**Azadirachta indica A. Juss**

**Scientific Name:** *Azadirachta indica* A. Juss  
**Family:** Meliaceae  
**Genus:** Azadirachta  
**Species:** indica  

**Synonyms:** *Antelaea azadirachta* (L.) Adelb., *Melia azadirachta* L., *Melia indica* (A. Juss.) Brandis  

**Local Name:** Neem, neem tree, Indian-lilac (Canada), margosa, nimtree and margosier.  

**Description of Plant:** Neem is a fast-growing tree that can reach a height of 15–20 metres (49–66 ft), rarely to 35–40 metres (115–131 ft). It is evergreen, but in severe drought it sheds most or nearly all of its leaves. The branches are wide and spreading. The fairly dense crown is roundish and may reach a diameter of 15–20 metres (49–66 ft) in old, free-standing specimens. The neem tree is very similar in appearance to its relative, the Chinaberry (*Melia azedarachta*).

The opposite, pinnate leaves are 20–40 centimetres (7.9–15.7 in) long, with 20 to 31 medium to dark green leaflets about 3–8 centimetres (1.2–3.1 in) long. The terminal leaflet is often missing. The petioles are short.

The (white and fragrant) flowers are arranged in more-or-less drooping axillary panicles which are up to 25 centimetres (9.8 in) long. The inflorescences, which branch up to the third degree, bear from 150 to 250 flowers. An individual flower is 5–6 millimetres (0.20–0.24 in) long and 8–11 millimetres (0.31–0.43 in) wide. Protandrous, bisexual flowers and male flowers exist on the same individual tree.

The fruit is a smooth (glabrous) olive-like drupe which varies in shape from elongate oval to nearly roundish, and when ripe is 1.4–2.8 centimetres (0.55–1.10 in) by 1.0–1.5 centimetres (0.39–0.59 in). The fruit skin (exocarp) is thin and the bitter-sweet pulp (mesocarp) is yellowish-white and very fibrous. The mesocarp is 0.3–0.5 centimetres (0.12–0.20 in) thick. The white, hard inner shell (endocarp) of the fruit encloses one, rarely two or three, elongated seeds (kernels) having a brown seed coat.

The ovary is syncarpous, superior, three-celled with 1–2 ovules per cell. The fruit is a glabrous, olive-like drupe, 1–3 cm in diameter, varying in shape from elongate oval to roundish. It is yellow when ripe and comprises a sweet pulp enclosing a single seed (rarely 2–3 seeds) (Figure 3). Neem has a strong root system with a deep tap root and extensive lateral roots. Suckers can be produced following damage to the roots.

**Part Used:** Flowers, Fruit, Seeds, Kernel, Bark, Occasionally bark of root, oil from seed, Exudate or gum and sap.  

**Chemical Constituents:** The different plant part contains mostly terpenoids (limonoids). The trunk bark contains nimbin (0.001%), nimbidin (0.04%), nimbsterol (0.03%), essential oil (0.02%), tannin (6%), and a bitter principle margosine. Neem oil contained various acids, sulphur etc. Azadirachtin is an important constituent which is a highly oxygenated terpinoid. The petroleum ether extract of dry flowers gave waxy substance which yielded β-sito-sterol, Kempferol, Quercertin and Myricetin. The following compounds were also obtained from dry flowers green amorphous bitter toxic substance, nonacosane C12 H30, Highly pungent essential
oil and a sesquiterpene and a fatty acid fraction. Amino acids (Asparatic acid, serine, threonine, tyrosine, arginine, methionine, phenylalanine, histidine, glutamic acid, aminocaproic acid, isoleucine); acids (oxalic acid, Indole acetic acid, Indole pyruvic acid (E)-2-methyl-2-butanoic acid (tiglic acid), Fatty acid); flavonoids (Kaempferol, quercetin, myricetin, quercetin-3-galactoside, laempferol-3-glucoside, myricetin-3-l-arabinoside, Quercetin); Sugars (Galtose, arabanose mannose, xylose, fucose, rhamnose, 4-O-(4-O-methyl-α-D-galactose, 4-O-(α-D-glucopyranosyluronic acid)-D-galactose, Aldoblouronic acid, Aldotriueneonic acid, D-glucosamine; steroids and terpenoids (Nimbosterol, B-sitosterol-B-D-glucoside, 4,14-α-dimethyl-5-aergota-8, 24-(28)-dien-β-ol, 4-methyl-5a-ergoosta-8, 24,28-dien-3β-ol). β-sitosterol, 24-methylene cycloartenol, β-sitosterol, Nimboide, vepeine, nimbinine, vilasisnin, alimonoid. Azadiarchtin, salanin, Mellantriol, azadirone, epoxy azadiradone, Nimbidine, nimbidica acid, nimbin, deacetyl-nimbin, Nimbin, nimbidin, nimbinin, nimbosterol).

**Isolated chemical constituents of *Azadirachta indica***

- Azadirachtin
- 2’, 3’- dehydrosalannol
- Nimboide
- Salannin
- Azadiradione

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**Actions of herb:** anti-inflammatory, anti-histamine, anti-ulcer, anti-pyretic, anti-malarial, anti-microbial, diuretic, anti-pyretic, analgesic, immunostimulant, hypoglycaemic, anti-fertility, anti-viral, hepatoprotective, anti-oxidant.

**Medicinal Uses:** Neem oil and the bark and leaf extracts have been therapeutically used as folk medicine to control leprosy, intestinal helminthiasis, respiratory disorders, and constipation and also as a general health promoter. Its use for the treatment of rheumatism, chronic syphilitic sores and indolent ulcer has also been evident. Neem oil finds use to control various skin infections. Bark, leaf, root, flower and fruit together cure blood morbidity, biliary afflictions, itching, skin ulcers, burning sensations and phthisis. Neem is used as a pesticide.

**Side effects:** Vomiting, diarrhea, drowsiness, blood disorders, seizures, loss of consciousness, coma, brain disorders, infertility, kidney damage, liver damage, low or no urine production, allergic reactions, difficult breathing and death.

**Contraindications:** Pregnancy, lactation, auto-immune diseases such as multiple sclerosis (MS), lupus (systemic lupus erythematosus, SLE), rheumatoid arthritis (RA), or other conditions; diabetes, organ transplant, surgery.

**Drug Interactions:** Neem might have an effect like a diuretic. Taking neem might decrease how well the body gets rid of lithium. This could increase how much lithium is in the body and result in serious side effects. Talk with your healthcare provider before using this product if you are taking lithium. Your lithium dose might need to be changed.

Neem might decrease blood sugar. Diabetes medications are also used to lower blood sugar. Taking neem along with diabetes medications might cause your blood sugar to go too low. Monitor your blood sugar closely. The dose of your diabetes medication might need to be changed. Some medications used for diabetes include glimepiride (Amaryl), glyburide (DiaBeta, GlynasePresTab, Micronase), insulin, pioglitazone (Actos), rosiglitazone (Avandia), chlorpropamide (Diabinese), glipizide (Glucotrol), tolbutamide (Orinase), and others.

Neem might increase the immune system. By increasing the immune system, neem might decrease the effectiveness of medications that decrease the immune system. Some medications that decrease the immune system include azathioprine (Imuran), basiliximab (Simulect), cyclosporine (Neoral, Sandimmune), daclizumab (Zenapax), muromonab-CD3 (OKT3, Orthoclone OKT3), mycophenolate (CellCept), tacrolimus (FK506, Prograf), sirolimus (Rapamune), prednisone (Deltasone, Orasone), corticosteroids (glucocorticoids), and others.

**Dose:** 1 – 3 gm of the leaf drug in powder form; 10 – 20 ml of the leaf drug for decoction. 2 – 4 gm of the bark drug in powdered form. Bark decoction should be used externally.

**Macroscopic examination of A. indica leaf**
Leaves are compound, alternate, rachis 15-25 cm long, 0.1 cm thick; leaflets with oblique base, opposite, exstipulate, lanceolate, acute, serrate, 7-8.5 cm long and 1.0-1.7 cm wide, slightly yellowish-green; odour, indistinct; taste, bitter.

**Macroscopic examination of A. indica bark**
Azadirachta indica bark varies much in thickness according to age and parts of tree from where it is taken. External surface is rough, fissured and rusty-grey; laminated inner surface yellowish and foliaceous, fracture fibrous, odour characteristic and taste bitter.

**Microscopic examination of A. indica leaf**
Midrib of leaf
Leaflets through midrib show a biconvex outline; epidermis on either side covered externally with thick cuticle; between epidermis 4-5 layered collenchyma were present. Stele composed of
one crescent-shaped vascular bundle towards lower and two to three smaller bundle towards upper surface; rest of tissues composed of thin-walled, parenchymatous cells having secretory cells and rosette crystals of calcium oxalate; phloem surrounded by non-lignified fibre strand; crystals also present in phloem region.

**Lamina of leaf**
The structure of lamina was dorsiventral. Epidermis on either surface was composed of thin walled, tangentially elongated cells, covered externally with thick cuticle. Anomocytic stomata present on lower surface only; palisade single layered; spongy parenchyma composed of 5-6 layered, thin-walled cells traversed by a number of veins, rosette crystals of calcium oxalate present in a few cells, palisade ratio 3-4.5, stomatal index 13-14.5 on lower surface and 8-11.5 on upper surface.

![Upper epidermis of leaves of A. indica](image1) ![Lower epidermis of leaves of A. indica](image2)


**Microscopic Examination of bark powder**
Bark contains entirely dead elements of secondary phloem, alternating with discontinuous tangential bands of compressed cork tissue, former composed of several layers of stone cells occurring in regularly arranged groups together with collapsed phloem elements filled with brown contents; in between the successive zones of cork tissue 3-5 layers of fibre groups with intervening thin-walled and often collapsed phloem elements present; each zone of cork tissue consists of several layers of regular, thin-walled cells occasionally with a few compressed rows of thick-walled cells towards outer surface; within exfoliating portion a number of layers of newly formed cork composed of thin walled, rectangular cells and one or two layers of cork cambium, below which a wide zone of secondary phloem present; secondary cortex absent in most cases; secondary phloem commonly composed of well-developed fibre bundles traversed by 2-4 seriate phloem rays and transversely separated by bands of parenchymatous tissue of phloem; phloem elements of outer bark mostly collapsed; a few fairly large secretory cavities also occur in phloem; most of phloem parenchyma contain starch grains and prismatic crystals of calcium oxalate; starch grains, simple, round with central hilum, measuring 2.75-5µ structure of bark varies considerably according to gradual formation of secondary cork bands.

**Powder Microscopy of A. indica leaf**
The green powdered drug of *A. indica* revealed vessels, fibers, rosette crystals of calcium oxalate, fragments of spongy and palisade parenchyma.
**Powder microscopy of A. indica bark**
Reddish-brown powder of *A. indica* showed numerous prismatic crystals of calcium oxalate, phloem fibres with narrow lumen and pointed ends; cork cells, stone cells mostly in groups, lignified rectangular to polygonal, having wide lumen and distinct striations, simple starch grains, measuring 2-75 – 5 µ in diameter.

**Physico-chemical Parameters of A. indica**
- Foreign matter – not more than 2%
- Total ash – not more than 10%
- Acid-insoluble ash – not more than 1%
- Alcohol-soluble extractive – not less than 13%
- Water-soluble extractive – not less than 19%

**Phytochemical analysis of A. indica**
*A.indica* powder (50 gm) was extracted using a percolation method that involved 3 consecutive extractions of 48 hours with methanol/H2O (80:20 v/v) at room temperature. Preliminary phytochemical tests of the extracts for alkaloids, phytosteroids, flavonoids, tannins, coumarins, saponins and anthraquinone were carried out using specific reagents through prescribed standard methods.

<table>
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<tr>
<th>Phytochemicals</th>
<th>Test name</th>
<th>Extract</th>
<th>LN</th>
<th>PN</th>
<th>PN</th>
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<tbody>
<tr>
<td>Alkaloids</td>
<td>Wagner</td>
<td>Potassium mercuric iodide</td>
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<tr>
<td></td>
<td>Mayer</td>
<td>Iodine in potassium iodide</td>
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<td>Flavonoids</td>
<td>Cyanidin test</td>
<td>HCl (37%) + Mg powder + amyl alcohol (50%)</td>
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<td>Lembergmann–Burchard test</td>
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<td>Salkowski test</td>
<td>Conc. H$_2$SO$_4$</td>
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<tr>
<td>Tannins</td>
<td>FeCl$_3$</td>
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<td></td>
<td>Gelatin test</td>
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<td>Anthraquinones</td>
<td>Borntrager test</td>
<td>NH$_3$</td>
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**Thin-layer Chromatography of A. indica bark extract**
Thin-layer chromatography of alcoholic extract of *A. indica* on Silica gel ‘G’ plate using Chloroform: Ethyl acetate: Formic acid (5:4:1) shows under UV (366nm) three fluorescent zones at Rf 0.72 (blue), 0.86 (blue), and 0.90 (green). On spraying with 5% methanolic phosphomolybdic acid reagent and heating the plate for about ten minutes at 105°C revealed four blue spots at following Rf values: 0.20, 0.45, 0.63 and 0.90.

**UV-Visible Spectroscopy of A. indica extract**
Azadirachtin showed absorbance at 220 nm in the UV Spectrophotometer, Correlation coefficient of Azadirachtin was found to be 0.998. The calibration curve of Azadirachtin is shown in figure below.
HPLC Analysis

Retention time of Azadirachtin was found to be 3.8 minutes using the optimized chromatographic conditions.

The chromatogram below reveals the method developed for quantitation of Azadirachtin A & B in bovine muscle.

Larvicidal Activity
Reared larvae were exposed to 1, 2, 3, 4 and 5 ppm concentrations of aqueous extract of *Azadirachta indica* A Juss. *A. indica* elicited 70 – 99% mortality. *A. indica* extract was found to be significantly effective in controlling Culex larvae.

**Anti-bacterial activity**
The petroleum ether, methanol and aqueous extracts of the leaves of *Azadirachta indica* were screened for their anti-microbial activity using the cup plate agar diffusion method. They were tested against six bacteria: two gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and four gram-negative (*Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and *Salmonella typhi*). The methanolic extract of *Azadirachta indica* exhibited pronounced activity against *Bacillus subtilis* (28 mm).

**Anti-diabetic activity evaluation**
The pharmacological hypoglycemic action of *A. 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. *A. indica* significantly reduce glucose levels at 15th day in diabetic rats.

**Anti-oxidant activity**
*A. indica* extract from young flowers and leaves have strong anti-oxidant potential potential. An indicator of oxidative malondialdehyde (MDA) was reduced by 46% and 50.6% for flower and leaf-based extracts respectively, prompting the recommendation of *A. indica* extract to promote good health.

**Anti-HIV/AIDS**
In HIV/AIDS patients, a 12 weeks oral administration of acetone water neem leaf extract had a significant influence *in vivo* on CD4 cells without any adverse effects in the patients. Of the 60 patients who completed treatment, 50 were completely laboratory test complaint. The mean levels of CD4 cells increased by 159% in 50 patients that is a significant increase. The number of HIV/AIDS pathologies decreased from the 120 baseline to 5 and significant increases were observed in body weight (12%), hemoglobin concentration (24%) and lymphocyte differential count (24%).

**Anti-ulcer activity**
*A. indica* bark extract reduced gastric acid hyper secretion, gastro-esophageal and gastro duodenal ulcers. After six weeks one case of esophageal ulcer and gastric ulcer were fully healed while after 10 weeks, the duodenal ulcers were almost healed.

**Anti-malarial activity**
The anti-malarial activities of the tablet suspension of the bark and leaf of *A. indica* were evaluated on *Plasmodium yoellinigeriensis* infected mice, the tablet suspensions exhibited high prophylactic, moderate suppressive and a very minimal curative schizonticidal effect. The tablet suspensions from the leaf and bark at a concentration of 800 mg/kg and chloroquine at a concentration of 62.5 mg/kg body weight produced average % parasitaemia of 79.6%, 68.2% and 99.5% for leaf, bark and chloroquine respectively in chemosuppression. For the purpose of prophylactic treatment, the tablet suspensions at 800 mg/kg and pyrimethamine at a concentration of 0.35 mg/kg gave an average parasitaemia reduction of 75.3%, 65.6% and 98.3% for the leaf, bark and pyrimethamine respectively.
Anti-tumor effect
A. indica showed chemopreventive capability by regressing the hepato-carcinogenesis induced by di-ethyl-nitrosamine/2 acetyl-aminofluorene carcinogens on Sprague-Dawly rats.

Anti-fertility effect
A. indica leaf and its seed extracts administered orally at the beginning of the post-implantation stage resulted in pregnancy termination in rodents and primates, without any permanent effects. Praneem is a poly-herbal vaginal tablet that has proven to be effective in immobilizing sperms.

Anti-dental caries effect
A. indica extract dental gel exhibited significantly reduced plaque and bacteria (Streptococcus mutans and Lactobacilli species) over the control group that used commercially available mouthwash containing the germicide chlorhexidine gluconate (0.2% w/v).

Anti-inflammatory, anti-pyretic and analgesic effects of A. indica
The chloroform extract of stem bark is effective against carrageenan induced paw oedema in rat and mouse ear inflammation. Inflammatory stomatitis in children is cured by the bark extract. Anti-pyretic activity has been reported in neem oil. A methanolic extract of the leaves exert anti-pyretic effect in male rabbits. The plant also possesses analgesic activity mediated through opioid receptors in laboratory animals.

Anxiolytic effect
Low dose of A. indica extract have sedative effects that may be helpful in reducing anxiety and stress.

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