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## Chemistry behind in neem (*Azadirachta indica*) as medicinal value to living forms-A review

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**Abstract**

The Azhadirachtin in Indian society has been considered higher than kalpavriksha, the mythological and ethanobotanical beneficial properties. The efficacy of neem as a medicine has been documented in several different ancient treatments like the Atharvana Veda, the Ghrhyasutra and Sutragrantha and in puranas. The acidic principles in neem as margosic acid with three active constituents, viz., nimbin, nimbidin and nimbinene. Chemically related and biogenetically derivable from a tetracycliterpene are the key features of them. These chemicals, for example, pesticides, antifeedants and cytotoxic properties, also show a whole range of biological activity.

**Keywords:** Nimbin, nimbidin, nimbinene, tetracycliterpenes

**Introduction**

The Sanskrit word "nimba" means (Nimbati sincati svasthyamiti, svastha vrtikaramiti yavat) that which gives health (Kumar and Navaratnam, 2013) [5]. The neem tree is an extraordinary plant that has been proclaimed by the United Nations as the 'Tree of the 21st Century'. The neem twigs are used as tooth brushes as it possess prophylactic effect widely used by 500 million people of India alone (Srirangarayan *et al.*, (2020) [19]; Lekshmi, (2012)) [7]. Neem is used in Ayurveda, Siddha, Unani and Homeopathic medicine. In India, pharmaceutical chemists isolated margosic acid during 1919, an acidic principle in neem oil containing three active constituents, such as nimbin, nimbidin and nimbinene, since they were chemically identical and biogenetically derived from tetracycliterpenes (Neem foundation, 2012) [13]. The components are also referred to as liminoids as it contains azhadirachtin, meliantrol, salanin etc., (Chen *et al.*, 2018). These compounds also exhibit a wide range of biological activity.

**Medicinal uses of neem**

Neem has more than 140 compounds isolated from different parts of the tree (Subapriya *et al.*, 2005) [20]. The parts of neem such as leaves, flowers, seeds, fruits, roots and bark have been used traditionally in treating inflammation, infections, fever, skin diseases, dental disorders and removing the evil effects of spirits. Quercetin (flavonoid) and nimboesterol ( $\beta$ -sitosterol) are present in the leaves, as is of the liminoids (nimbin and its derivatives). Quercetin is a polyphenolic flavonoid that tends to have antibacterial and antifungal properties and possess curative effects for sores and scabies (Singh, 2009) [18]. At a dosage ranging between 100 and 500 ppm, limonoids such as nimocinolide and isonimocinolide affect fertility in house flies (*Musca domestica*) and mutagenic properties are also found against mosquitoes (*Aedes aegypti*) yields intermediates. New matured leaves develop an odorous viscous essential oil that exhibits fungal antifungal activity against *Trichophyton mentagrophytes* at invitro conditions (Lim, 2014) [8]. White crystalline flakes obtained from petroleum ether extract of leaves has C 14, C 24, C 31 alkanes were found to exceed or equal the larvicidal activity of pyrethrum extract (Singh *et al.*, 2014) [17]. Proteins (7.1 percent), carbohydrates (22.9 percent), minerals, calcium, phosphorus, vitamin C, carotene, etc. are the main constituents of neem leaves (Abdel-Zaher *et al.*, 2018) [1]. Amino acids such as glutamic acid, tyrosine, aspartic acid, alanine, praline, glutamine, cystine and other fatty acids such as dodecanoic acid, tetradecanoic acid, elcosanic acid, etc. are present.

**Table 1:** Valuable products extracted from the neem

1. Antimalarial	2. Antituberculosis	3. Antiviral
4. Anti allergic	5. Anti Enzemic	6. Antiscabic
7. Anti Dermatic	8. Anti Gingivitis	9. Antiinflammatory
10. Anti Periodontitic	11. Ameobocidal	12. Diuretic
13. Spermicidal	14. AntiPythoeic	15. Anti Seborrhoeic
16. Anti freedant	17. Anti fungal	18. Anti furancular
19. Bactericide	20. Insecticidal	21. Larvicidal
22. Piscidal	23. Anti cardiac arrest	24. Nematicidal

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Nimboesterol and flavonoids such as kaempferol, melicitrin are present in flowers which are one of the essential oil consisting of sesquiterpene derivatives while flowers yields a waxy material which contains fatty acids such as behenic (0.7 percent), arachidic (0.7 percent), stearic (8.2 percent), palmitic (13.6 percent), oleic (6.5 percent) and linoleic (8.5 percent) (Saini *et al.*, 2018) [16]. There are several amino acids in the neem pollen, including glutamic acid, tyrosine, arginine, methionine, phenylalanine, histidine, arminocaprylic acid, and isoleucine (Mishra *et al.*, 2013) [11]. Nimbin (0.04 percent), nimbinin (0.001 percent), nimbidin (0.4 percent), nimboesterol (0.03 percent), essential oil (0.02 percent), tannin (6.0 percent), bitter margosin and 6-desacetyl nimbinene are found in the trunk bark (Singh, 2009) [18]. The stem bark is rich in tannins (12-16 Percent) and non-tannin (8-11 Percent). The bark contains anti-inflammatory polysaccharide consisting of glucose, arabinose and fructose at a molar ratio 1:1:1 with molecular weight of 8,400 (Chitra *et al.*, 2017) [3]. The bark also yields an antitumor polysaccharide (Priyadarsini *et al.*, (2010) [15]; Othman *et al.*, (2012)) [14]. Stem bark and root bark yields diterpenoids such as nimbinone, nimbolicin, margocin, nimbidiol and nimbine. Though heartwood contains iron salts, potassium and calcium, heartwood provides charcoal (30 percent) and pyroligeneous acid (38.4 percent) by the process of destructive distillation. (Kumar *et al.*, 2017) [6]. Neem wood contains cellulose, hemicellulose (14.00%) and lignin (14.63%), while wood oil contains  $\beta$ -sitosterol, cycloecalenol and 24-ethylenecycloartenol (Manimaran *et al.*, 2018) [10]. The gum exuded by the tree on hydrolysis yields, D-glucuronic acid, L-arabinose, D-galactose and L-fucose as the older tree exudes a sap which has free sugars such as glucose, fructose, mannose and xylose and amino acids includes asparagines, praline, alanine, aminobutyric acid, arginine, aspartic acid, glycine, norvaline and organic acids *viz.*, citric, malonic, succinic and fumaric acids. (Kumar *et al.*, 2017) [6]. The sap is reported to be useful in the treatment of general weakness and skin diseases. Seed is very important both because of its high lipid content and because of the presence of a large number of bitter principles that include, in substantial amounts, azadirachtin, azadiradione, fraxinellone, nimbin, salannin, salannol, vepinin, and vilasinin.

**Table 2:** Chemical Composition of Neem leaves

S. No.	Chemical composition	Unit as prescribed in parenthesis
1.	Moisture	59.4(%)
2.	Fat	1.0(%)
3.	Carbohydrates	22.9(%)
4.	Calcium	510(mg/100g)
5.	Iron	17(mg/100g)
6.	Niacin	1.40(mg/100g)
7.	Carotene	1998( $\mu$ g/100g)
8.	Glutamic acid	73.30(mg/100g)
9.	Aspartic acid	15.50(mg/100g)
10.	Proline	4.00(mg/100g)
11.	Proteins	7.1(%)
12.	Fiber	6.2(%)
13.	Minerals	3.4(%)
14.	Phosphorus	80(mg/100g)
15.	Thiamine	0.04(mg/100g)
16.	Vitamin C	218(mg/100g)
17.	Calorific value	1290 (kcal/kg)
18.	Tyrosine	31.50(mg/100g)
19.	Alanine	6.40(mg/100g)
20.	Glutamine	1.00(mg/100g)

(Redrawn from Singh, 2009 & Neem Foundation, 2012) [18]

Azadirachtin has been shown to be effective against around 200 insect species as a pesticide and is confirmed to be non-toxic to humans (National Research Council, 2002) [12]. Neem kernel lipids are similar to the normal glycerides from other oilseeds and contains oleic acid (50-60 percent), palmitic acid (13-15 percent), stearic acid (14-19 percent), linoleic acid (8-16 percent) and arachidic acid (1-3 percent) (Singh, 2009) [18]. Neem kernel oil is brownish yellow, non-drying oil with unpleasant odour and acrid taste. The oil content varies with the processing system. Depending on the raw material used for expulsion, the composition of neem cake after oil extraction varies widely. The range of the proximate composition in neem leaves includes crude protein 13-35, carbohydrates 26-50, crude fibre 8-26, fat 2-13, ash 5-18, acid insoluble ash 1-7 (Neem Foundation. 2012) [13]. As feed for animals or poultry, the bitter cake has no appeal. Cake extraction followed by hexane with 70 percent alcohol produces a meal free of bitterness and odor that will be adequate as feed. Neem cake is rich in amino acids. It is one of the potential organic manure source which was rich in plant nutrients, including 2-3 percent nitrogen, 1.0 percent phosphorus and 1.4 percent potassium, 1.0-1.5 percent tannic acid and sulphur content of 1.07-1.36 percent. (Singh, 2009) [18]. The bark of neem, leaves, fruits, flowers, oil, everything (bark, leaves, fruit, flower and oil) combination. Researchers reported that tender neem leaves are effective against parasitic infections and anti-viral properties have been discovered in a 10 percent of aqueous extract dosage. Plasma coagulation period tests using Russel's viper venom have shown that a clotting agent is present in the leaf extract which was used in treating poisonous bites. (Gunadharini *et al.*, 2011) [4]. Neem leaves total extract is a potent hepatoprotective agent, as neem leaves water extract showed significant antiulcer activity, while mild fungicidal action was observed in fresh leaves essential oil, significant anti-inflammatory effect, decreased frequency and severity of gastric mucosal lesions induced by stress. The extracts of neem leaf, bark and seed on intraperitoneal administration revealed immuno-stimulatory properties which are responsible for its anti-HIV effect. Among more than 100 compounds found in Neem (Neem seed kernel) (Srirangarayan *et al.*, 2020) [19]. Twelve Azadirachtin compounds are identified while all of them shows high biological activity levels. Azadirachtin in only single low dose was reported to have immunized a transmission of Chagas disease from the kissing bug. Azadirachtins have been shown to inhibit the larval, pupal and adult moults and reproduction and fitness of both plant-feeding and aquatic larvae such as mosquitoes. It has been shown that Gedunin, contained in whole fruit possess antimalarial activity. The antipyretic and non-irritant, nimbidin found in neem bark proved to be effective in treating of skin diseases such as eczema, furunculosis, arsenic dermatitis, burn ulcers, *Herpes labialis*, scabies and seborrheic dermatitis (Srirangarayan *et al.*, 2020) [19]. It is also effective in treating skin diseases, such as warts, dandruff and skin diseases of unknown origin. Bark extracts have potent properties that are diuretic and anti-inflammatory. Spermicidal activity is reported to include nimbidin and sodium nimbidinate found in neem bark. Neem Bark has demonstrated antibacterial activity against different species that are gram-positive.

## Conclusion

Neem (*Azadirachta indica* Linn) is a spiritual divine tree mainly grown in Indian subcontinent, all parts of the neem is used as medicine for curing various diseases in human as well

as animal beings. The active compound present in neem play a major role to relieve different pains, fevers, infections and other problems. The multipurpose benefit behind in neem tree as a uncountable and more valuable gift to living forms in the ecosystems.

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