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The Application of Neem in Traditional and Modern Medicine. A Review.

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Abstract

Neem has become important in the global context today because it offers answers to the major concerns facing mankind. Azadirachta indica is a fast-growing evergreen popular tree found commonly in India, Africa, and America. This review gives a bird's eye view mainly on the biological activity and its preventive-promotive medicinal uses and applications overall this review also tells that how the "neem is the one solution of thousand problems

Azadirachta indica, commonly known as neem, has attracted worldwide prominence in recent years, owing to its wide range of medicinal properties. Neem has been extensively used in Ayurveda, Unani and Homoeopathic medicine and has become a cynosure of modern medicine. Neem elaborates on a vast array of biologically active compounds that are chemically diverse and structurally complex. More than 140 compounds have been isolated from different parts of the neem. All parts of the neem tree-leaves, flowers, seeds, fruits, roots, and bark have been used traditionally for the treatment of inflammation, infections, fever, skin diseases, and dental disorders. Neem leaf and its constituents have been demonstrated to exhibit immunomodulatory, anti-inflammatory, antihyperglycaemic, antiulcer, antimalarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic, and anticarcinogenic properties. Its twigs have been used to clean teeth (1).

Neem is a unique plant in that all its parts — its leaves, flowers, seeds, fruit, root, and bark — exhibit medicinal properties.

Although scientific research on this supplement is still in its early stages, evidence suggests that it may treat dandruff, lice, gingivitis, and dental plaque, as well as promote wound healing.

Keywords:- Neem extracts Nutritional components Systemic diseases, Anti Oxidant, Inflammation, and Dental Disorder

Introduction

The plant product or natural products show an important role in disease prevention and treatment through the enhancement of antioxidant activity, inhibition of bacterial growth, and modulation of genetic pathways. The therapeutic role of the number of plants in disease management is still being enthusiastically researched due to their fewer side effect and affordable properties. It has been accepted that drugs based on allopathy are expensive and also exhibit a toxic effect on normal tissues and various

biological activities. It is a largely accepted fact that numerous pharmacologically active drugs are derived from natural resources including medicinal plants (2, 3)

Neem ingredients are applied in Ayurveda, Unani, Homeopathy, and modern medicine for the treatment of many infectious, metabolic, or cancer diseases [4, 5]. Different types of preparation based on plants or their constituents are very popular in many countries in disease management. In this vista, neem (Azadirachta indica), a member of the Meliaceae family, commonly found in India, Pakistan, Bangladesh, and Nepal, hash as therapeutics implication in diseases cure and formulation based on the fact that neem is also used to treat various diseases.

Azadirachta indica has a complex of various constituents including Nimbin, Nimbin, nimbolide, and limonoids, and such types of ingredients play role in disease management through modulation of various genetic pathways and other activities. Quercetin and ß-sitosterol were the first polyphenolic flavonoids purified from fresh leaves of neem and were known to have antifungal and antibacterial activities.

Active Compounds of Azadirachta indica L. (Neem)

Azadirachta indica L. (neem) shows therapeutics' role in health management due to the rich source of various types of ingredients. The most important active constituent is azadirachtin and the others are nimbolinin, Nimbin, Nimbin, 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-diacetyl-7-benzoylazadiradione, 7-diacetyl-7-benzoylgedunin, 17-hydroxyazadiradione, and nimbiol (4,5).

Quercetin and ß-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 azadirachtin.

The mechanism of action of *Azadirachta indica* is presented as follows

Neem (*Azadirachta indica*) plant parts show an antimicrobial role through an inhibitory effect on microbial growth/potentiality of cell wall breakdown. Azadirachtin, a complex tetranortriterpenoid limonoid present in seeds, is the key constituent responsible for both antifeedant and toxic effects in insects [6]. Results suggest that the ethanol extract of neem leaves showed *in vitro* antibacterial activity against both *Staphylococcus aureus* and MRSA with the greatest zones of inhibition noted at 100% concentration [7].

1. Neem plays the role of free radical scavenging properties due to its rich source of antioxidants. Azadirachtin and nimbolide showed concentration-dependent antiradical scavenging activity and reductive potential in the following order: nimbolide > azadirachtin > ascorbate [8].
2. Neem ingredient shows an effective role in the management of cancer through the regulation of cell signaling pathways. Neem modulates the activity of various tumor suppressor genes (e.g., p53, pTEN), angiogenesis (VEGF), transcription factors (e.g., NF-κB), and apoptosis (e.g., bcl2, bax).
3. Neem also plays the role of anti-inflammatory via regulation of proinflammatory enzyme activities including cyclooxygenase (COX), and lipoxygenase (LOX) enzyme.

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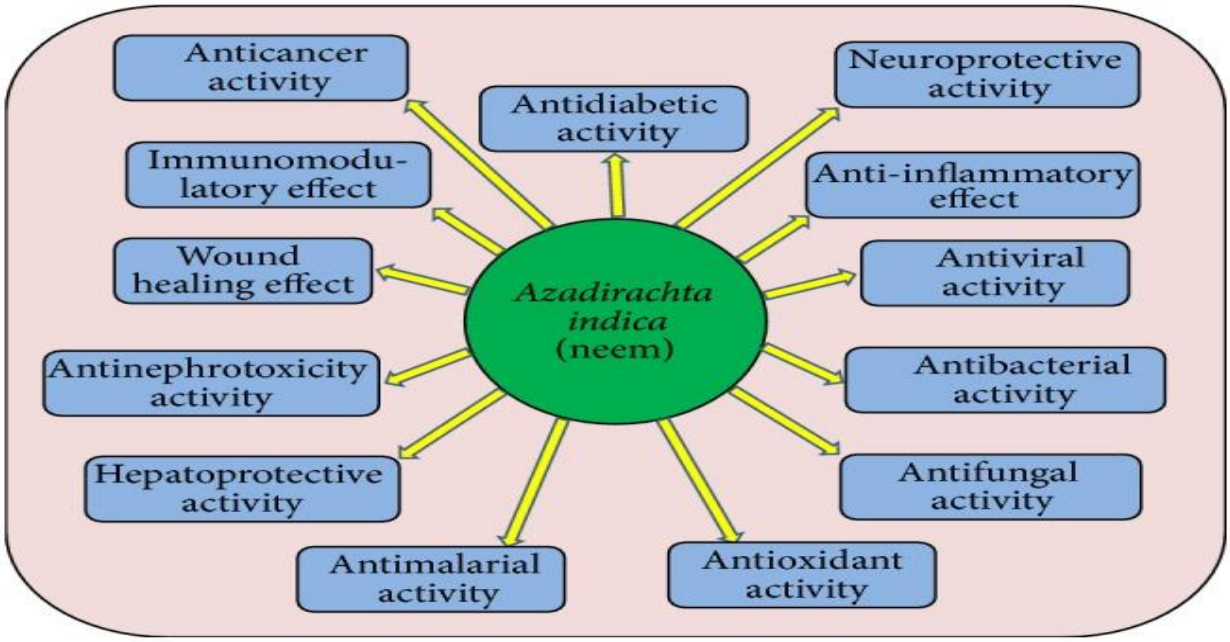

Antioxidant effect

Free radicals or reactive oxygen species (ROS) are a major source of inflammation, as they act upon many biological molecules, exerting damage by taking out electrons as a way of entering a stable state, unleashing in the cell a state of oxidative stress (Alzohairy, 2016, Kiranmai et al., 2011). Therefore, there is a need for providing adequate compounds (termed antioxidants) to stabilize or neutralize these radicals as a step in preventing or blocking an exacerbation of oxidative stress, which can lead to many diseases. These antioxidant molecules will supplement the work of the body's natural antioxidant defenses: superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), glutathione (GSH), nitric oxide dioxygenase (NOD) (Basir and Shailey, 2012, Gautam et al., 2015). To provide the body with such compounds, a simple way is to supplement them in the diet. One way is to supplement with natural extracts like those derived from Neem; in forms such as teas and oils, which seem to be a simple and cost-effective way to introduce antioxidants (Alzohairy, 2016, Farjana et al., 2014, Khamis Al-Jadidi and Hossain, 2015, Page and Hawes, 2013, Yerima et al., 2012), and although much debate and research continue on the efficacy and safety of extracts, we can still consider certain preparations, like those typically used in medicinal folklore as safe, although again these preparations are artisanal-crafted the potential benefits vary from preparation to preparation. With that in mind, we should not disregard that certain natural compounds can further alter certain pathological states. (9)

Antimicrobial and Anti Parasitic Effect of Neem Tree *Antibacterial effect* Neem possesses a wide spectrum of antibacterial action against Gram-negative and Gram-positive microorganisms. The antibacterial activity of neem extracts against 21 strains of foodborne pathogens was evaluated and the result of the study suggested that it possesses compounds containing antibacterial properties that can potentially be useful to control bacteria and spoilage organisms [10]. Another experiment was made to evaluate the antibacterial activity of the extracts of A.indica on bacteria isolated from adult mouths and results revealed that bark and leaf extracts showed antibacterial activity against all the test bacteria used[11].

Water extracts of neem twigs inhibit the growth of dental caries organisms Streptococcus mutans, S. salivarius, S. mitis, and S. sanguis [12]. Neem has suppressed several species of pathogenic bacteria, including Staphylococcus aureus, a common source of food poisoning and manypus-forming [13]. The susceptibility of the microorganisms to the extracts of neem leaves was compared with certain specific antibiotics. Its leaves possessed good anti-bacterial activity, confirming the great potential of bioactive compounds, and are useful for rationalizing the use of this plant in primary health care [14]. The methanol extract of A. indica exhibited pronounced activity against Bacillus subtilis [15].

Antifungal effects Nimbidin, Nimbin, Nimbidol, and Neem oil are very effective against fungi like Tinea rubrum ringworm fungus, Trichophyton interdigitale, Coccidioides immitis, and species of Trichophyton at very low concentrations. High antimycotic activity with extracts of different parts of neem has already been reported. Extracts of leaf, oil, and seed kernels are effective against certain human fungi; due to this property is given great importance in the field of science. A.indica leaf extract has antifungal activity against three fungal species: Aspergillus flavus, Alternaria solani, and Cladosporium. Neem oil has been the cure for many fungal diseases caused by the above fungi which have been a lifesaver [16].

A study done by [17] shows that the ethanolic extract of A.indica leaves is more effective against Rhizopus compared to aqueous leaf extract. Aqueous and ethanolic extracts of neem leaves were found effective against Candida albicans by which this organism shows sensitivity at the concentration of 15% and 7.5% on aqueous extract [18]. Neem oil is used to prevent aflatoxin which is produced due to contamination of the poultry feed by fungus and the neem leaves extract antagonizes the production of Patulin caused by Penicillium expansion [19].

Antiviral effect Neem leaves are found to be effective against Dengue virus type -2 in which it halts the replication of the virus itself in an in-vitro environment and the laboratory animals. The aqueous extract of its bark was found to be effective against Herpes simplex virus type 1 by blocking its entry into the natural target cell [20]. Even though it does not cure it shows the ability to prevent smallpox, chickenpox, and fowl pox[21]. In HIV/AIDS patients, a 12-week oral administration of acetone water neem leaf extract (IRAB) had a significant influence in vivo on CD4 cells (which HIV reduces) without any adverse effects in the patients [22]. It may be applied topically to appropriate parts of the body during an outbreak or just prior, when stress is high and we begin to get that ‘feeling’ that often occurs just before an outbreak. To speed relief, one may also take oral supplements, such as neem leaf capsules [20].

Conclusion

The popularity of natural products or their derivatives role in disease cure and prevention is increasing worldwide due to fewer side effects properties. Neem and its ingredients have therapeutic implications and have been traditionally used worldwide especially in Indian Subcontinent since ancient times. Clinical-based studies confirmed that neem plays a pivotal role in the prevention of various diseases. The role of active ingredients as a chemopreventive effect has been noticed in various tumors via modulation of numerous cell signaling pathways. A detailed study should be made based on an animal to know the exact mechanism of action in the management of the diseases.

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