

Neem (Azadirachta Indica): Medicinal Kalpavriksha

Giram Pratik Dilip, Prof. Sul S. A.

Dr. Babasaheb Ambedkar Technological University, Lonere.
ADITYA INSTITUTE OF PHARMACEUTICAL
Nalwandi Road, Beed - 431 122

Submitted: 10-01-2024

Accepted: 20-01-2024

ABSTRACT

Neem, has thrown the light worldwide in recent years, due to its wide range of medicinal properties. The tree has been largely used in Naturopathy, Unani and Homoeopathic medicine and has become a lodestar of current medicine. Further it elaborates a vast array of biologically active compounds that are chemically diverse and structurally complex. More than 150 compounds have been isolated from different parts of neem and these have been divided into two major classes isoprenoids and non-isoprenoids, which are proteins and carbohydrates.

Further, it consists of sulphurous compounds, polyphenolic compounds such as flavonoids and their glycosides, dihydrochalcone, coumarin, tannins and aliphatic compounds. All parts of the neem tree viz., leaves, flowers, seeds, fruits, roots and bark have been used traditionally for the treatment of inflammation, infections, fever, skin diseases, dental disorders, etc. Every part of the neem tree viz., roots, seeds, flowers, bark, leaves, fruit pulp and its constituents have been demonstrated to exhibit immune modulatory, anti-inflammatory, anti hyperglycaemic, antiulcer, antimalarial, antifungal, antibacterial, antiviral, antioxidant, anti-mutagenic, anti-diabetic and anti-carcinogenic properties.

Azadirachta indica, also known as the neem tree, has been used for millennia as a traditional remedy for a multitude of human ailments. Also recognized around the world as a broad-spectrum pesticide and fertilizer, neem has applications in agriculture and beyond. Currently, the extensive antimicrobial activities of *A. indica* are being explored through research in the fields of dentistry, food safety, bacteriology, mycology, virology, and parasitology.

KEYWORDS: Azadirachata, chemistry, medicinal properties, neem, pharmacological.

I. INTRODUCTION

Azadirachta indica is popularly known as Indian neem or margosa tree. It's been extensively used in ayurveda, unani and homoeopathic medicine since time immemorial. In Sanskrit a "good health" condition is expressed as "Nimba", which on due time derived in to "Neem", further the tree is considered as "Sarvaroga nivarini" means cure all ailments. In Ayurveda neem is known as "Arishtha" meaning 'reliever of sickness'. The tree is still regarded as "village pharmacy" or "Divine tree" due to presence of medicinal properties in India. If the developing countries are considered more than 80% of the population is believed to be dependent on medicinal plants for curing various diseases or disorders. Further, the total trade in medicinal plants in India during 2004-05 has been 4,530 crore. India ranks second in the world in terms of the volume and value of medicinal plants export.

Neem is one of the indigenous medicinal plants of India which possess medicinal properties in each and every part viz., roots, seeds, flowers, bark, leaves, fruit pulp etc.. Neem is one of the examples of complementary medicine through phytotherapy. Each of the plant part has been used in the Indian Ayurvedic and Unani systems of medicine and has become a cynosure of modern medicine.



Fig. 1

In Ayurvedic literature neem is well known for its medicinal properties viz., Neem bark is cool, bitter, astringent and acrid. In addition to this, it is used to cure tiredness, cough, fever, loss of appetite, worm infestation etc. It also heals wounds and vitiated conditions of kapha, vomiting, skin diseases, excessive thirst and diabetes. Along the bark, chemical compounds present in the leaves are reported to be valuable for eye disorders and insect poisons. It treats Vatik disorder and acts as anti-leprotic. Its fruits are bitter, purgative, anti-hemorrhoids and anthelmintic'. In the view of its immense utilities, this review summarizes the wide range of medicinal uses, pharmacological activities, biological activities of neem tree and its compounds and their chemistry.

Human society used the medicinal plants to combat diseases, since the dawn of civilization. A number of alternative medicine systems exist in the eastern region of the Mediterranean. For thousands of years nature has been a source of medicinal agents and based on their uses in traditional medicine an impressive number of modern drugs have been isolated from natural sources. In fact, plants are rich source of different types of medicines because they produce a diverse range of bioactive molecules. In the pharmaceutical industries natural products play an important role in drug development programs, therefore, over 50% of all modern clinical drugs are of natural product origin. In the addition of the importance of synthetic medicinal chemistry, there is huge interest in herbal medicine, there has been a revival of interest in herbal medicines to control major diseases and to discover new molecular structures as lead compounds from the plant kingdom.



Fig 2

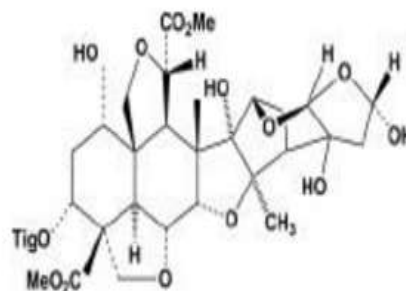
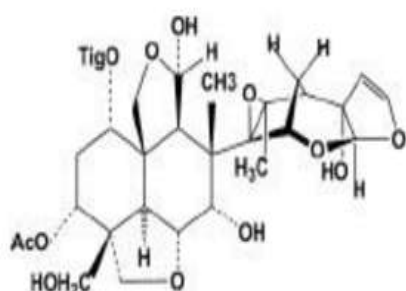
Azadirachta indica A. Juss. is a tree of small to medium-sized around 18 m, tall up to 15-30 m, with large crown up to 10-20 m diameter. The leaves are light green simply pinnate alternate with 20-40 cm long. The flowers are pentamerous, small, white or pale yellow, slightly sweet and bisexual. The plants fruits are greenish yellow to yellow or purple and have one or two seeded drupe, ellipsoidal, 1-2 cm long. They are greenish when ripe and their seeds are ovoid or spherical. Neem's leaves, seeds, bark, roots, fruits and oil have become a cynosure of modern medicine and used medicinally for treatment various diseases specially in Indian Ayurvedic medicine, Homoeopathic medicine. This plant was used for centuries by many cultures for their medicinal values. The advantages of this plant (very popular in many Asian and African countries) are easily available, cheap and low toxicity. *Azadirachta indica* is commonly known as Neem. It has great medicinal values and distributed widespread in the world. It is native of India and naturalized in most of tropical and subtropical countries. Their uses and attribution as one of medicinal plants is due to its various different active compounds which can be extracted from each of its parts. This review stated a detailed description on the existing chemical constituents and traditional uses of *Azadirachta indica* (neem) tree.

Method of Data Extraction

The procedure of collecting the available information on *Azadirachta indica* was via library search for articles published in peer reviewed journals and ethno botanical textbooks, as well as via electronic search (using Google Scholar, Pubmed, Web of Science, Scopus, and other web search engines).

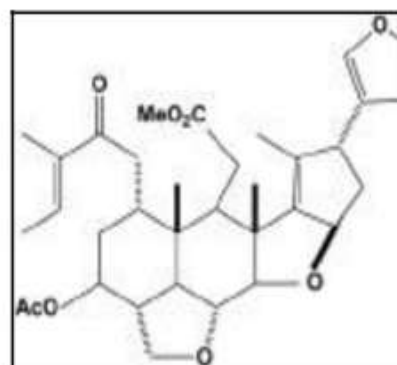
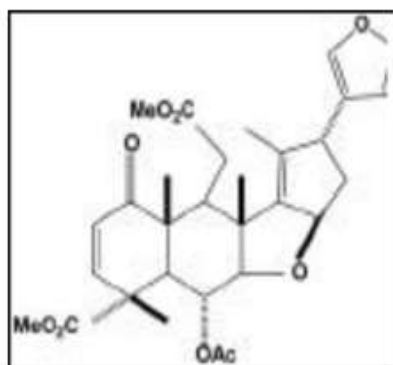
CHEMICAL CONSTITUENTS

Neem (*Azadirachta indica*) elaborates a vast array of biologically active compounds which are structurally complex and chemically diverse. Every part of this plant is used as herb. During the past two decades, the chemical constituents and biological activities of *Azadirachta indica* were intensively investigated in



both developing and developed countries. Several published studies revealed a lot of biological compounds and effects of these compounds on insects, and other inhibitory activities such as antitypanosomal and antiprotozoal extracted different constituents from the flowers of *Azadirachta indica* and analyzed their insecticidal activity, they found around 38 compounds in the flowers with insecticidal activity (such as: n-Hentriacontane, n-Nonacosane, n-Pentacosane, 2-Methoxy-5, 40-dimethylbenzenebutanal, Methyl octadecanoate acid, etc). The group of tetranortriterpenoids, especially azadirachtin analogues is responsible for most of the active principles as it has many antiinfective and antimicrobial properties. The extracted chemical constituents of different parts of neem tree contained many biologically active compounds, including triterpenoids, alkaloids, phenolic compounds, flavonoids, carotenoids, ketones and steroid. The most biologically active compound is azadirachtin. This compound belongs to the C-seco limonoids which was classified as tetranortriterpenes. It is actually a mixture of seven isomeric compounds labelled as azadirachtin M and azadirachtin N. These two compounds is more effective and play major role in medicinal activities when compared against second-instar larvae (L2)

of *Plutella xylostella* L. The structure of chemical compounds of *Azadirachta indica* is complex. Therefore, many years of study and research were done to elucidate the exact structure of azadirachtin. In 1968 Azadirachtin was first isolated by Butterworth and Morgan. Since that, more than 100 related compounds had been isolated from the neem tree, and these could be assigned to one of three groups: azadirachtols, azadirachtins, and meliacarpins. The Neem oil comprised of the bitter principles which was formed from biologically active compounds that were isolated from different parts of the plant including meliacin, azadirachtin, gedunin, nimbidin, nimbolides, nimbin, salanin, meliacin and valassin. Besides, the seeds also contains tignic acid responsible for the distinctive odour of the oil. Around 30-50 % of the oil was extracted from neem kernels. This oil mainly used as pesticide, contain many active ingredients which are together called triterpene or limonoids. The four best limonoids compounds were included Azadirachtin, Salannin, Meliantriol, and Nimbin. Limonoids contain insecticidal and pesticidal activity which lead to its role as an antifeedants, repellents, growth inhibitors, attractants, chemosterilants or as insecticides.



NEEM COMPOUNDS AND BIOLOGICAL ACTIVITY

More than 150 compounds have been isolated from different parts of neem. The compounds have been divided into two major classes; isoprenoid like diterpenoids and triterpenoids containing protomeliacins, limonoids, azadirone and its derivatives, gedunin and its derivatives, vilasinin type of compounds and C-secomeliacins such as nimbin, salannin and azadirachtin) and non-isoprenoids, which are proteins, carbohydrates, sulphurous compounds, polyphenolics such as flavonoids and their glycosides, dihydrochalcone, coumarin and tannins, aliphatic compounds, etc. Nimbidin, is responsible for crude bitter principle extracted from the oil of seed kernels of *A. indica* which possess several biological activities, from this crude principle some tetranortriterpenes, including nimbin, nimbinin, nimbidinin, nimbolide and nimbidic acid have been isolated. Further, have reviewed the biological activities some of the neem compounds, pharmacological actions of the neem extracts, clinical study and plausible medicinal applications of neem along with their safety evaluation. Further, neem also possess compounds acts as Antiinflammatory, Antiarthritic, Antipyretic, Hypoglycaemic, Antigastric ulcer, Spermicidal, Antifungal, Antibacterial, Diuretic, Antimalarial, Antitumour, Immunomodulatory etc.

Besides, several biological and pharmacological activities of neem compounds have been reported such as antioxidant, anti-inflammatory, antiarthritic, antipyretic, antiviral, spermicidal, hypoglycemic, anthelmintic, antigastric ulcer, and antitumour activities.

• Active Compounds of Neem

Azadirachta indica shows therapeutics role in health management due to rich source of various types of ingredients. Different parts of the Neem

tree contain numerous types of ingredients such as azadirachtin and the others are nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinat, gedunin, salannin and quercetin. Leaves of Neem tree contain ingredients such as nimbin, nimbanene, nimbandiol, ascorbic acid, 6-desaacetylnimbinene, nimbolide, n-hexacosanol and amino acid, 7-desaacetyl-7-benzoylgedunin, 7-desaacetyl-7-benzoylazadiradione, 17hydroxyazadiradione, and nimbiol [5, 6, 7]. Quercetin and Beta-sitosterol are polyphenolic flavonoids were purified from Neem fresh leaves and they are known to have antibacterial and antifungal properties [1]. Seeds of Neem tree hold valuable constituents including gedunin and azadirachtin. The active constituent of *Azadirachta indica* show therapeutic implications in the modulation of cell signaling pathway involved in the management of cancer. Neem and its active ingredient play a role in prevention and treatment of tumor due to its broader pharmacological activities. Neem tree extracts have been extensively used in health management since ancient times and have a variety of health promoting properties.

CHEMISTRY OF NEEM COMPOUNDS

Natural compounds present in neem are triterpenes or limonoids. New limonoids are still being discovered in neem. Azadirachtin, salannin, meliantriol and nimbin are well known. The bitter constituent, the nimbin contains an acetoxy, a lactone, an ester, a methoxy and an aldehyde group. Nimbidin contains sulphur.

1. Bark

The bark exudes a clean bright amber coloured gum which is collected in small tears or fragments. It contains a bitter alkaloid named "margosine". Leaves also bitter principles but in small quantity which are much more soluble in water. This substance is a hydrate of the resin.

2. Flowers

Flowers have been found to contain a flavonoid. Nimbicetin is identical to kaempferol. In the dried bark the same bitter components as in the seed oil have been found and in the pericarp of the fruit a bitter principle bakayanin was found.

3. Neem oil

Neem oil contains Sulphur 0.427%; a very bitter yellowish substance obtained from the alcoholic extract of the oil, which is supposed to be an alkaloid; resins; glucosides and fatty acids

4. Seeds

Meliacins found in the seeds include gedunin, 7-desacetylgedunin, desacetylnimbin and azedarachtin. The seed oil mainly contains nimbidin, nimbin and nimbinin, which also occur in the stem bark. **5. Toddy**

The toddy or sap contains glucose, sucrose, gums and coloring matter.

MEDICINAL USES

• Ayurveda

Neem tree has occupied a prominent place in the traditional Ayurvedic medicine in India from time immemorial. Neem bark, leaf extracts and neem oil have been under use as folk medicine to control various problems viz., leprosy, intestinal helminthiasis, constipation, etc. Further, it plays vital role in treating rheumatism, chronic syphilitic sores and indolent ulcers. Neem oil is well known to control various skin problems. Bark, leaf, root, flower and fruit together cure blood morbidity, biliary afflictions, itching, skin ulcers, burning sensations and pruritus. The root bark and young fruits are used as an alterative, antiperiodic and as a tonic. Green twigs are used as toothbrushes for cleaning teeth and as a prophylactic for mouth and teeth complaints. The bark, gum, leaf and seed are used in snake bite and scorpion sting. The bark is used as a bitter tonic, astringent, antiperiodic, antipyretic and against nausea and vomiting. Gum is demulcent tonic in catarrhal affections. Leaves are used as poultice for boils. Decoction of leaves used as an antiseptic in ulcers and eczema. Dry flowers are stomachic. Seed oil is a stimulant, antiseptic, alterative in rheumatism and skin diseases. Berries are purgative, emollient and anthelmintic. An extract of leaves is used in toothpastes. Neem oil is effective in the treatment of leprosy and skin diseases.

• Homoeopathy

Used against rheumatic pains. Pain in sternum and ribs, in the extremities and aches in hands and toes. Also used against eczema, pemphigus and scabies.

• Unani

Neem finds use as a resolvent and blood purifier. Leaves expel wind, heal ulcers in urinary passages. Used as an emmenagogue and in skin diseases. Fruit is used as an astringent and in leprosy and bronchitis.

• Immunostimulant activity

Various studies have revealed that the aqueous extract of leaf and bark possesses anticomplement and immunostimulant activity. Neem oil has been shown to possess activity by selectively activating the cell-mediated immune mechanisms to elicit an enhanced response to subsequent mitogenic or antigenic challenge.

• Hypoglycaemic activity

Neem leaf extracts showed promising results in decreasing blood sugar level and prevents adrenaline as well as glucose-induced hyperglycaemia. Recently, hypoglycaemic effect was observed with leaf extract and seed oil in normal as well as alloxan-induced diabetic rabbits.

• Antiulcer effect

Neem leaf and bark aqueous extracts produce highly potent antiacid secretory and antiulcer activity. A significant antiulcer effect was observed with nimbidin in preventing acetylsalicylic acid, indomethacin, stress or serotonin-induced gastric lesions as well as histamine or cysteamine-induced duodenal ulcers.

• Antifertility effect

Neem seed and leaf extract possess the chemical constituents which can act as anti-fertility sources. Studies on this concept have revealed that intravaginal application of neem oil, can prevent pregnancy, thereby stating it as a novel method of contraception. NIM-76, a refined product from neem oil, was studied in 10 human volunteers, where intravaginal application before sexual intercourse could prevent pregnancy with no adverse effect on vagina, cervix and uterus, further, the study revealed that intrauterine treatment is safe. Aqueous extracts of seeds and leaves contain sodium nimbinate (triterpene) which showed antifertility activity.

- **Antimalarial activity**

Neem seed and leaf extracts are effective against both chloroquin-resistant and sensitive strain malarial parasites. One of the neem's components, "gedunin" (a limonoid), is as effective as quinine against malaria. Malaria is one of the pandemic diseases causing millions of deaths every year in India and several other countries. China has adopted neem in a big way to reap the antimalarial effects of neem. The antimalarial formulation "Quinahausa" prepared in China will be available in India as well. Neem oil treated mosquito nets and mosquito-repellent cheap tablets are also becoming popular, due of growing problems of resistance to conventional treatments, it is becoming more and more difficult to control malaria. Clinical trials have been conducted to check the efficacy of neem extracts to control hyperlipidemia in a group of malarial patients severely infected with *P. falciparum*. The lipid level, especially cholesterol, was found to be lower during therapy when compared to non-malaria patients.

- **Antifungal activity**

From time immemorial it is believed that Neem is effective against certain fungi that infect the human body. Some important fungi against which neem preparations have been found to be effective are: athlete's foot fungus that infects hair, skin and nails; a ringworm that invades both skin and nails of the feet, fungus develops in intestinal tract, bronchi, lungs, and mucous membranes and a fungus that is part of the normal mucous flora that can get out of control leading to lesions in mouth (thrush), vagina, etc. Extracts of neem leaf, neem oil seed kernels are effective against certain fungi including *Trichophyton*, *Epidermophyton*, *Microspor*, *Trichosporon*, *Geotricum* and *Candida*.

- **Antibacterial activity**

Neem derives compounds especially Azadirachtin is well known for its role as antibacterial agent. It is a complex tetranortriterpenoid limonoid present in the seeds as well as leaves which is highly responsible for toxic effect on microbes. Extracts of the leaves, seed and bark possesses a wide spectrum of antibacterial action against Gram-negative and Gram-positive microorganisms, including *M. tuberculosis* and streptomycin resistant strains. In vitro, it inhibits *Vibrio cholerae* *Klebsiella pneumoniae*, *M. tuberculosis* and *M. pyogenes*. Antimicrobial effects of neem extract have been

demonstrated against *Streptococcus mutans* and *S. faecalis*. Apart from azadirachtin, other components such as nimbidin, nimbin, nimbolide, gedunin, mahmoodin, margolone, and cyclic trisulfide contribute to the anti-bacterial activity of neem. Further, neem extracts are a ray of hope to cure deadly diseases viz., Chagas disease in Latin America which was uncontrolled by any other means of medicines. This disease is caused by a parasite which is carried by an insect called kissing bug. Research has shown that feeding neem to the bugs not only frees them of parasites, but azadirachtin prevents the young insects from molting and the adults from reproducing.

- **Antiviral activity**

Aqueous leaf extract offers antiviral activity against Vaccinia virus, Chikungunya and measles virus. Nimbin and nimbidin have been found to have antiviral activity. They affect potato virus X, vaccinia virus, and fowl pox virus.

- **Anticancer activity**

Neem leaf aqueous extract effectively suppresses oral squamous cell carcinoma induced by 7, 12-dimethylbenz[a] anthracene (DMBA), as revealed by reduced incidence of neoplasm. Conducted a study in chemoprotective neem compounds viz., azadirachtin, nimbolide and limonoid enrich extracts on models of buccal carcinogenesis in hamsters. Overall studies were tested positive to reduce the expression and cell proliferation antigens. Further, researchers have shown prominent anti-cancerous activities from limonoidderived compounds from neem. Amongst these, both 1-Odeacetyllochchinolide B and 15-O-deacetylnimbolindin-B are proved to be beneficial to hinder cell growth in human cervical adenocarcinoma. A very recent study discovered that alkaloid-derived limonoid, azadiramide-A, is primarily found in Neem leaf ethanolic extracts, showed to stop cell growth and induce apoptosis in both the estrogen independent MDAMB-231 and estrogen dependent MCF-7 cell lines of breast cancer in human beings.

- **Antioxidant activity**

The antioxidant activity of neem seed extract has been demonstrated in vivo during horse-grain germination which is associated with low levels of lipooxygenase activity and lipid peroxides. An antioxidant principle has also been isolated, which is a potent inhibitor of plant lipooxygenases. Antioxidants derived from neem is

simple and cost effective way to supplement with natural extracts like those derived from Neem, in forms such as teas and oils, seem to be a simple and cost-effective way to introduce antioxidants.

- **Anti-diabetic effect**

Diabetes is one of the major chronic degenerative disorders now the world is facing. According to the health survey conservatively by 2030 there is expectancy for diabetes to be the 11th leading cause of death. Keeping in view of the severity of disease searching the ways for lower cost treatments must be need of hour. Among the various methods and pharmaco therapies being developed, the use of Neem extracts has steadily grown in interest. Several studies carried out in induced-diabetic rat models have revealed rescue of the G6PD when treated with Neem extracts.

- **Effect on central nervous system**

Varying degrees of central nervous system (CNS) depressant activity in mice was observed with the leaf extract. Fractions of acetone extract of leaf showed significant CNS depressant activity. Leaf extract up to a dose of 200 mg/kg body weight produces significant anxiolytic activity in rats. The crude ethanolic extracts of stem bark and root bark showed hypotensive, spasmolytic and diuretic activities.

- **Other activity**

The gum from bark is a stimulant and demulcent tonic. It possesses antileprosy, antispasmodic, and immunomodulatory properties. Neem is widely used for treating fevers. It has antipyretic (fever-reducing) property. Apart from these benefits, neem products also have analgesic (pain-relieving) and antiinflammatory effects, i.e. for most common ailments neem can provide organic, cheap, easily available and local medicines, thereby neem can bring sustainable livelihood to many people especially in rural and tribal regions.

II. RESULT

Neem acts as a bio-pesticide at different levels and in various ways. Primarily it acts as anti-feedant i.e., when an insect larva is hungry and it wants to feed on the leaf but if the leaf is treated with neem product, because of the presence of azadirachtin, salanin and melandriol there is an anti peristaltic wave in the alimentary canal and this produces something similar to vomiting sensation in the insect. Because of this sensation the insect does not feed on the neem treated surface and

ability to swallow is also blocked. Secondly it acts as oviposition deterrent i.e. by not allowing the female to deposit eggs comes in very handy when the seeds in storage are coated with neem kernel powder and/or neem oil.

III. CONCLUSION

Neem is one of the best nontoxic biological sources for development of modern drugs. Therefore, wide variety of neem extracts extend their benefits beyond traditional medical folklore, hence through the use of scientific and technological advance now we can use neem extracts as current medical adjuvants, on humans, animals and plants by understanding their potential. Considering the immense importance of this "Kalpavriksha" it can be explored for economic and therapeutic utilization for a sustainable development.

Clinical based examinations affirmed that Neem assumes essential job in aversion of different maladies. The job of dynamic fixings as chemo preventive impact has been seen in different tumor by means of balance of various cell signaling pathways.

ACKNOWLEDGEMENT

I express my sincere thanks to my project guide, **Miss. Sul S. A.** Designation Professor, for guiding me right from the inception till the successful completion of the research project. I sincerely acknowledge him for extending their valuable guidance, support for literature, critical reviews of project and the report and above all the moral support he had provided to me with all stages of this project.

I would also like to thank the supporting staff of Department, for their help and cooperation throughout our project.

REFERENCES

- [1]. Al Akeel, R., Mateen, A., Janardhan, K., Gupta, V.C., 2017. Analysis of antibacterial and anti-oxidative activity of *Azadirachta indica* bark using various solvents extracts. *Saudi Journal of Biological Sciences* 24(1), 11– 14.
- [2]. Alzohairy, M.A., 2016. Therapeutic role of *Azadirachta indica* (Neem) and their active constituents in diseases prevention and treatment. *Evidence-Based Complementary and Alternative Medicine*, 1–10.

- [3]. Amritalingam, M., 2001. Neem Tree- A Review. The Indian Forester 127(12), 1336–1342.
- [4]. Ara, I., Siddiqui, B.S., Faizi, S., Siddiqui, S., 1989. Antifungal and antibacterial activities of Neem. Journal of chemical society Perkin Transactions 87, 343–345.
- [5]. Balasenthil, S., Arivazhagan, S., Ramachandran, C.R., Nagini, S., 1999. Chemopreventive potential of neem (*Azadirachta indica*) on 7,12dimethylbenz[a]anthracene (DMBA) induced hamster buccal pouch carcinogenesis. Journal of Ethnopharmacol 67(2), 189–195.
- [6]. Basir, S., Shailey, S., 2012. Strengthening of antioxidant defense by *Azadirachta indica* in alloxan-diabetic rat tissues. Journal of Ayurveda and Integrative Medicine 3(3), 130.
- [7]. Baswa, M., Rath, C.C., Dash, S.K., Mishra, R.K., 2001. Antibacterial activity of Karanj (*Pongamia pinnata*) and Neem (*Azadirachta indica*) seed oil: a preliminary report. Microbios 105, 183–189.
- [8]. Bhakuni, D.S., Dhar, M.L., Dhar, M.M., Dhawan, B.N., Gupta, B., Srimal, R.C., 1971. Screening of indian plants for biological activity. Indian Journal of Experimental Biology 9(1), 91–102.
- [9]. Biswas, K., Chattopadhyay, I., Banerjee, R.K., Bandyopadhyay, U., 2002. Biological activities and medicinal properties of Neem (*Azadirachta indica*). Current Science 82(11), 1336–1345.
- [10]. Chatterjee, A., Pakrashi, S.C., 1991. The treatise on Indian Medicinal Plants. New Delhi, Publications & Information Directorate.
- [11]. Chen, J., Fan, X., Zhu, J., Song, L., Li, Z., Lin, F., Zi, J., 2018. Limonoids from seeds of *Azadirachta indica*, A. Juss. and their cytotoxic activity. Acta Pharmaceutica Sinica 8(4), 639–644.
- [12]. Chopra, I.C., Gupta, K.C., Nair, B.N., 1952. Biological activities and medicinal properties of neem (*Azadirachta indica*). Indian Journal of Medicinal Research 40, 511–515.
- [13]. Elumalai, P., Gunadharini, D.N., Senthilkumar, K., Banudevi, S., Arunkumar, R., Benson, C.S., Arunakaran, J., 2012. Ethanolic neem (*Azadirachta indica* A. Juss) leaf extract induces apoptosis and inhibits the IGF signaling pathway in breast cancer celllines. Biomedicine and Preventive Nutrition 2(1), 59–68.