IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

Medicinal Properties of Azadirachta Indica

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Abstract: *Neem oil (Azadirachta Indica A. Juss.) was tested for its antifungal properties against Drechsleraoryzae and Fusariumoxysporum and tenuis, and the results revealed that the active antifungal fraction is a combination of tetranortriterpenoids. [1Bandyopadhyay et al., Life Sciences, 71, 2845-2865, 2002] We have previously demonstrated that Neem (Azadirachtaindica) bark aqueous extract has effective antisecretory and antiulcer properties in animal models and has no significant side effect. Examining if neem bark extract had comparable antisecretory and antiulcer effects in human participants was the goal of the current study. [2] The antioxidant activity, total phenolic (TP), and total flavonoid (TF) contents of bark extracts from four different trees (Azadirachtaindica, Terminaliaarjuna, Acacia nilotica, and Eugenia jambolana Lam.) were assessed. The solvents used were 80% methanol, 80% ethanol, and 80% acetone (solvent:water, 80:20 v/v). By assessing reducing power, inhibiting peroxidation using the linoleic acid method, and DPPH scavenging activity, antioxidant activity (AA) was measured. Different bark extracts' TP, TF, suppression of linoleic acid oxidation, and DPPH• scavenging activity varied significantly (P 0.05). However, a slight difference in decreasing power was seen.[3].*

Keywords: Azadirachta Indica

I. INTRODUCTION

Reactive oxygen species (ROS) are a broad category of chemical substances that include the super oxide anion, hydrogen peroxide, hydroxyl radicals, nitric oxide, and peroxynitrite. According to Wang et al. (2002), these radicals have the ability to start degenerative processes in the human body. Effective defense systems protect us from the oxidative stress brought on by ROS; nevertheless, the capability of the defensive system is influenced by factors like age, food, and overall health (Chun, Kim, & Lee, 2003) Antioxidants must be included in the diet to aid in maintaining the right balance between ROS and defense system components (Yu et al., 2002). According to Vagi et al. (2005), antioxidants are crucial in avoiding the oxidative deterioration of food and indirectly removing radicals from it. To stop oxidative destruction, foods frequently contain synthetic antioxidants like tertiary butylhydroquinone, butylatedhydroxyanisole, butylatedhydroxytoluene, and propyl gallate. Due to safety and health effects, consumers have a negative perception of the use of synthetic antioxidants in foods (Iqbal et al., 2007, Jeong et al., 2004).It is sometimes referred to as the "village pharmacy" because the neem tree has been used for generations in Ayurvedic treatment. It was originally indigenous to the countries of India, Pakistan, Nepal, and Sri Lanka, but it finally made its way to the Philippines and flourished there.[4]

II. MATERIALS AND METHODS

2.1 Chemicals

Hexane, ethyl acetate, chloroform, butanol, and methanol were all purchased from BDH in the UK for use in this investigation. Sigma provided the DPPH (2,2-diphenyl-1-picrylhydrazyl). The additional substances were of analytical grade.

2.2 Plant sample

Samples of neem were gathered in Manah, Nizwa, and the Sultanate of Oman. On March 15, 2012, the plants were harvested, and they were taken at 5 o'clock in the afternoon. The samples were immediately placed in plastic bags after collection. Until extraction, the samples were maintained frozen at 4 °C. To get rid of dust, the samples were first cleaned with water and then with distilled water. For three days, the samples were dried at room temperature in the

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shade. A grinder (Japan, Supper Deluxe, and India) was used to grind 150 g of leaf sample material for 20 s. The dry leaf samples were finally ground into powder form.

2.3 Extraction procedure

Using a Soxhlet extractor, 127 g of powdered neem leaves were extracted for 72 hours with 500 cc of methanol. After extraction, it was filtered and a rotary evaporator (Yamato Rotary Evaporator, Model RE 801) was used to entirely evaporate the methanol solvent. 9.6 g of the solvent-free methanol crude extract were suspended in 100 ml of distilled water. Into a separatory funnel was transferred the suspension. Then, it was successively extracted with different organic solvents of increasing polarity, such as hexane, chloroform, ethyl acetate, and butanol, yielding, respectively, fractions of hexane (1.327 g), ethyl acetate (4.425 g), butanol (1.20 g), and residual methanol (2.09 g) [5]. To get crude extract devoid of particles, all of the crude extracts were filtered using filter paper (Whatman No. 41). The fat-free

2.4 Evaluation of antioxidant activity

Different neem crude extracts' antioxidant activity was assessed and described by Prieto [6] with modifications. In order to create the serial concentrations (12.5, 25, 50, 100, and 200 ppm, which translate to 12.5, 25, 50, and 100 g/ml, respectively), the crude extracts such as hexane, chloroform, ethyl acetate, methanol, and butanol were diluted with the appropriate solvents. Each concentration was given its own functioning test tube (4 ml). The test tube was then filled with DPPH (2,2-diphenyl-1-picrylhydrazyl) and forcefully shaken by hand after being added (1 ml, 0.1 mM, methanol). All of the test tubes were shaken, and then they were left to stand at 27 °C in the dark for 45 minutes. The same process was used to prepare the control sample, which included no extract. The evaluated samples' absorbance was

2.5 GC–MS analysis

Using a Perkin Elmer GC-MS (Model Perkin Elmer Clarus 500, USA) fitted with a fused silica capillary column (30 m 0.25 i.d., film thickness 0.25 m) paired with a Perkin Elmer Clarus 600C MS, the various crude extracts from the leaves of neem samples were examined. For the purpose of detecting chemicals, an electron ionization device with an ionization energy of 70 eV was employed. As a carrier gas, helium, an inert gas, was used at a constant flow rate of 1 ml/min. Temperatures for the mass transfer line and injector were set at 220 and 300 °C, respectively. The oven's temperature was set to increase from 50 to 150 °C at a rate of 3 °C per minute, hold for 10 minutes, and then increase to 300 °C at a rate of 10 °C per minute The raw materials were filtered after being diluted with the proper solvent (1/100, v/v). A syringe containing one milliliter of the particle-free, diluted crude extracts was used to inject it into an injector set to split mode. There was a 1:120 split. The crude extract constituents' composition was expressed as a percentage by peak area. Based on GC retention duration, the organic chemical components were located and described in various crude extracts. The mass spectra were computer matched with standards found in the database (Mainlab, Replib, and Tutorial data of GC-MS systems).[7]

2.6 Free radical scavenging activity

The antioxidant activity of Neem (leaf and bark) was assessed using a slightly modified version of the method reported by Bracca et al. (2003), based on the scavenging activity of the stable 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical. In a nutshell, 4 ml of 0.15 mM methanol solution (80% in water v/v) of DPPH was added to an aliquot of 1 ml of extract at a concentration of 0.1 mg/ml. After giving the mixture a thorough shake, it was allowed to stand for 30 minutes in the dark and at room temperature. A positive control was taken, which was 0.1 mg/ml of vitamin C. The % inhibitory activity was determined by measuring the solution's absorbance spectrophotometrically at 517 nm.[8]

2.7 Collection of plant materials Neem

Early June of 2008 saw the collection of (leaf and bark) from the Eastern province (MechiAnchal) of Nepal's foothills (subtropical zone). The old barks and young leaves (eight to twelve leaflets each) were gathered, cleaned, and washed under running water before being dried in the sun. The seeds were taken from the same location at the end of August 2008 and brought to Kangwon National University (South Korea) for examination.[8]

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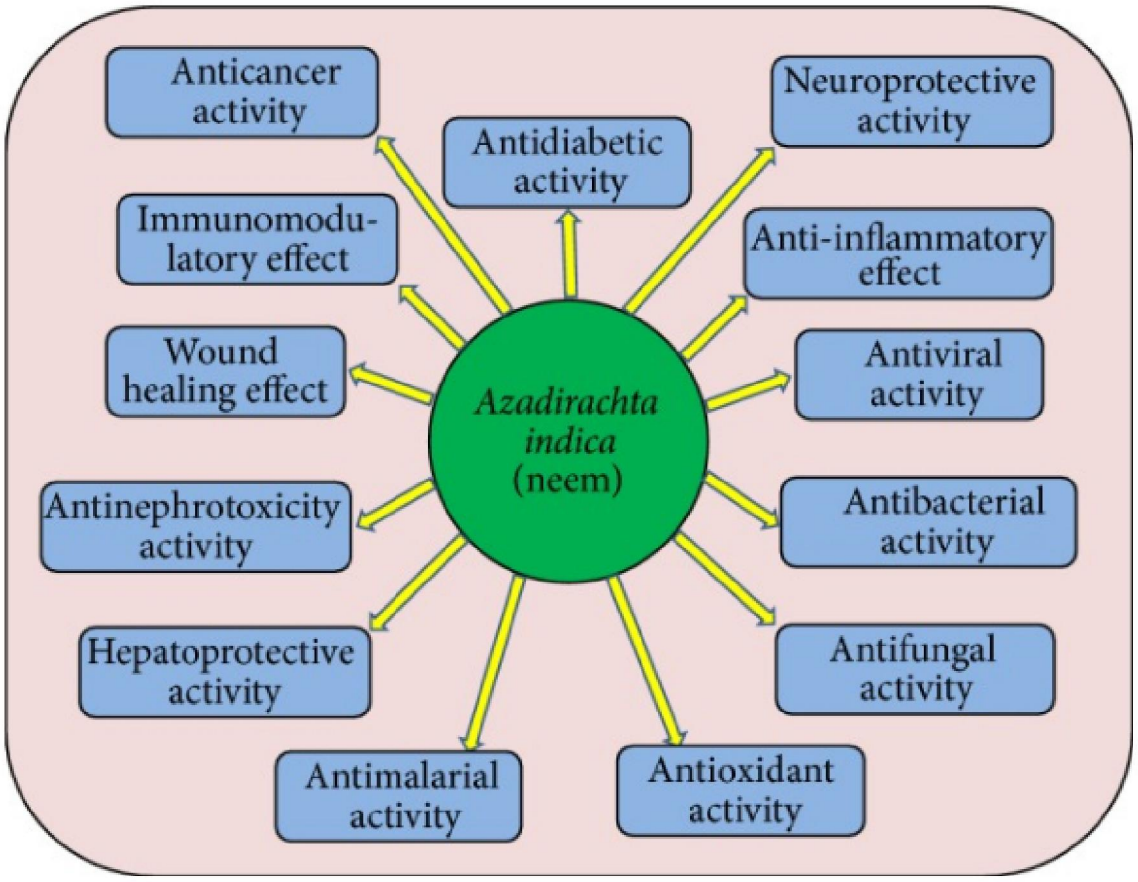
III.ACTIVITIES OF AZADIRACTA INDICA



3.1 Objective of the Literature Review

An evergreen tree with possible therapeutic uses is called Azadirachtaindica. It has been discovered to be effective against a wide range of terrible diseases, including cancer, viral infections, hepatitis, and malaria. Additionally, it works well against oral acidogenic bacteria that cause tooth plaque and cavities as well as periodontal infections. The objective of the current review is to concentrate on the dental features of distinct Neem extract components with their chemical make-up and biological functions. The miracle tree's various historical applications have also been briefly touched upon. This information might provide a bird's-eye view for the dentist, and as a result, this database might be crucial to future dental research.

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3.2 Therapeutic role of Azadirachtaindica in Dentistry

Nimbidin, a crucial substance isolated from the seed kernels of A. indica, has a variety of biological effects. Nimbidin also contains the biologically active substances nimbin, nimbinin, nimbidinin, nimbolide, and nimbidic acid.[9] Neem dental care products contain neem leaf or bark extract. The antioxidant component of neem leaf enhances the immune response in the tissues of the gum and mouth.[10,11] Neem is effective in treating tooth decay, mouth ulcers, and toothaches by acting as an analgesic.

IV. ANTIMICROBIAL EFFECT

Numerous microorganisms, including viruses, bacteria, and dangerous fungi, have their growth inhibited in part by neem and the components that make it up. The following is a description of each aspect of neem's function in preventing microbiological development.

4.1. Antibacterial Activity

When compared to sodium hypochlorite, the standard endodontic irrigant, a study was conducted to determine the antimicrobial efficacy of herbal substitutes [12]. The results confirmed that leaf extracts and grape seed extracts showed zones of inhibition, indicating that they had antimicrobial properties. Furthermore, compared to 3% sodium hypochlorite, leaf extracts displayed considerably larger zones of inhibition [12]. The antibacterial activity of guava and neem extracts was assessed against 21 strains of foodborne pathogens, and the study's findings indicated that these extracts may contain compounds with antibacterial properties that may be useful in controlling foodborne pathogens and spoilage organisms [13].Another test was conducted to determine the antibacterial effects of Azadirachtaindica (neem) bark, leaf, seed, and fruit extracts on bacteria isolated from adult mouths. The results showed that bark and leaf extracts had antibacterial effects on all of the test microorganisms employed [14]. Additionally, only at greater doses did fruit and seed extracts exhibit antibacterial action [14].

4.2. Antiviral Activity

At doses ranging from 50 to 100 g/mL, the results demonstrated that neem bark (NBE) extract strongly inhibited HSV-1 entrance into cells [14]. Additionally, when the extract was pre-incubated with the virus but not with the target cells, inhibiting action of NBE was seen, pointing to a direct anti-HSV-1 capability of the neem bark [15]. According to

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results from a virus inactivation and yield reduction assay, neem (Azadirachtaindica A. Juss.) leaf extract (NCL-11) exhibited virucidal action against coxsackievirus virus B-4 in addition to interfering with an early stage of its replication cycle [16].

4.3. Antifungal Activity

An experiment was conducted to test the effectiveness of different neem leaf extracts on the seed-borne fungus Aspergillus and Rhizopus. The results showed that both alcoholic and water extract strongly suppressed and controlled both fungal species' growth. Additionally, neem leaf alcoholic extract was superior to neem leaf aqueous extract in terms of slowing the growth of both fungal species [17]. Another finding showed the antimicrobial role of aqueous extracts of neem cake in the inhibition of spore germination against three sporulating fungi such as C. lunata, H. pennisetti, and C. gloeosporioides f. sp. mangiferae [18] and results of the study revealed that methanol and ethanol extract of Azadirachtaindica showed growth inhibition against Aspergillusflavus, Alternariasolani, and Cladosporium [19]. Previous researchers have noted that aqueous extracts of different neem sections, including neem oil and its main constituents, exhibit antifungal properties [20–21]. An investigation into the antifungal activity of Azadirachtaindica L. against AlternariasolaniSorauer was conducted, and the results showed that the fraction of ethyl acetate, which has a MIC of 0.19 mg, was most effective in slowing fungal growth [22]. This fraction was also more effective than the fungicide (metalaxyl + mancozeb), which has a MIC of 0.78 mg.

4.4. Antimalarial Activity

Neem leaf and stem bark extracts significantly decreased the level of parasitemia in infected mice by about 51–80% and 56–87%, respectively, according to an experiment done using Plasmodium berghei-infected albino mice [23]. Additionally, other studies revealed that azadirachtin and other limonoids present in neem extracts are active on malaria vectors [24–25]. In a separate 72-hour culture of mature gametocytes and asexual parasites treated with IRAB (0.5 microg/mL), parasite numbers were less than 50% of the numbers in control cultures, which had 8.0% and 8.5% parasitemia, respectively. This finding was based on crude acetone/water (50/50) extract of leaves (IRAB), which was used to evaluate the activity against the asexual and sexual forms of the malaria parasite, Plasmodium falciparum

V. ROLE OF NEEM IN DENTISTRY

A. indica mouthwash is just as good at lowering periodontal indices as chlorhexidine, according to a study conducted to evaluate the effectiveness of neem-based mouthwash's antigingivitis impact [27] In another study, three bacterial strains that cause dental caries were tested for their ability to inhibit the growth of organic neem extracts. The results showed that petroleum ether and chloroform extract had the strongest antibacterial action against S. mutans. Streptococcus salivarius was strongly inhibited by chloroform extract, while the third strain, Fusobacteriumnucleatum, was extremely sensitive to both ethanol and water extract [28]. Previous research verified that dried neem chewing sticks had the strongest antibacterial effect on S. mutans when compared to S. salivarius, S. mitis, and S. sanguis [29].

VI. ANTINEPHROTOXICITY EFFECT

A study was conducted to determine the effects of Azadirachtaindicamethanolic leaf extract (MLEN) on cisplatin (CP)-induced nephrotoxicity and oxidative stress in rats. The results showed that the extract is beneficial in protecting the kidney from CP-mediated oxidative damage [30]. Additionally, downregulation of the caspase-3, caspase-9, and Bax genes was observed in the MLEN treated groups according to PCR data [31].

VII. NEUROPROTECTIVE EFFECTS

An investigation into the neuroprotective properties of Azadirachtaindica leaves against cisplatin- (CP-) induced neurotoxicity was conducted, and the findings suggested that well-preserved brain tissue from morphological observations of neem before and after CP injection. Biochemical parameters did not alter in the neem-treated groups [32].

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VIII. IMMUNOMODULATORY AND GROWTH PROMOTING EFFECT

Neem infusion successfully increased antibody titre, growth performance, and gross return at the level of 50 mL/liter of fresh drinking water in an experiment to evaluate the growth-promoting and immunomodulatory effects on broiler chicks [33]. Another study examined how feeding broilers powdered dry leaves of A. indica (AI) affected humoral and cell-mediated immune responses. The findings revealed that AI (2 g/kg) administration significantly increased antibody titres against the antigen of the new castle disease virus (NCDV) [34].

IX. SAFETY, TOXICITIES, AND LD50 VALUES OF NEEM

Prior to their use in the treatment of health, it is essential to test the toxicities of natural compounds. Neem is safe at specific doses, according to numerous research based on animal models and clinical trials, although neem and its constituents also revealed hazardous or detrimental effects.

Neem oil poisoning has been linked to several studies in children, including vomiting, hepatic toxicity, metabolic acidosis, and encephalopathy [35–36]. Another rat study found that administration of leaf sap had an antianxiety effect at low doses but not at higher doses [37]. Azadirachtin did not exhibit toxicity even at 5 g/kg body weight, according to a significant study using rats as a model [38]. To test the validity of the toxicological analysis, a rabbit study was conducted. According to the study's findings, both the test and control animals' body weights increased gradually, and neither group showed any signs of toxicity for the entire time the neem extract was administered [39].

According to a study finding, neem oil has an acute toxicity test LD50 value of 31.95 g/kg [40]. Another investigation was conducted to determine the toxicity in chickens, and the results indicated that the acute toxicity of neem leaf aqueous extract exhibited an intraperitoneal LD50 of 4800 mg/kg, and clinical symptoms were dose-dependent [41].

Neem leaf and stem bark extracts were shown to have lethal median doses (LD50) of 31.62 and 489.90 mg/kg body weight, respectively, according to a study [42]. A. indica leaves and seeds had LD50s of 6.2 and 9.4 mL kg1, respectively [43]. Using probit analysis, the LD50 and LD90 values of neem extract were determined to be 8.4 and 169.8 g/fly, respectively [44]. The LD50 value of approximately 13 g/kg body weight was discovered in a mouse test for acute oral poisoning [45]

X. CONCLUSION

It is clear from the review that the structural variety of polysaccharides is significantly influenced by their botanical or biological sources. Numerous polysaccharides have demonstrated great potential as anti-cancer drugs due to their distinctive structure diversities and physiochemical properties, which can be successfully used in a variety of medical applications. Three methods have been revealed to be the main mediators of polysaccharides' anti-cancer effects: direct cytotoxicity, and two

XI. ACKNOWLEDGEMENT

The laboratory space for this research was provided by Prof. M. Michael Aruldhas, Head of the Department of Endocrinology at the University of Madras, and is gratefully acknowledged by the authors.

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IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 1, January 2024

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