

Phytochemicals of *Azadirachta Indica* Source of Active Medicinal Constituent Used for Cure of Various Diseases: A Review

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Abstract: In the world of Ayurveda, Neem is a popular medicinal herb that's been part of traditional remedies that date back almost 4000 years. *Azadirachta Indica* is the botanical name of Neem and known as Neemba in devbhasha Sanskrit. The medicinal tree is good example of how nature holds the problem and cures both. Neem tree is bank of many phytochemicals which are active against many microbial as well as chronic diseases.

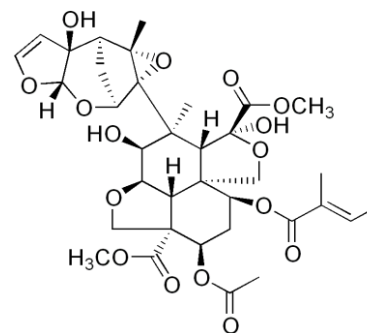
Index Terms: Extract, Antibiotic, Antiviral, Antimicrobial and Antifungal.

I. INTRODUCTION

The plants present in our surroundings help to not only clean our environment but also its plant products are rich sources of antioxidants as well as contain phytochemicals of medicinal uses. In India since ancient time we are highly depend on the plant products for prevention and cure of diseases. Allopathic medicines are not only expensive but also have many side effects. It is established fact that number of medicinally active phytochemicals are obtained from plants (Zong, Cao & Wang, 2012; Efferth & Koch, 2011). Extracts and phytochemicals obtained from the *Azadirachta Indica* are used against many infectious metabolic diseases and cancer disease (Brahmachari, 2004; Ketkar & Ketkar, 2004). Dried Neem leaves are placed in cupboards to prevent the clothes from insects and also in stored rice (Jumpupto:^{a b c}, 17 April 2006). Polyphenolic flavonoids extracted from fresh leaves of neem, Querestien and sitosterol shows antibacterial and antifungal activities (Govindachari et al, 1998). Antifungal (Singh & Sastry, 1997), antibacterial (Kher & Chaurasia, 1997) and anti-inflammatory and also the various biological activities of neem are reported. Many investigators have confirmed phytochemicals of *A. Indica* as anti-inflammatory, antiarthritic, antipyretic, hypoglycemic, antigastric ulcer, antifungal, antibacterial, and antitumour

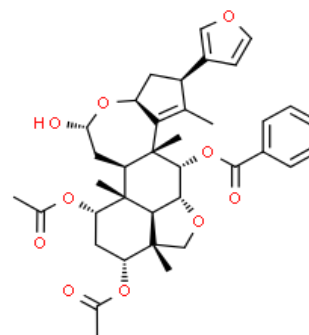
activities (Bandyopadhyay et al, 2004; Sultana, Anwar & Przybylski, 2007; Ebong, Atangwho, Eyong, & Egbung, 2008; Paul, Prasad & Sah, 2011).

II. ACTIVE PHYTOCHEMICALS OF *A. INDICA* AND STRUCTURES

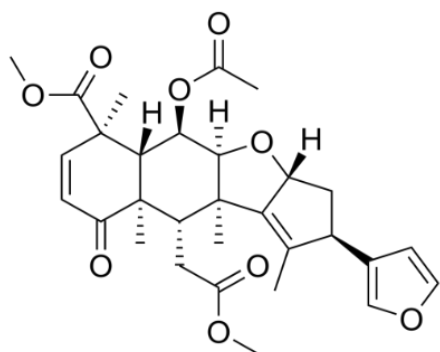


Azadirachtin

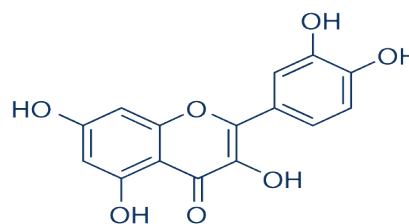
Azadirachtin is the most important phytochemical of *A. Indica*. This phytochemical has antimalarial activity.



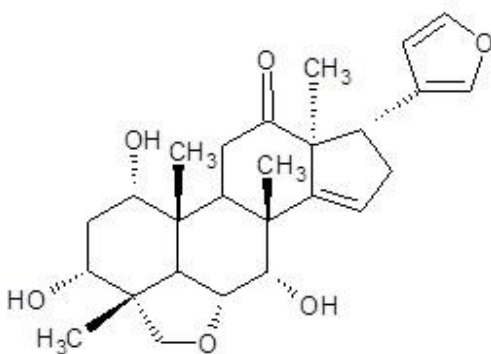
Nimbolinin A



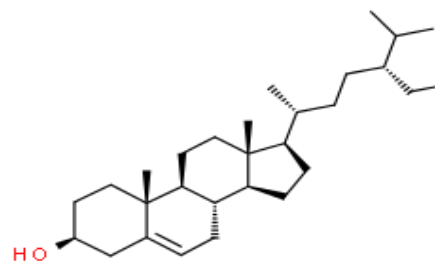
Nimbin



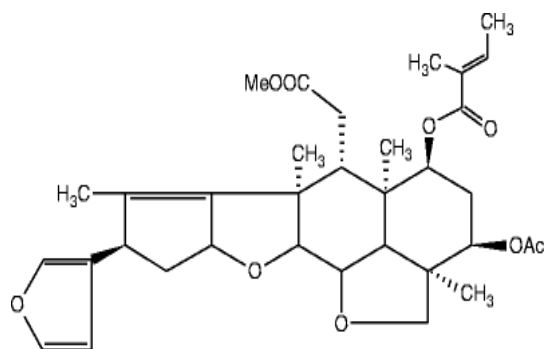
Quercetin



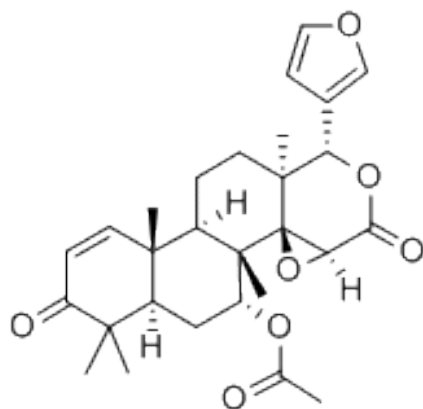
Nimbin



Sitosterol



Salannin



Gedunin

“The phytochemicals which are active against different pathogens, nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinat, gedunin, salannin, and quercetin. Leaves contain ingredients such as nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione, and nimbiol” (Ali, 1993; Hossain, Shah & Sakari, 2011; Kokate, Purohit, and Gokhale, 2010). “Fresh leave extract of Neem give the following active biological compounds, i.e. Quercetin and -sitosterol, polyphenolic flavonoids, they have antibacterial and antifungal properties (Singh & Sastry, 1997), and the neem seeds contains constituents including gedunin and azadirachtin in it”.

A. Phytochemicals shows antioxidant activities

The free radicals present in our body are responsible for the generation of many diseases. One can prevent himself from the diseases generate by action of free radicals only by deactivation of free radical. Antioxidants have property to stop the activity of free radicals before its action to words the biological cell of human body (Nunes, Silva, Guedes & Almeida, 2012).

Neem and other medicinal plants have been reported for their medicinal activity (Rahmani & Aly, 2015). All the parts of plant *A. indica* like leaves, fruit, seed, flower, and bark extracts shows strong antioxidant activity (Ghimeray, Jin, Ghimire & Cho, 2009; Sithisarn, Supabphol & Gritsanapan, 2005).

B. Anticancer activity of phytochemicals of *A. Indica*

The flavonoid present in Neem plant shows its activity against the spread of cancer cells. High dose of flavonoid may decrease the risk of cancer (Le Marchand, 2002). Limonoids present in oil of *A. Indica* active against the mutagenic effect of 7,12 Dimethylbenz(a)anthracene (Kumar et al, 2010).

C. Activity of phytochemicals of *A. Indica* against bacteria

The oil obtained from seed, bark and leaves of Neem shows its strong activity against gram positive, gram negative and mycobacterium tuberculosis organism (Chopra, Gupta & Nazir, 1952). In *in-vitro* antibacterial activity shown by Neem seed oil and the extract of other parts of Neem and its seed in water against microflora of cervico vaginal mucus of cows with endometritis. Neem oil extract in organic solvent methanol with hexane yielded four fractions. The first fraction is methanol miscible (a), the second fraction is methanol immiscible (b), the third fraction is hexane miscible (c) and the fourth fraction is hexane immiscible (d). The first fraction shows highest antibacterial activity i.e. 95%, second and third fraction shows 85% activity and fourth fraction shows 65% activity (Barman et al, 2009).

It has been reported that 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 bacteria (*Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and *Salmonella typhi*). The susceptibility of the microorganisms to the extracts of this plant was compared with each other and with selected antibiotics. The methanol extract of *Azadirachta indica* exhibited pronounced activity against *Bacillus subtilis* (28mm) (Aditi, Bhandari & Rai, 2011).

D. Activity of phytochemicals of *A. Indica* against virus

Neem bark extract at the ranging concentration of 50 to 100 µg/ml have ability to stop the entry of HSV-1 in to cells (Yerima et al, 2012). Neem leave extract is active against coxsackievirus virus B-4 (Badam, Joshi & Bedekar, 1999).

E. Activity of phytochemicals of *A. Indica* against fungus

Alcoholic Neem leaf extract was found very much effective to retard the growth of *Aspergillus* and *Rizopous* fungal species. Antifungal activity have been found in aqueous extracts of Neem oil, leaf extract, bark extract and the other parts of Neem extracts (Natarajan, Venugopal & Menon, 2003; Mahmoud et al, 2011; Amadioha & Obi, 1998).

F. Activity of phytochemicals of *A. Indica* against inflammation

Many plant extracts contain anti-inflammatory phytochemicals. Extracts obtained from different parts of Neem plays effective role anti-inflammatory agent. Fruit skin of *A. Indica* and phytochemical azadiradione are very good anti-inflammatory agents (Ilango, Maharajan & Narasimhan, 2013).

G. Activity against diabetes

It is a metabolic disease. It causes high blood sugar. *A. Indica* root bark extract shows very effective results against diabetes

(Patil et al, 2013). Neem leaves extracts are very effective for the treatment of diabetes (Akter et al, 2013).

Shravan et al (2011) evaluated the pharmacological hypoglycemic action of *Azadirachta indica*. In diabetic rat after treatment for 24 hrs, *Azadirachta indica* 250mg/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.

H. Antimycobacterial activities of phytochemicals of *A. Indica*

Passosa et al (2019) has been isolated two new terpenoids, limonoid morenolide and diterpene 17-hydroxy-sandaracopimar-8,15-dien-11-one, in addition to the three diterpenoids nimbidiol, ferruginol, and 6,7-dehydroferruginol and four well-known limonoids nimbinene, nimbinal, nimbadiol and salannin. These terpenoids exhibited the anti-inflammatory, cytotoxic and antimycobacterial activities.

Akpuaka, et al (2013) evaluated the antimicrobial activities of n-Hexane extract and 5 Column Chromatography fractions, of *Azadirachta indica* leaves. The n-hexane extract showed antimicrobial activities against human pathogenic bacteria (*Salmonella typhi*) and yeast fungus (*Candida albicans*). "Antimicrobial properties of *Azadirachta indica* fractions were tested using ditchwell diffusion method. Analysis of the data projected that upon bioassay with n-Hexane neem leaves extract and 5 fractions of Column Chromatography zone of inhibition for *Salmonella typhi* observed was 17mm, 12mm, 5mm, 3mm and 11mm respectively. While for the yeast fungus *Candida albicans* the zones of inhibition, seen were 28mm, 25mm, 20mm, 3mm, 21mm and 20mm for *Azadirachta indica*, respectively. Results were compared to conventional drugs. GC/MS identified 45 bioactive compounds in the n-Hexane extract of *Azadirachta indica* leaves out of which 33 have antifungal activity. Conclusively based on the data analysis it can be said *Azadirachta indica* A. juss leaves extract have biological activity as good as the conventional drugs against such microorganisms".

I. Activity against malaria

The antimalarial activities of the tablet suspension of the bark and leaf of *Azadirachta indica* were evaluated by Isah et al. on *Plasmodium yoelli nigeriensis* 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 percentage (%) parasitaemia of 79.6%, 68.2% and 99.5% for leaf, bark and chloroquine, respectively, in chemosuppression. Also in the 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". There was indication of moderate beneficial effect (Isah, Ibrahim & Iwalewa, 2003).

J. Activity against tumour

A study done by Manal et al (2009) on *Azadirachta indica* has revealed a chemopreventive capability by regressing the hepatocarcinogenesis induced by diethyl Nitrosamine (DEN) / 2 Acetylaminofluorene (AAF) carcinogens on Sprague-Dawley rats.

K. Activity against ulcer

Bandhopadhyay et al (2004) were evaluated that the neem bark extract reduced human gastric acid hypersecretion, and gastro-esophageal and gastroduodenal ulcers. After 10 weeks, the duodenal ulcers were nearly fully healed; after 6 weeks one case of esophageal ulcer and gastric ulcer were fully healed.

L. Activity Against Larvae

Aqueous extracts of four plants were tested by Aditi, Bhandari & Rai (2011) for larvicidal properties. Laboratory reared larvae were exposed to 1, 2, 3, 4 and 5 ppm concentrations of the extracts of *Azadirachta indica* A. Juss, *Gymnema sylvestre*, *Nerium indicum* mill and *Datura metel* L. respectively. Result showed that the *Azadirachta indica* elicited 70-99% mortality, followed by *G. sylvestre* 44-89%, *N. indicum* 41-74% and *D. metel* elicited 19-54% mortality to larvae. The extracts of *A. indica* and *G. sylvestre* were found to be significantly effective in controlling *Culex* larvae.

M. Activity against dental caries

"A neem-extract dental gel significantly reduced plaque and bacteria (*Streptococcus mutans* and *Lactobacilli* species were tested) over the control group that used commercially available mouthwash containing the germicide chlorhexidine gluconate (0.2% w/v)" has been evaluated by Pai, Acharya and Udupa, (2004). In preliminary findings done by Vanka et al (2001) neem inhibited *Streptococcus mutans* (bacterium causing tooth decay) and reversed incipient carious lesions (i.e. primary dental caries).

N. Activity against hypertension and hypercholesteremic effect

Administration of aqueous extract of neem along with DOCA salt prevented the development of hypertension in rats (Obiefuna & Young, 2005).

Administration of the mature leaf extract decreased serum cholesterol significantly without changing serum protein, protein urea and uric acid level in rats (Ogbuewu et al, 2011).

III. SOME EXCELLENT WAYS TO USE NEEM LEAVES

1. Its paste work as wound healer.
2. Extract of green leaves is strong anti-dandruff.
3. Neem leaves extract is also used for the removal of redness, irritation and tiredness of eyes.
4. Its paste with turmeric used to cure itching,eczema,ring worms and mild skin diseases.
5. It can boost immunity of human body.

A. Uses of Neem Flowers

It can be used to treat anorexia, nausea, belching and intestinal worms. It is sweet in taste and used to cook many dishes in south India. According to a study done in year 2008, its alcoholic extract is an effective contraceptive.

B. Use of Neem Twigs

It is used as tooth brush. It fights germs, maintains the alkaline level of saliva, keeps away bacteria, treats swollen gums and gives whiter teeth.

CONCLUSION

In coming years our interest in medicinal phytochemicals will increase due to its effectiveness against pathogens. These are nontoxic herbal products. *Azadirachta indica* is an herb of multiple interests and its use as medicine will save our social interest.

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