

The Antibacterial Activities of Neem [Azadirachta Indicia] Seed Oil, A Review

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Abstract: In traditional medicine most of the diseases have been treated by administration of plant or plant product. Neem (*Azadirachta indica*) is the most useful traditional medicinal plant in India. Each part of the neem tree has some medicinal property. During the last five decades, apart from the chemistry of the neem compounds, considerable progress has been achieved regarding the biological activity and medicinal applications of neem. It is now considered as a valuable source of unique natural products for development of medicines against various diseases and also for the development of industrial products. This review gives a bird's eye view mainly on the biological activities of the neem seed and some of their compounds isolated from the neem seed oil, pharmacological actions of the neem extracts, clinical studies and plausible medicinal applications of neem seed along with their safety evaluation.

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I. Introduction

Nature has provided a complete store house of remedies to cure all ailments of mankind. The natural or herbal remedies are still the backbone of medicines. Phytotherapy is a medicinal practice based on the use of herbal plants and their extracts. These herbs or plants and their active ingredients are used in traditional herbal remedies. The easy availability, low cost and negligible side effects, natural products are popular in the nowadays in the world [1-7]. All the herbs produced bewildering variety phytochemicals like primary metabolites [carbohydrates, fats, proteins] and secondary metabolites [Alkaloids, flavonoids, steroids, saponins, polyphenols, etc.] for their normal metabolic activities[8-10]. These secondary metabolites showed various biological activities and act in plant defense mechanisms. The chemical profile of a single plant may vary over time as it reacts to changing conditions. The secondary metabolites have therapeutic actions, which produced drugs.[11]

In 1830, De Jussieu[12] described the neem tree as *A. Indica* and its taxonomic position is as follows:

Order	Rutales
Suborder	Rutinae
Family	Meliaceae (mahogany family)
Subfamily	Melioideae
Tribe	Melieae
Genus	<i>Azadirachta</i>
Species	<i>Indica</i>

From the report by Siddiqui in 1942 on the isolation of nimbin from neem oil, more than 130 compounds have been isolated from different parts of neem and several reviews have also been published on the chemistry and structural diversity of these compounds. These compounds have been divided into two major classes: **isoprenoids and others**. The isoprenoids includes protomeliacins, limonoids, azadirone and its derivatives, vilasinin type of compounds, gedunin and its derivatives and Csecomeliacins such as nimbin, and azadirachtin. The nonisoprenoids include proteins and carbohydrates (polysaccharides), sulphurous compounds, polyphenolics such as flavonoids and their glycosides, aliphatic compounds etc[13-15].

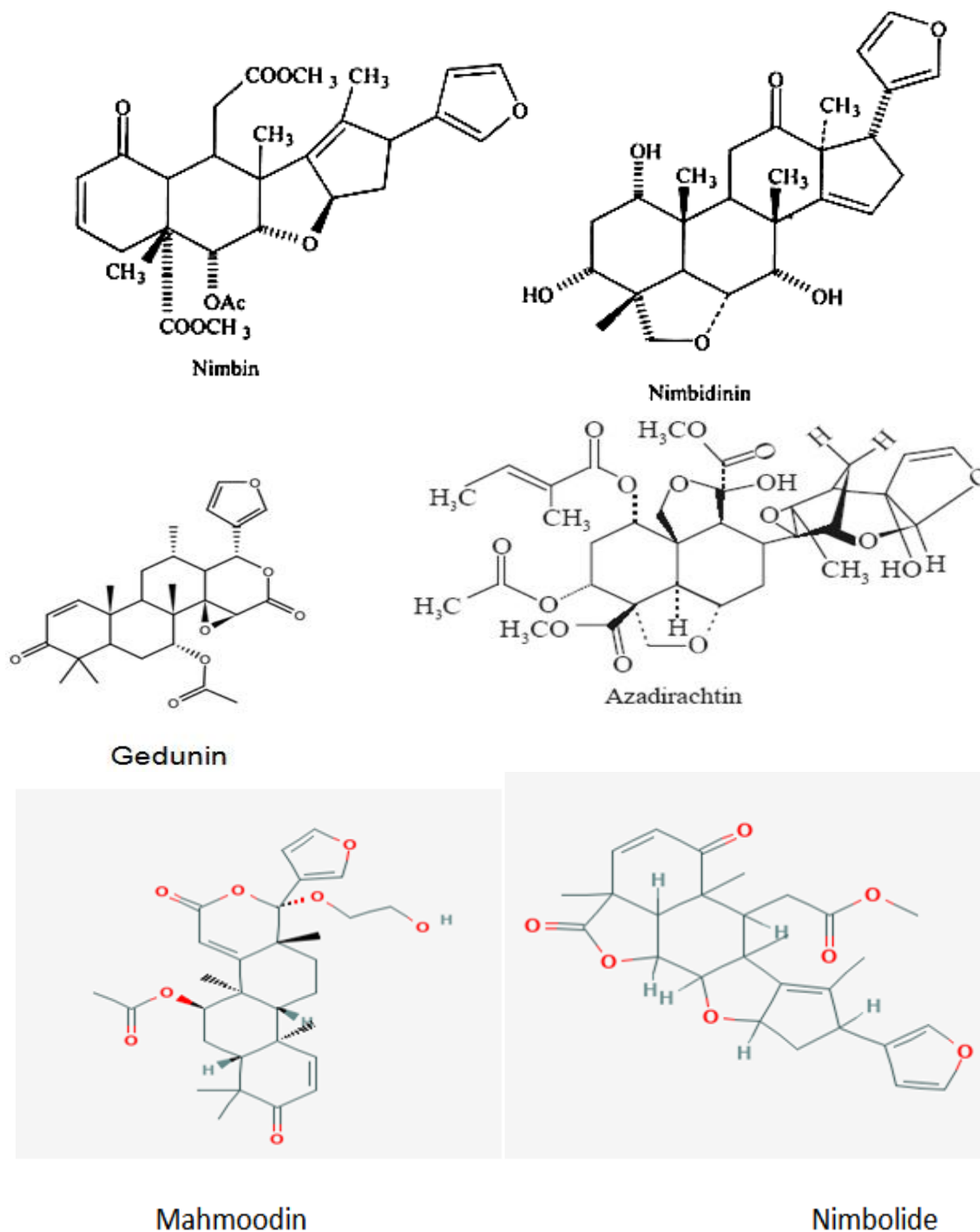
Azadirachta indica

Neem tree [*Azadirachta indica*] is a tree in the mahogany family Meliaceae, is evergreen tree found in most tropical countries. It is one of two species in the genus *Azadirachta*, native to India and Burma, growing in tropical and semi-tropical regions. It is a fast growing tree, average height 15-20 m but rarely to 35-40 m. It is evergreen but under severe drought it may shed most or nearly all of its leaves. For thousands of years the beneficial properties of neem have been recognized in the Indian tradition[16-18]. Each part of the neem tree has some medicinal property. Almost every part of the tree has been in use since ancient times to treat a number of human ailments and also as a household pesticide[19-22].

Active Compounds of *Azadirachta indica* L. (Neem)

Azadirachta indica L. (neem) shows therapeutic role in health management due to rich source of various types of ingredients. The most important active constituent is azadirachtin and the others are nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, 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. Quercetin and β sitosterol, polyphenolic flavonoids, were purified from neem fresh leaves and were known to have antibacterial and antifungal properties and seeds hold valuable constituents including gedunin and azadirachta[23].

II. Structure of Bioactive Need Seed Oil Compounds [24]



Compound Name	Source	Biological activity
Nimbi din	Seed oil	Anti-inflammatory An arthritic Diuretic Hypoglycemic Antifungal Spermicidal Ant gastric ulcer Antibacterial Antipyretic
Azadirachtin	Seed oil	Ant malarial
Numbing	Seed oil	Spermicidal
Nimbolide	Seed oil	Ant malarial Antibacterial
Gedunine	Seed oil	Ant malarial Antifungal
Mahmoodin	Seed oil	Antibacterial

[25-39]

NIMBIN

Nimbin is a triterpenoid isolated from Neem. Nimbin is thought to be responsible for much of the biological activities of neem oil, and is reported to have anti inflammatory, antipyretic, fungicidal, antihistamine and antiseptic properties.[24]

AZADIRACHTIN

Azadirachtin, a chemical compound belonging to the limonoid group, is a second- ary metabolite present in neem seeds. It is a highly oxidized tetranortriterpenoid which boasts a plethora of oxygen-bearing functional groups, including an enol ether, acetal, hemiacetal, tetra-substituted epoxide and a variety of carboxylic esters. [24]

GEDUNIN

Gedunine is an organic compound that is classified with the meliacines and as such with the triterpenoids. The substance is found in trees from the Mahogany family (Meliaceae), including the neem (Azadirachta indica), the krappa (Carapa guianensis) and the tiam (Entandrophragma angolense). It also occurs in the mangrove Xylocarpus granatum. The medicinal effects of gedunine have been shown against filariasis, cancer, gastric ulcers and malaria. It also has an effect against the dengue mosquito, Culex quinquefasciatus and the European corn borer [24].

Physical properties of Neem Seed Oil

Properties	Observation
Colour	Greenish yellow
Quality	Non-drying oil
Taste	Acrid and bitter
Odour	Repulsive (Garlic)
Solubility	Insoluble
Density	0.908 g /cm ³

Biological Activities of Neem Seed Oil(based on researches)

Since neem tree has been a point of focus of research to study the biological activity of its different products like seed oil, leaves(dry and fresh) and bark, a number of researches has been done using different methods and materials resulting important facts to discuss. Some of the properties of neem seed oil are as follows:

Immunostimulant activity:

Neem oil has been shown to possess immunostimulant activity by selectively activating the cell-mediated immune mechanisms to elicit an enhanced response to subsequent mitogenic or antigenic challenge[40].

Hypoglycaemic activity:

A significant hypoglycaemic effect was also observed by feeding neem oil to fasting rabbits. Recently, hypoglycaemic effect was observed with leaf extract and seed oil, in normal as well as alloxan-induced diabetic rabbits. The possible mechanisms underlying the hypoglycaemic activity of the aqueous leaf extract have also been discussed[28,41].

Antifertility effect:

Neem oil proved spermicidal against rhesus monkey and human spermatozoa in vitro. In vivo studies showed that intravaginal application of neem oil prior to coitus can prevent pregnancy. Antifertility effect of neem oil has also been studied and suggested to be a novel method of contraception. Purified neem seed extract (Praneem) has also been demonstrated to abrogate pregnancy in both baboons and bonnet monkeys, when administered orally. From the hexane extract of neem seed, an active fraction containing six components has been found to completely abrogate pregnancy in rodents when given orally up to a concentration of 10%, with no apparent side effect. The effect is possibly due to activation of cell-mediated immune reaction. The mechanism of action of neem oil appears to be non-hormonal, probably mediated through its spermicidal effect and may have less side effects than steroidal contraceptives[42-44].

Antimalarial Activity:

Nimbolide isolated from neem extracts shows the antimalarial activity by preventing the growth of plasmodium falciparum . Gedunin isolated from neem seed oil has been reported to show antimalarial activities[45-46].

Antitumor and Antiviral Activity:

Scientists in India, Europe and Japan have now found that limonoids and polysaccharides found in neem seed oil, bark and leaves reduced tumors and cancers and revealed effectiveness against lymphocytic leukemia. Aqueous extracts of neem leaf and also the some of fraction from neem oil showed antiviral activity against HIV and Polio Viruses[47].

Antioxidant activity:

Neem seed extract has demonstrated the antioxidant activity in vivo during horse grain germination, associated with low levels of lipooxygenase activity . An antioxidant principle has also been isolated, which is a potent inhibitor of plant lipooxygenases[48].

Activity against Oral Pathogens:

The antibacterial activity of Neem oil is screened against the bacterial pathogens using agar well diffusion assay and the zone of inhibition is measured in mm diameter. The area of inhibition where the growth of microorganisms was inhibited by neem oil was observed to be significant with all the three pathogens used when compared with the control. Through this study it was found that neem oil is effective against the oral pathogens. Many of the synthetic drugs present cause various side effects. Hence the drugs which are developed through plant based compounds have minimal side effects. The neem oil has got very good antibacterial activity[49].

Toxicity Of Neem Oil:

Neem oil shows toxicity to fish species like tilapia and carp. Oral administration of neem oil at 200 mg/rat produces severe hypoglycaemic effect.. Neem seed oil produces toxic effect in humans in several isolated cases. Intoxication of neem oil by humans causes vomiting, acidosis, diarrhoea, nausea, encephalopathy, etc. These toxic effects might be due to presence of aflatoxin and other toxic compounds present in neem oil. After further researches for mechanisms, it indicates that neem oil uncouples mitochondrial oxidative phosphorylation, thus inhibiting the respiratory chain. It also decreases intramitochondrial levels of acetyl CoA and acid-soluble CoA esters and reduces the mitochondrial ATP content[50-52].

Safety Evolution of Seed Oil

Toxic/adverse effect	Animal in which toxicity is manifested
Lethal toxicity	Tilapia and carp
Acute toxicity	Rat, rabbit
Severe hypoglycaemia	Rat
Produces vomiting, diarrhoea, drowsiness, acidosis, encephalopathy	Human
Spermicidal Rhesus	Monkey and human
Antifertility	Baboons and monkey
	Rodent

III. Conclusion

Neem oil is a unique source of various types of compounds with different chemical structure. A drug-development programme should be undertaken to develop modern drugs with the compounds isolated from neem oil. As the era is now changing towards the use of nontoxic plant products having traditional medicinal use, development of modern drugs from neem should be emphasized for the control of various diseases. This is the time to use this novel product (neem oil) in medical field by the coordination of the knowledge gifted by the ancestors and modern approaches of drug development. As seed oil consists of so many beneficial properties to fight against several diseases, quite a significant amount of research has already been carried out during the past few decades in exploring the chemistry of different parts of neem. Several therapeutically and industrially useful preparations and compounds have also been marketed, but an extraordinary work should be done in the field of research and development to ensure the uses of neem seed oil and also other products of neem in a better and more effective way.

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