

REFERENCES

NEEM
NIMBA
MARGOSA
AZEDARACHA
INDIAN LILAC TREE
NIM
CHINABERRY TREE
PERSIAN LILAC

Melia azedirachta
Azardirachta indica
Azadirachta indica
Melia Azedarach

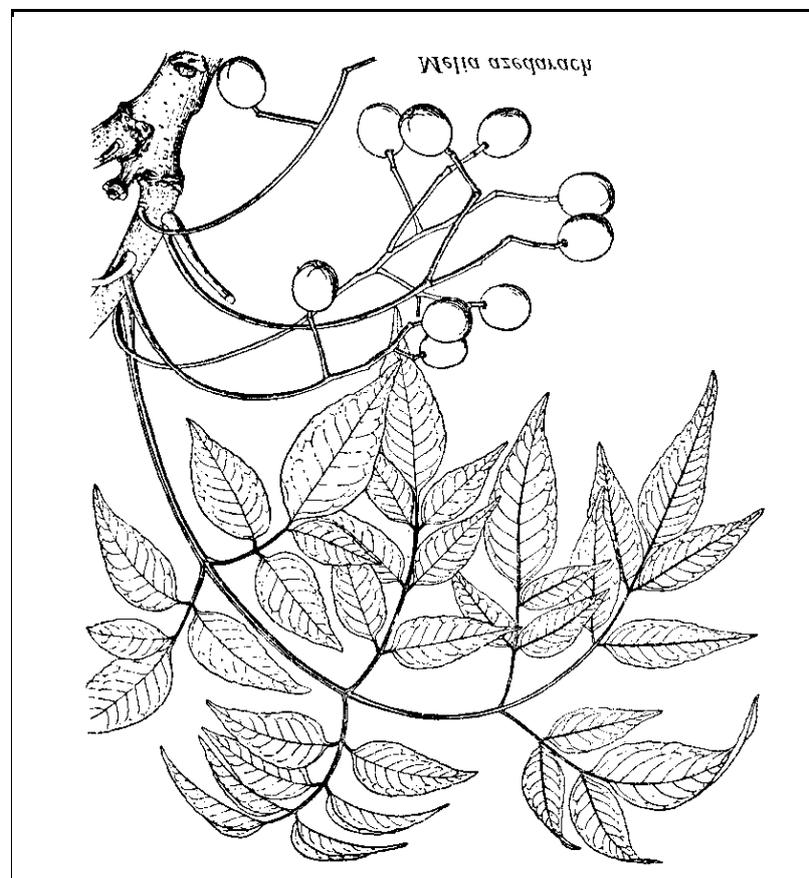
1. In a reference from Folicon (through CPL Fragrances) we learn that it is a part of Ayurvedic medicine. It contains alkaloids - nimbin, margosine, nimbinin, nimbidin. Dermatologically it offers complete skin and mucous membrane compatibility.

It is also known by the Sanskrit name Nimba. Every part of the plant is used:- bark, root-bark, young fruit, nut or seed, flowers, leaves, gum and toddy or sap.

Neem is alterative, antihelminthic (anthelmintic in text), antiarthritis, antimalarial, antiperiodic, antiseptic, appetiser, astringent, bitter tonic, constipative, cooling, demulcent, digestive, emmenagogue, emollient, expectorant, febrifuge, flatulent, ophthalmic, purgative, stimulant, stomachic, tonic and vermifuge.

Neem is indicated in boils, bronchitis, catarrhal affections, diabetes, debility, eczema, eye trouble, fever, glandular swelling, indigestion, jaundice, leprosy, liver complaints, lumbago, malaria, night-blindness, piles, prurigo, purgative, pustular eruptions, rheumatism, scrofula, skin diseases, ulcers, urinary diseases, urticaria, vomiting in fevers and worms.

Neem is commonly used as tooth brushes for cleaning the teeth and mouth and to prevent



pyorrhoea; skin diseases, vermiside, softens hard and rough skin, skin antiseptic, allergy, hair care, checks hair loss, stimulates hair growth and darkens them. (for dark hair).

2. In a data sheet from Midland Biocides we read that Midecol CF is a naturally occurring oil with pronounced antimicrobial properties, extracted from the seeds of a tropical tree, *Azadirachta indica*. Its widespread use over many years in native medicine gives indication that its safety to humans is much greater than almost any synthetic biocide, even though its antimicrobial activity is similar to that of many commonly used industrial biocides. Toxicological studies have verified this initial impression, allowing Midecol to be presented as a broad-spectrum antimicrobial agent suitable for use in a wide range of applications from personal care products (subject to appropriate registration) to industrial systems.

It has shown exceptionally low toxicity and appears to be almost completely non-irritant. Usage in personal care products is recommended at between 0.1 - 0.5%.

The document then goes on to give the minimum inhibition concentrations for various yeast, bacteria and fungi. The report continues by giving some preservative challenge test results, and shows that at 1% it will satisfy the BP criteria for topicals. At 0.1% it has a kill value, but not sufficient to satisfy the stringent criteria of the BP code. It does this for a range of typical products.

The material is a complex mixture of limonoids, tetranortriterpenoids and fatty acids. The exact mode of action has not been determined for its action, as many different mechanisms may be involved. More than 50 different components have been identified and isolated. Nimbin (0.19%), Nimbinin (1.0%), Salannin (0.945%), Azadiradione (0.8%), 17-epi-Azadiradione (0.0267%), 7-deacetylazadiradione 7-benzoate (0.0389%), epoxyazadiradione 7-benzoate (0.0667%), gedunin 7-benzoate (0.0833%), meldenin (0.0005), 1,3-diacetylvilasinin (0.0255%), 17beta-hydroxyazadiradione (0.194%), 1alpha-methoxy-1,2-dihydroepoxyazadiradione (0.0167%), 1beta,2beta-diepoxyazadiradione (0.0167%), 7-acetylneotrichelenone (0.0389%), 3-deacetylsalannin (0.04%), salannol (0.005%), salannolide (0.008%), nimbinene, 6-deacetylnimbinene, nimbandiol, 6-O-acetylnimbandiol.

The documents contain a summary of the toxicological data and an impressive reference list.

3. In a reference from CTMS (Cosmetics, Toiletries, Manufacturers, Suppliers) April May 1991, Preserving Cosmetics could come naturally. Richard Corbett.

He says that the medicinal and antimicrobial activity of plant extract has been known from time immemorial. The earliest use of a plant being used as human medication is found on an Egyptian papyrus dated about 1550 BC. (The Ebers Papyrus - ACD). The paper continues to discuss the development of natural materials and leads into food and antioxidants. He then leads into preservatives and mentions that some of the synthetic preservatives can lead to the conversion of some ingested materials into toxic substances or carcinogens by the increase of microsomal enzymes.

Oregano and thyme were highly toxic to *Vibrio parahaemolyticus* when present in growth media at 0.5%.

The essential oils of heartwood of *Santalum album* and of the whole of *Glossogyne pinnatifida* exhibited antibacterial activity against some pathogenic bacteria such as *Bacillus*

mycoides and *Escherichia coli*.

The essential oil from *Capillipedium foetidum* displayed high antibacterial activity against Gram-positive bacteria and moderate to excellent activity against Gram-negative bacteria.

Farag et al. showed that spice essential oils, in particular thyme and clove oils, can be applied as antimicrobial agents and food treatments to prevent the deterioration of stored foods. They also showed the use of thyme and cumin oils to prevent butter deterioration during storage.

The ayurvedic system of medicine has long claimed antimicrobial activity for many plant extracts. These have been studied by Maruzzella et al. for some fixed and volatile oils. Neem, Darudi, Malkanguni and Karanja oils were studied by Patel and Trevedi who found that the crude oils had no distinct effect, but an ethanolic extraction provided maximum antimicrobial effect after 4 hours of refluxing.

Jain et al, Chaurasia et al have confirmed the antimicrobial activity of *Azadirachta indica* (Neem seed oil) using the cup-plate inhibition test.

There are indications reported by Thaker and Anjara that *Azadirachta indica* led to effective wound healing with an indigenous ointment formulation, comparable to nitrofurazone and significantly better than the zinc oxide base, in mice infected with microorganisms. The indigenous plant material under study shows significant inhibition of pathogenic microorganisms to the extent of 75-99% and effective wound healing.

Nimbin, nimbinin were isolated from the oil, later nimbidin (an amorphous bitter principle) through solvent partitioning avoiding its prior saponification.

Nimbidin is anti-arthritic and anti-inflammatory in its action and possesses significant anti-ulcer potential, whereas other fractions have antipyretic and anti-inflammatory properties.

The extracts and various factors derived from Neem also produce diverse biological effects on insects, such as repellency, phagodeterrence, reduced growth, abnormal development and reduced oviposition. The article goes on to discuss the further composition as listed above.

The article has a good discussion on the toxicology, and concludes that there would be little, if any, hazard in use.

4. In the Lawrence review of natural products, we read that *Azadirachta indica* was formerly known as *Melia azadirachta*. It is often confused with *Melia azedarach* (the chinaberry or Persian lilac).

Almost every part of the neem tree is used in traditional medicine in India, Sri Lanka, Burma, Indochina, Java and Thailand. The stem, root bark, and young fruits are used as a tonic and astringent and the bark has been used to treat malaria and cutaneous diseases. The tender leaves have been used in the treatment of worm infections, ulcers, cardiovascular diseases and for their pesticidal and insect-repellant actions. The tree yields a high quality timber and a commercial gum.



The seed kernels of neem yield about 10% of a fixed oil, comprised primarily of glycerides. The yellow bitter oil has a garlic-like odour and contains approximately 2% of bitter principles including nimbidin, nimbin, nimbinin, nimbidol and other related minor components. All parts of the tree yield β -sitosterol. Azadirachtin is the most active insecticidal component of neem with a yield of about 5g from 2Kg of seeds.

The variety of components in neem give the plant and its extracts a number of pharmacologic activities. Neem is being investigated for its potential as a contraceptive agent. The oil has been shown to inhibit sperm motility in vitro, and its intravaginal application to rabbits did not induce mucosal irritation. Sodium nimbin and nimbidin have weak spermicidal activity in vitro and the oil immobilises human sperm within 30 seconds of contact. In women, the intravaginal application of 1ml of neem oil prior to intercourse did not affect cycle regularity and provided effective contraception for 10 couples over four cycles. Initial acceptance problems due to the unpleasant smell of the oil were overcome by masking the odour with lemongrass scent.

It has been suggested that the lack of hormonal effect may offer a contraceptive alternative with fewer side effects than traditional steroidal contraceptives.

Studies support the traditional use of neem in the management of diabetes.

Neem oil and azadirachtin are effective pesticides and insect repellants. Azadirachtin is one of the most potent insect antifeedant and ecdysis inhibitory compounds known from a botanical source. Because of the complex chemical structure of azadirachtin, only naturally derived products have been used commercially. This compound is effective in concentrations as low as 0.1 ppm and has been shown to be biodegradable, nonmutagenic and nontoxic to warm-blooded animals, fish and birds.

The Environmental Protection Agency has approved the use of a neem formulation (Margosan-O) as a pesticide for limited use on nonfood crops. Other insecticidal compounds from neem include deactyl-azadirachtinol and salannin.

Gedunin and nimbolide, both isolated from neem have shown antimalarial activity in vitro. One survey of the in vitro antibacterial effect of neem oil against 200 clinical bacterial isolates resulted in 92% susceptibility.

Neem oil has been used as a traditional dentifrice and the oil has been found to be an anti-inflammatory, aseptic and healing in gingivitis. In toothpaste, the extract has low abrasiveness and good antimicrobial activity against oral flora.

Neem oil is non-mutagenic in the Ames mutagenicity test. It is considered a relatively safe product in adults. The LD/50 is 14ml/Kg in rats and 24ml/Kg in rabbits.

The seeds of neem, which are poisonous in large doses have caused severe poisoning in 13 infants who received 5ml to 30ml doses of margosa oil. Toxicity was characterised by metabolic acidosis, drowsiness, seizures, loss of consciousness, coma and death in 2 infants. These children exhibited Reye's syndrome-like symptoms, with death from hepatoencephalopathy.

Neem oil has been used in traditional Indian medicine for thousands of years, practically as a panacea.

The oil and its extracts are insecticidal, can reduce blood sugar levels and may be the source of a contraceptive substance. It is not toxic in adults, but has caused mortality in infants.

5. Potter (B5) says that it is native of the Levant and Northern India, but cultivated in the Southern United States. It is a large deciduous tree, the bark of which is used medicinally.

It is anthelmintic; it is also said to be cathartic and emetic. It is used in the Southern States of America for worms in children, and generally given in form of a decoction.

6. Trease and Evans (B37) say that since antiquity, the seed oil (margosa oil) has been widely used in Asian medicines. Recent work has tended to confirm the therapeutic value of the oil as an anti-inflammatory and antibacterial agent. In addition, some antipyretic and hypoglycaemic activity has been noted. Particular attention has been focused on its effects in two other areas; toxicity and antifertility. As an antifertility agent it appears to have potential, both in inducing male infertility and as a vaginal and oral contraceptive; it may also prevent implantation. Poisoning in young children produces an effect similar to Reye's syndrome. Aflatoxins have been found in some toxic oil samples owing to fungal contamination. However, the toxicity of the oil exceeded that due to its aflatoxin content, suggesting that other unidentified components may act synergistically with aflatoxins.

Neem leaf extracts have been found to exert some anti-malarial activity, although this is not great, whereas considerable effectiveness against gastric ulcers has been demonstrated. There is also potential for the development of insecticides. Phytochemical investigations extend to polysaccharides from the bark and glycoproteins from the gum.

7. Martindale (B90) says that *Azadirachta indica* or *Melia azadirachta* is also known as

margosa or neem and is made from the dried stem bark, root bark, and leaves of the plant.

Azadirachta has been used as a bitter. It is widely used in Asia and has been reported to have insecticidal and spermicidal properties.

Severe poisoning in Indian children given margosa oil as a remedy for minor ailments (Lancet 1981,1,487)

There is a dental product called Silvose, which is an extract from the bark of Azadirachta. It is claimed to reduce dental caries and inflammation of the mouth when used as an ingredient in dental preparations.

8. Lust (B8) says that *Melia azedarach* is known as Pride of China, Azedarach, Africa Lilac, Bead Tree, Chinaberry, Hagbush, Hoptree, Pride Tree. It has purplish, fragrant flowers which turn into a fruit which is a yellow drupe.

It is antihelminthic, astringent, bitter tonic, emetic, emmenagogue, purgative. A decoction of the bark root acts as a purgative and emetic, especially in large doses; it is also said to promote the onset of menstruation. The bark of the tree is bitter and astringent, and has been commonly used in India as a tonic. The seeds and the oil of the fruit promote the elimination of intestinal worms. The tree also exudes a gum which has been considered by some to have aphrodisiac powers.

9. Keys (B115) says that *Melia azedarach* is Chinaberry tree. The fruit is a glabrous drupe, the seeds black. It is found in China, Indochina, India, Iran, Syria, Madagascar, Guiana, Antilles. (Syn. *Melia japonica* G.Don., *Melia toosendan* Sieb. et Zucc.)

The root epidermis and fruit are officinal. The taste is bitter. The drug is mildly poisonous. The bark of the tree contains tannin and the alkaloid margosine; the seeds yield 60% of a fatty oil comprising stearic, palmitic, lauric, valerianic and butyric acids, and traces of a sulphurated essential oil. The drug is known to produce symptoms of narcotic poisoning as giddiness, dimness of sight, mental confusion, stertorous breathing, dilated pupils, and stupor; large doses are necessary to cause these effects, and the occurrence of such effects has been questioned.; the drug is, however, a gastrointestinal irritant, producing vomiting and purging, and is anthelmintic against *Ascaris*.

Used as anthelmintic. Dose 15-20g in decoction every 2 hours; or 0.5g powdered 3 times per day.

10. Tyler, Brady and Robbers (B128) refers to *Melia azedarach* Linné (Chinaberry tree) as a small, thickly branched tree with large compound leaves, purple flowers, and smooth ovoid fruits (drupes) that are yellow when mature. The plant is common in the southern United States, Puerto Rico and Hawaii. Poisoning most often results from ingestion of the fruits whose toxicity is associated with a resinous fraction. Severe irritation, nervous symptoms, and fatty degeneration of the liver and kidneys characterise toxic effects.

11. Kew Scientist April 1993, issue 3. Activity of Azadirachtin. Azadirachtin (A), one of the active components of neem (*Azadirachta indica*), shows potent antifeedant and growth disruptive activity against insects. Recent studies on the newly synthesised decalin (B) and dihydrofuranacetal (C) fragments of azadirachtin showed that they only exhibit potent

antifeedant activity against the caterpillar *Spodoptera littoralis* when tested in combination. They are looking to see whether the activity of these fragments can be enhanced.

12. In a file from Dr Stephen Greenburg (Lipo Chemicals Inc.) entitled "Ethnic Botanical Literature) author anon.

Azadirachta indica, *Melia azadirachta* or Neem oil tree. There has been some confusion in the nomenclature between *Melia azedarach* and *Melia azadirachta* (*Azadirachta indica*). Oil obtained from the latter (*Melia azadirachta*) is known as margosa oil, neem oil, nim oil and oleo margosa. These names have been erroneously applied to the oil of *Melia azedarach* as well. Therefore, caution must be exercised when reporting the uses and constituents of botanical sources with nearly similar scientific names. (ref. Watt, J.M. and M.G. Breyer-Brandwijk. The Medicinal and Poisonous Plants of Southern and Eastern Africa. London: E & S Livingstone Ltd, 1962.)

A. indica is used throughout West Africa and especially in Nigeria for a wide variety of skin problems, ranging from simple acne vulgaris to syphilitic sores. It also is used as a hair tonic to relieve an itching, scaling scalp and to improve the texture and strength of the hair itself. (ref. Bep Oliver-Bever. Medicinal Plants in Tropical West Africa. Cambridge University Press 1986)

The natives of India use neem leaves in various forms such as poultices, ointments, and liniments for everything from leprosy, burns, gangrene, scabies, herpes lesions, eczema, and skin ulcers. Its use dates back into antiquity in Hindu Ayurvedic medicine. (ref. Colonel Sir R.N. Chopra, M.D., et al. Chopra's Indigenous Drugs of India. Calcutta: U.N. Dhur and Sons Ltd. 1958)

Negritos in various parts of the Philippines take the juice of the green fruit of *A. indica*, with a third of its weight of sulphur and an equal quantity of curds heated together in a copper pot, is used as an application to scabies, and to sores infested with maggots. (ref Eduardo Quisumbing. Medicinal Plants of the Phillipines. Manila: Dept of Agriculture and natural Resources, Bureau of Printing, 1951.)

Chemical constituents

The seed oil contains bitter constituents. Those reported have been mainly 1.1% nimbidin (containing sulphur) and 0.1% nimbin and 0.01 nimbinin (both free from sulphur), which also occur in the stem bark. (ref. Mitra and Siddiqui Chatterjee in Indian Journal of Scientific and Industrial research 69B (1948). Cited in R.Hegnauer, Chemotaxonomie des Pflanzen (5 vols) Basel: Birkhauser, 1962-1968, vol.5).

Meliacins found in the seeds include gedunin, 7-desacetylgedunin, desacetylnimbin and azedarachtin. (ref. R.H.F.Manske and H.L.Holmes. The Alkaloids (13 vols). New York: Academic Press, 1950-1971; Vol.5)

Azedarachtin, together with warburganal from the East African *Warburgia cyanensis*, is considered to be one of the most powerful antifeedants of African army worms ever discovered. (ref: I.Kubo et al. "Muziigadial and warburganal, potent antifungal, antiyeast and African worm antifeedant agents". Tetrahedron Letters 52:4553-6.

An aqueous extract of the root has been reported to reduce sarcoma and other skin cancers. (ref. B.H.Abbot, et al. "Screening data from the Cancer Chemotherapy National Service Center Screening Laboratories. XIL. Plant extracts 51-54." Cancer research 364-536.

An attempt has been made to scientifically demonstrate neem tree's anti-inflammatory properties. A tincture of *A. indica* when compared with aspirin (200mg/g gave 10%) and indomethacin (4mg/Kg gave 29.97) reduce inflammation by 18% for 800 mg/Kg of dry extract. The experiment was performed on carrageenin-induced rat paw edema and three doses of neem were used - 400, 800 and 1600 mg/Kg. (ref. Abayomi Sofowora. Medicinal Plants and Traditional Medicine in Africa. New York: John Wiley and Sons Ltd. 1982.)

13. Abbiw (B136) recommends the plant for wounds, cuts and sores. *Azadirachta indica* - Neem Tree, acrid oil of the seeds used.

14. Kew Scientist April 1993. Issue 3.

Activity of Azadirachtin.

Azadirachtin, one of the components of neem (*Azadirachta indica*), shows potent antifeedant and growth disruptive activity against insects. Monique Simmonds with Prof. Wally Blaney (Birkbeck College) have been undertaking structure-activity relationship studies on derivatives of azadirachtin, in order to optimise its activity and identify which parts of the molecule are involved in its different types of activity. Recent studies on the newly synthesised decalin and the dihydrofuranacetal fragments of azadirachtin showed that they only exhibited potent antifeedant activity against the caterpillar *Spodoptera littoralis* when tested in combination.

Molecular structures are given in the text.

15. Merck (B54). It is a tetranortriterpinoid isolated from the seeds of the neem tree, *Azadirachta indica* A.Juss. (*Melia azadirachta*), Meliaceae, and the Chjinaberry tree, *Melia azedarach* L. Highly active insect feeding deterrent and growth regulator. Isolation from *A. indica* and identification as feeding inhibitor in locusts, numerous other references on this subject. Used experimentally as an insect control agent.

16. Manning (B141) says that it is a member of Meliaceae. *Melia azedarach* is known as Persian Lilac. It is a tree up to 40' high. Leaves alternate, 9-18" long, 2-pinnate and occasionally 3-pinnate with pointed egg- or lance-shaped leaflets 0.5" long. Flowers lilac, fragrant, 0.25" long, in panicles in leaf-axils. Calyx short, deeply 5-6 lobed. Petals 5-6, free, spreading, narrowly spoon-shaped. Anthers 10 or 12. Filaments united in a cylindrical staminal-tube which is purple, marked with 10-12 striations. Ovary superior, 5-celled. Ovules 2. Style slender.

Habitat: Forests, mountain slopes. Also widely cultivated.

Fruit a drupe 0.5-0.75" across, 5-celled, 5-seeded or fewer by abortion.

Range: Baluchistan. Persia. India. Jamaica. Central America. Cultivated in Europe.

Various parts used medicinally. Stones of fruit made into necklaces and rosaries (hence the

name "Bead Tree"). Leaves used as a fodder.

17. Cosmetics and Toiletries. Vol.108. October 1993 p.85-88. Preservative Encyclopaedia update. CAS: 84696-25-3 EINECS: 283-644-7

Recommended use: 0.1 - 0.5%

USA - CTFA/INCI name applied for.

Japan - not listed

Comments: Naturally occurring oil (from seeds of *Azadirachta indica*) with pronounced antimicrobial properties; active components are carried in a mixture of fatty acids; therefore, this should be added to the oil phase for even distribution.

18. Phelps Brown (B161) refers to the Pride of China or Bead Tree as *Melia Azedarach*. The bark of the root is used.

This is an elegant tree, which attains heights of 30-40 ft., with a trunk about a foot and a half in diameter. The bark is rough; leaves bipinnate; flowers lilac colour; calyx five-parted; corolla has 5 petals; stamens deep violet; anthers yellow. The fruit is a five-celled bony nut.

It is a native of China but cultivated in the warm climates of Europe and America. It does not grow to any great extent north of Virginia, and flowers early in the spring. Its name Bead Tree is derived from the use to which its hard nuts are put in the Roman Catholic countries, viz., for making rosaries. The recent bark of the root is the most active part for medicinal purposes. It has a disagreeably bitter taste and a very unpleasant odour, and imparts its properties to boiling water.

Properties and uses:- The bark is anthelmintic, and in large doses narcotic and emetic. It is useful in worm fevers and in infantile remittents, in which, although worms are absent, yet the symptoms are similar to those accompanying the present of worms.

The fruit is somewhat saccharine, and is an excellent remedy to expel worms. Its pulp is used as an ointment for destroying lice and other ectozoa, as well as in treatment of scald head and other diseases of the skin. The oil of the nuts is useful as a local application in rheumatism, cramps, obstinate ulcers, etc.

Dose:- Of the powdered bark, 20 grains; of the decoction (which is the best form of administration - 2 oz. of the bark to a pint of water, and boiled down to half a pint), a tablespoon every one, two, or three hours, until the desired effect is obtained.

19. The U.S. Dispensatory 1883 (B148) refers to the bark of the root of *Melia azedarach* Linné (Nat ord. Meliaceae). It is known as the Pride of India, the Prie of China, Common Bead Tree; Ecorce d'Azédarach, Ecorce de Margousier.

Properties

The bark is in curved pieces or quills of variable size and thickness; outer surface red-brown, with irregular, blackish, longitudinal ridges; inner surface whitish or brownish. longitudinally striate; fracture more or less fibrous; upon transverse section tangentially striate, with yellowish bast-fibres; inodorous, sweetish, afterward bitter and nauseous. If collected from old roots, the bark should be freed from the thick, rust-brown, nearly tasteless corky layer.

Jacobs (A.J.P., 1879. p.444) believes that the active principle is a yellowish white resin, and that the activity of the bark resides in the liber. Hanousek (1878) states that two kinds of oil of azedarach are used in Eastern Asia, - one from the fruit and the other from the seeds; the former is used medicinally, the latter only for burning. The closely related *Azadirachta indica*, according to Broughton (P.J.Tr., 1873, p.992) contains a bitter amorphous resin, C₃₆H₅₀O₁₁, which fuses at 92°C, and a crystallised principle, melting at 175°C. Cornish (Indian Annals of Med. Sci., 4, p.104) had previously announced the presence of a bitter alkaloid, to which he gave the name margosine, from the Portuguese name for the tree, Margosa.

Medicinal properties and uses.

The decoction of this bark is cathartic and emetic, and in large doses is said to produce narcotic effects similar to those of spigelia, especially if gathered at the season when the sap is mounting; but in a number of experiments made by Dr. H.C.Wood with extracts of the dried bark and fruit, it was found impossible to produce toxic symptoms in frogs or rabbits. Robins eating of the sweetish fruit, of which they are very fond, are often rendered so far insensible as to be picked up under the tree; though they usually recover in a few hours. It has been suggested that sufficient alcohol is produced by the spontaneous fermentation of the berries to cause intoxication. Children are said to eat the fruit without inconvenience and possibly the robins simply choke themselves with the large berries. The bark is considered in the Southern States an efficient anthelmintic, and appears to enjoy, in some places, an equal degree of confidence with the pinkroot. The form of decoction is usually preferred. A quart of water is boiled with 4 oz. of the fresh bark to a point, of which the dose for a child is a tablespoon every two or three hours, till it affects the stomach or bowels. Another plan is to give a dose morning and evening for several successive days and then to administer an active cathartic. The **fresh** bark and fruit are said to be superior as vermifuges, but are not to be found in our Northern drug stores. A fluid extract and syrup of Azedarach are proposed by J.J.Miles (A.J.P., Aug. 1874)

In a later section.

Azedarach indica or Nim Tree. The inner bark of this tree is extensively used in India as a febrifuge and tonic, in the form of powder, or more usually in that of decoction. The roots are said to be vermifuge, and the seeds yield an oil largely used for lighting purposes and sometimes as a medicine. Reference made to J. Broughton as above.

20. British Pharmaceutical Codex 1923 (B147) refers to *Azadirachta indica* as Indian Azadirach, Neem Bark or Margosa Bark.

Indian Azadirach is the dried stem bark of *Melia azadirachta* Linn., a tree indigenous to India, Ceylon, and the Malay archipelago. The description of the bark is described (see above).

Constituents: The chief constituents of the bark are a bitter, amorphous resin, a crystalline, bitter alkaloid (margosine), margosic acid, a crystalline substance, and tannin.

Action and uses: Indian azadirach is used as a simple bitter, in the same way as gentian or quassia, for which it is employed as an equivalent in India and the eastern Colonies, being administered usually in the form of tincture or infusion.

Dosage levels quoted.

21. In a data sheet from Honeywill and Stein on Mahanimba. *Melia azadirachta* or *Azadirachta indica* is Neem tree, Margosa, Nim tree, Nimba tree. Akshadru - Sanskrit. The flowers or inflorescences are used.

Active substances

carotenoids	granulaiton promoting
amino acids	tightening
phytosterols	protective care
mucins	hydration
polyacetylenes	bacteriastatic/fungicidal
sesquiterpenes	anti-inflammatory

Ethnobotany

Throughout the entire Indian sub-continent, this is a tree of a thousand uses. Virtually all parts of the tree are utilised for uses ranging from medicines, cosmetics, agrochemicals, furniture and farm tools. Traditional cosmetics and pharmaceutical use are almost unlimited. It is particularly effective for the treatment of skin complaints and has a special reputation for curing itching of all kinds. It facilitates wound healing, skin softening, and the treatment of dandruff and greasy hair. Neem extract is a unique insecticide which is believed to enter the leaves of other plants to which it is applied making the recipient plants poisonous to insect predators.

After 100 years of life, a neem tree is believed, on a day that can not be predicted, to begin to secrete a nectar or sap that is believed to be its very essence. That nectar is believed to be capable of curing many diseases.

Application and dosage recommendation

The properties of mahanimba have already been utilised by several cosmetic manufacturers in Japan, where it is known as Tnimpa or Kshadoo. It is being used as a functional ingredient in skin care products where it exhibits beneficial properties in day creams, night creams and special preparations for the treatment of greasy skin. Also used for greasy hair and dandruff.

22. In a data sheet from Honeywill and Stein we read of Vaipillai, Latin name *Azadirachta indica* A.Juss. or *Melia azadirachta*. It is the Neem tree, Margosa, Nim tree, Nimba tree. Nimba is the Ayurvedic name.

The dried and cured leaves are used - cured in accordance with ancient Siddha texts. This is to reduce: 1. the concentration of certain toxic compounds which occur in the fresh leaf and which will cause blisters and skin redness if used in skin care preparations. 2. To remove the bitter and garlic-odour of certain fragrance compounds in the fresh leaf.

carotenoids	granulaiton promoting
amino acids	tightening
chlorophyll	deodorant

acetylcholine	vasodilatory
tannins	astringent
azadirachtin	fungistatic, bacteriostatic
nimbidin	healing

Nimbidin is one of the bitter principles in Neem leaf. In the preparation of the extract, the leaves are dried and cured by traditional methods, in accordance with the texts of the Siddha sage, Agasthiyar. This reduces the nimbidin concentration to 0.005ppm. At higher concentrations, say in excess of 100ppm., it will cause skin redness and possible blistering. In traditional Siddha medicinal cosmetic preparations usage of Vaili pilla Taila is well known using similarly cured Neem leaves.

Ethnobotany

Green twigs of the Neem tree are used as tooth brushes. Leaves soaked overnight are used as a prophylactic for teeth, mouth and skin complaints.

Uncured seed oil is used in leprosy and for the treatment of skin disorders resulting from serious venereal diseases.

Garlands of leaves and stones from the fruit are hung on sick rooms and sick room doors during epidemics of smallpox and chicken pox.

Application

The extract may be used for hair regeneration where hair is as a result of fungal infection, and as a general scalp stimulation remedy. Neem leaf extract may be used for the treatment of slow healing skin conditions and in day and night moisturising and skin tightening formulations. In bath care preparations Neem acts as a vasodilator and deodorant.

1Kg extract = 1.05 Kg cured Neem leaves.

23. SIDDHA MEDICINAL HERBS AS COSMETICS INGREDIENTS

An article for SPC, March 1994.

BY: Dr. Alan Onions

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The fabled Margosa Tree, or Neem Tree, *Azadirachta indica*, in Tamil **mahanimba**, or in traditional Sanskrit, *Nimba* has hit the headlines recently in the West as a source of a potential new insecticide. But this is just one of its attributes. Throughout the entire Indian sub-continent, it is a sacred tree of a thousand uses and, having been identified on seals excavated from the Indus Valley civilisation, its history can be traced back over 5000 years. In mythology, the Amrita (the elixir of immortality) was being carried to heaven by Garuda, a part-man, part-bird Hindu demi-god, a few drops fell on the neem tree and medicinal healing properties were gifted to the tree.

Traditional cosmetics and pharmaceutical uses are almost unlimited. Green twigs are used as toothbrushes, leaves soaked overnight are used as a prophylactic for teeth, mouth and skin complaints. The uncured seed oil is used in the treatment of leprosy and garlands of leaves

and the stones from the fruit are hung around the doors of sick rooms during smallpox and chickenpox epidemics. Dried leaves are burned as a mosquito repellent.

The functional properties of Neem have been recognised in Japan, where extract of the flowers and inflorescence, known as Tnimpa, is already being used in skin and hair care products. Additionally, it is being used in shampoos, conditioners and rinses as a remedial for greasy hair and dandruff.

The leaves also provide cosmetics functionality and in Tamil a preparation made from the cured and dried leaves is known as **Vaipillai**. Traditional methods described by the ancient Siddha sage, Agathiyar, (8) are used for the curing which is necessary to reduce the concentration of nimbidin. This is one of the bitter principals in neem leaves and in high concentrations can cause skin redness and blisters. The curing process also effectively reduces the concentration of disagreeable, bitter, garlic-like fragrance components. Neem leaves cured according to Afathiyar's *Sol Maruthavam* text are used in the well known Indian cosmetics preparations, *Vaili Pilla Taila*.

The extract of the cured leaves may be used for scalp stimulation and for hair regeneration, particularly when the original hair loss is caused by fungal infection. It may also be used in skin care products of acetylcholine and as a deodorant due the fungistatic and bacteriostatic properties of azadirachtin.

24. Kumkum Rani and Anand Akhila: "Synthetic relationship between nimocinol and nimocinolide in *Azadirachta indica*." Natural Product Letters. Vol.4, No.3, pp. 179-82.

25. Martindale - The Extra Pharmacopoeia
Topic: Azadirachta

PHYSICAL AND PHARMACEUTICAL PROPERTIES

Synonyms: Margosa; Neem .

The dried stem bark, root bark, and leaves of *Azadirachta indica* (=Melia azadirachta) (Meliaceae).

Azadirachta has been used as a bitter. It is widely used in Asia and has been reported to have insecticidal and spermicidal properties.

Severe poisoning in Indian children given margosa oil as a remedy for minor ailments. Sinniah D, Baskaran G. Margosa oil poisoning as a cause of Reye's syndrome. Lancet 1981; i: 487-9.

26. Tsarong (B247) refers to *Azadirachta indica* or *Neem-pah* in Tibet.

Taste: Bitter

Potency: Neutral

Action and uses: Febrifuge, carminative, clears mouth odour, promotes hair growth. Used against lack of appetite, excessive thirst, bad breath, skin disorders such as *Me-dBal* and loss of hair.

Parts used: Stem and leaves

27. Zakaria (B273) refers to *Melia azedarach* Linn. or *Azadirachta indica* (L.) a. Juss

(Meliaceae) by the local names *Mindi kecil*, *Margosa*.

Part used: Leaves, fruit, bark or root.

Traditional use: The oil from the fruit is used externally as an ointment. It is fatal when taken orally.

Scientific study: The oil contains a bitter compound known as nimbin, nimbidin and nimbidol. Other compounds are nimbolin A, nimbolin B and margosin.

28. ANTIDIABETIC AND ANTIHYPERLIPAEMIC EFFECTS OF NEEM SEED KERNEL POWDER ON ALLOXAN DIABETIC RABBITS

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SUMMARY

Objective: To study the effects of neem kernel powder(NP) and glibenclamide, alone or in combination, on alloxan diabetic rats.

Methods: The diabetic rabbits were given with NP alone or in combination with glibenclamide for thirty days and at the end of thirty days the serum lipid levels, blood glucose and activities of some serum, liver and intestinal enzymes were assessed.

Results: Administration of NP alone (500 mg/kg) as well as the combination of NP (250mg/kg) with glibenclamide (0.25mg/kg) significantly decreased the concentration of serum lipids, blood glucose and activities of serum enzymes like alkaline phosphatase (alk P), acid phosphatase (acid P), lactate dehydrogenase (LDH), liver glucose 6-phosphatase (G6P) and HMG CoA reductase activity in liver and intestine of alloxan diabetic rabbits. However, all the treatments produced an increased liver hexokinase activity. The changes observed were significantly greater when the treatment was given in combination of NP and glibenclamide than with NP alone.

Conclusion: Our data suggest a significant antidiabetic and antihyperlipaemic effect of NP in alloxan diabetic rabbits. (Indian J Pharmacol.1997, 29, 162-167)