ve, gram-ve organisms and fungi[13].

Antifertility Activity

A dose of 1 ml/animal administered intra-vaginally to humans and to rhesus monkeys prior to intercourse was 100% effective. The intra-vaginal dose of 20.0µl/animal was active in the rabbit. The seed oil, administered by gastric intubation to male rats at doses of 2 and 4 ml/kg was inactive. A dose of 6 ml/kg was equivocal[14].

Anti-inflammatory Activity

Chloroform extract of the fresh stem bark, applied externally to rats at a dose of 1.0 % was active versus Croton-oil -induced inflammation of the ear. The extract, when administered intragastrically to rats at a dose of 1 gm/kg was active versus carrageenin-induced pedal edema. Ethanol (70%) extract of fresh bark and leaf, administered by gastric intubation to rats at dose of 400 mg/kg was active versus carrageenin-induced pedal edema[15].

Antimalarial Activity

The water extract, when administered orally to mice at a dose of 0.1 gm/kg was active on *Plasmodium yoelii*. Ethanol (95%) extract of dried stem bark, in broth culture was inactive on *Plasmodium falciparum*[16].

CNS-depressant Activity

Methanol extract and the methanol insoluble fraction of the dried leaf, administered orally to mice at a dose of 100 mg/kg were active[17].

Hypercholesterolemic Activity

Water extract of the dried leaf, administered intraperitoneally to rats at a dose of 100 mg/kg was active versus stress induced hypercholesterolemia[18].

Antipyretic Activity

Chloroform, water and hexane extracts of a commercial sample of the seed, administered orally to rabbits at a dose of 150 mg/kg were inactive versus yeast induced pyrexia[19].

Antihyperglycemic Activity

A mixture containing *Gymnema sylvestre, Syzygium cumini, Azadirachta indica* and *Enicostema hyssopifolium*, administered intragastrically to rats at a dose of 40 mg/kg, was active versus anterior pituitary extract-induced hyperglycemia. Ethanol (95%) extract of the dried leaf administered intraperitoneally to rats at doses of 500 mg/kg and 75 mg/animal were active versus streptozotocin-induced hyperglycemia[20].

Antiulcer Activity

Water extract of the dried leaf administered intragastrically to rats at a dose of 160 mg/kg and a dose of 100 mg/kg administered intraperitoneally were active versus stress-induced ulcers (restraint). A dose of 40 mg/kg was active when the animals were pre-treated for 5 days. The effect of neem extract on gastric ulceration was studied in albino rats. Neem extract (100-800 mg/kg p.o.; 100-125 mg/kg i.p.) significantly inhibited gastric ulceration by indomethacin (40 mg/kg). Administration of (800 mg/kg p.o.) and (250 mg/kg. i.p.) caused 100% cytoprotection against indomethacin (40 mg/kg i.p.) induced gastric ulceration. In order to investigate the probable mechanism of neem antiulcer activity, the effect of extract alone and in combination with histamine (1 mg/kg) and cimetidine (0.12 mg/kg) on gastric acid secretion *in-situ* was studied. Neem (250 mg/kg) significantly inhibited the basal and histamine induced gastric acid secretion[21].

Antiplaque Activity

A 6 week's clinical study was conducted to evaluate the efficacy of neem extract dental gel with commercially available chlorhexidine gluconate (0.2% w/v) mouthwash as positive control. The results suggest that the dental gel containing neem extract has significantly reduced the plaque index and bacterial count than that of the control group[22].

Chemoprotective Effects

The modifying effect of ethanolic extracts of neem leaves on oxidative stress induced by the potent gastric carcinogen N-methyl-N'nitro-N-nitrosoguanidine (MNNG) in male wistar rats was investigated. The results demonstrate that neem leaf exerts its chemo protective effects on MNNG-induced oxidative stress by decreasing lipid peroxidation and enhancing the antioxidant status[23].

Antivirus Activity

Ethanol/water (1:1) extract of the dried twig, in cell culture at a concentration of 0.05 mg/ml was inactive on ranikhet and vaccinia viruses. Ethanol/water (1:1) extract of the dried root, fruit pulp, leaf and root wood in cell culture at a concentration of 0.05 mg/ml were inactive on vaccinia virus[24].

Larvicidal Activity

Ethanol/water extract, was tested against *culex pipiens* mosquito larvae and pupae in east of the Republic of Algeria under laboratory conditions[25].

CONCLUSION

In present scenario neem provides an answer to many incurable diseases. From time immemorial neem products have been used against a wide variety of diseases which include heat-rash, boils, wounds, jaundice, leprosy, skin disorders, stomach ulcers, chicken pox etc. Modern research also confirms neem's curative powers in case of many diseases i.e. abortifacient activity, analgesic activity, hypercholesterolemic activity, anti ulcer activity, antivirus activity, larvicidal activity etc. and provides indications that neem might in future be used much more widely.

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Figure 1. Morpholgical Structure of Neem