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NERIUM INDICUM: A COMPREHENSIVE REVIEW OF ITS MEDICINAL PROPERTIES AND PHARMACOLOGICAL ACTIVITIES

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ABSTRACT

Nerium Indicum, also referred to as Indian oleander, is a revered medicinal herb with a wide range of therapeutic uses. It is a member of the Apocynaceae family and has been used extensively in Ayurveda, Siddha, and traditional medicine to treat conditions like cancer, microbial infections, inflammation, cardiovascular disease, and skin conditions. Its pharmacological potential is enhanced by the presence of cardiac glycosides, flavonoids, alkaloids, terpenoids, and saponins, according to phytochemical analyses. Numerous actions, such as cardiotonic, anti-inflammatory, antioxidant, antibacterial, analgesic, anticancer, hepatoprotective, and wound-healing properties, have been shown in contemporary pharmacological research. The plant's strong cardiotonic glycosides make it extremely dangerous despite its promising bioactivities, therefore it must be used carefully and at a consistent dosage.

KEYWORS: *Nerium indicum*, Medicinal Properties, Pharmacological Activities, Hebral Plant.

INTRODUCTION

N.indicum, a plant in the Apocynaceae family native to India, Bangladesh, Nepal, Myanmar, and China, has been shown to inhibit viral infections and is utilized in treatments for cancer, asthma, and epilepsy. They further demonstrate antioxidant, antiproliferative, antiviral, and anti inflammatory effects, indicating that the isolated components of N. Indicum may be a promising therapeutic agen.[4,5,6] Nerium indicum (Apocynaceae), a medicinal herb, has been researched for antifungal properties. N.indicum has been shown to exhibit pharmacological properties.[7] Similarly, the plant is known to contain a variety of phytochemical elements, such as alkaloids, phenols, flavonoids, and others, which contribute to its effectiveness as an antibacterial agent.[8] The flowers and leaves have sedative, diuretic,

diaphoretic, expectorant, emetic, and sternutatory properties. External use of a leaf decoction has been used to treat parasitic skin worms, scabies, and swellings. The root has a strong ability to resolve issues.

It is only used externally due to its toxic nature. Leprosy and skin conditions are treated using oil extracted from the root. It is said that the entire plant has anticancer qualities.[19,20] The plant is also used as an insecticide, parasiticide, and rat poison. The bark and crushed leaves have insecticidal properties. Though it is too little for commercial use, the leaves do contain trace amounts of latex that can be utilized to produce rubber.[21] Parts of oleander is extensively used for the treatment of cardiac illnesses, diabetes, asthma, corns, cancer, and epilepsy.[25]

BOTANICAL DESCRIPTION

Nerium indicum is a huge, evergreen shrub with milky latex that can grow up to 3 meters tall. The leaves are linear-lanceolate and densely coriaceous. The flowers are crimson or white, sweet-scented, and grow in terminal polychasial cymes. Fruit paired follicles, cylindric and ribbed.Seeds topped with a coma of light brown hairs.

This flower is widely grown in India for ornamental purposes and is often seen near temples or gardens.[10] N. indicum root samples are characterized by their size, shape, exterior and inner surfaces, fracture type, and organoleptic properties such as color, odor, taste, and consistency.

OVERVIEW OF BOTANY

Scientific name: Nerium indicum Mill.

Family: Apocynaceae

Common names: Raktakarabi (in Sanskrit), Kaner, Arali, and Indian Oleander.

Habitat: Common in India; subtropical to tropical.

1. THE PLANT

Nerium indicum is a tiny tree or bushy shrub that can reach a height of 2 to 6 meters. Because of its hardiness and lovely blossoms, it is frequently seen in gardens and at the sides of roads. However, it must be handled with caution because every part of it is dangerous.

2. LEAVES

Leaves are long, thin, and leathery, the leaves grow in whorls of three or in pairs. They are lighter beneath and dark green above. A leaf's white, milky sap, or latex, is released when it breaks and is extremely poisonous.

The leaves contain unique channels and crystals (calcium oxalate) inside that can irritate skin and are toxic if consumed.

3. FLOWERS

Flowers At the tips of branches, the flowers develop in clusters. Usually pink, but also available in white, crimson, or yellow variations, they are stunning and ostentatious. Each flower smells somewhat pleasant and has five wide petals. They draw butterflies and bees, but once more, they are unsafe to eat. Some of the flavonoids and glycosides found in flowers have antioxidant properties, but if not properly processed, they might be harmful when consumed internally.

4. STEM AND BRANCHES

As they get older, the smooth, green stems turn woody and brown. White sap, like in the leaves, flows out if the stem is severed. Strong cardiac glycosides found in that sap can have fatal effects on the heart if consumed. Traditional medicine occasionally applies stem bark externally, but always with caution.

5. FRUIT

The fruit, which typically comes in pairs, resembles a long, narrow pod. It yields seeds with silky hairs that enable them float in the wind after drying and splitting. In addition to being poisonous, the seeds are flattened and brown. Because of the risks, they are rarely employed in medicine, despite the fact that they contain some oil and chemicals.

6. SEEDS

The size and germination behavior of Nerium indicum seeds vary greatly depending on the location, climate, and growing environment. The seeds of wild plants germinate less successfully than those of cultivated species, which typically have smaller seeds. Higher altitude or humid regions do not produce as good of a germination rate as drier places. Because of their silky hairs, they are scattered by the wind, and because the plant is hazardous, they must be handled carefully. Allelopathic effects are another way that Nerium affects the growth of neighboring plant species.

Part	Key Features	Active Compounds	Use	Toxicity
Leaves	Long, leathery	Oleandrin, Neriin	Medicinal, Pesticidal	High
Flowers	Showy, pink/red/white	Flavonoids, Glycosides	Decorative, Antioxidant	Moderate
Stem	Woody, smooth	Resin, Alkaloids	Medicinal (paste)	High
Roots	Fibrous, woody	Cardiac glycosides	External applications	Very High
Seeds	Hairy, light	Oils, Glycosides	Rarely used	Moderate
Latex	Milky, sticky	Cardiac glycosides	External use	Very High

CHEMICAL CONSTITUENTS

Nerium indicum bark includes cardio-active glycosides such as neriodorin, neriodorein, and karabin, as well as scopoletin and scopolin. The root bark's alcoholic extract contains α-amyrin and β-sitosterol, while the ether and chloroform fractions include kaempferol and odoroside.[11] According to additional data, the leaf has the largest concentration of thiamine, riboflavin, saponin, and tannins, while the root has the highest concentration of alkaloids and ascorbic acid. According to an in vitro study that examined the antioxidant and free-radical scavenging properties of oleander, the leaf has the highest flavonoid content (93.06 ± 0.03 mg/mL quercetin equivalent per 100 mg plant extract) and the highest total phenolic content (87.38 ± 0.16 mg/mL gallic acid equivalent per 100 mg plant extract.[26] Phytol, oleic acid, cis-vaccenic acid, vitamin E, dl-α-tocopherol, squa-lene, and 29 other phytochemicals were detected by GC analysis of an n-hexane fraction; several of these were also detected in the dichloromethane fraction.[28] Others have discovered quercetin, epicatechin, catechin, rutin, cinnamic acid, and chlorogenic acid in oleander leaf extract with strong antioxidant qualities using HPLC. Epicatechin and catechin have also been found in oleander leaves by others.[29]

TOXICITY

Acute toxicity studies were conducted on petroleum ether, chloroform, and water extracts of Nerium indicum leaves at doses of 5000 mg/kg body weight, as well as an alcoholic extract at 3000 mg/kg body weight. There were no significant toxicity indications identified within the first four hours, followed by daily observations for 14 days. The medicine was safe and did not cause any deaths.

The presence of several cardiac glycosides has been identified as the primary mechanism of action of oleander poisoning. Different cardiotonic steroids have different mechanisms of toxicity, but the most prevalent one is suppression of cardiac Na+/K+-ATPase.[24]

ANTIOXIDANT ACTIVITY

In traditional Chinese medicine, the flowers and leaves of Nerium indicum (Arali) have been used to stimulate cardiac muscles, relieve pain and eliminate blood stasis[1].Immunological active pectic polysaccharides have been isolated from Nerium indicum.[2] The antioxidant activity of flower and Leaves has been determined with a variety of methods. Many researches have indicated that Arali (Nerium indicum) possessed high antioxidant activity. The present investigation evaluated the levels of antioxidant compounds such as DPPH radical Scavenging activity, Total Phenolics, Total Flavonoid content, Superoxide radical Scavenging activity, Lipid Peroxidation activity and Enzymatic antioxidant factor such as Superoxide Dismutase, Glutathione Peroxidase and Catalase.

DPPH Radical Scavenging Activity: The antioxidant activity of methanol extract of Nerium indicum flowers and Leaves was measured using the DPPH radical Scavenging assay[3] **Superoxide radical Scavenging activity** shows higher in Crude Nerium indicum flower extract (66%), as compared to leaves 25%(9)

ANTI DIABETIC ACTIVITY

To assess antidiabetic efficacy, we used a glucose tolerance test and an alloxan-induced model. Diabetic control animals experienced significant hyperglycemia, as expected. The usual medicine glibenclamide significantly reduced blood glucose levels, putting them close to normal levels. At the 7th day of the trial, a single dosage of ethanolic extract (300 mg/kg b.w.) of Nerium indicum significantly ($P<0.01$) decreased blood glucose levels compared to the diabetic control group. Table 1 shows that chloroform extract (500 mg/kg b.w) significantly reduced blood glucose levels after one hour, while ethanolic extract exhibited significant reductions after three hours.[12] It has been reported that a hydromethanolic extract of oleander leaves with strong anti-diabetic properties has high levels of rutin, p-coumaric acid, jasmonic acid, gallic acid, vanillic acid, and 4-hydroxybenzoic acid.[27]

LARVICIDAL POTENTIAL

The extracts of various parts of N. indicum has been found toxic to ringer fly, Drosophila hydei and rice weevil, Sitophilus oryzae .The aqueous leaf extract of the plant also showed toxicity against Callosobruchus chinensis and C. maculatus.[13]

ANTI BACTERIAL ACTIVITY

The agar disc diffusion method was used to test various doses of N. indicum leaf extract. All of the N. indicum leaf extracts prepared were found to be efficient against Gram-negative bacteria and had a broad spectrum of activity.[14]

ANTI INFLAMMATORY ACTIVITY

The extract from N. indicum leaves showed strong immunomodulatory action, which could be advantageous with more research. Anti-inflammatory activity is mostly determined by the suppression of NO, TNF-a, and COX activity as well as a rise in IL-10 levels.[15]

ANTI ULCER ACTIVITY

The ulcer index and percentage of ulcer protection were significantly reduced by the Nerium indicum leaf extract. The ulcer index (4.833) and percentage of ulcer protection (69.63%) were both decreased more effectively by the high dose of Nerium indicum leaf extract (500 mg/kg) than by the lower dose (250 mg/kg) of Nerium indicum leaf extract (5.416) and (65.97%). Additionally, ranitidine effectively lowers the proportion of ulcer protection and the ulcer index. Nerium indicum leaf extract's effects on stomach volume, free acidity, total acidity, and ulcer in rats with pyloric ligation were investigated. The extract from N. indicum leaves decreased the control rats' gastric juice volume by 4.1 and 3.6 milliliters, respectively. There was a 60.6 and 43.81% decrease in free acidity, respectively. The highest ulcer prevention of 67.35% was demonstrated by the dosage of 500 mg/kg.[16]

ANTI HELMINTIC ACTIVITY

It was discovered that the ethanolic extract was more active than the other extracts. Compared to other extracts, the ethanolic extract showed that the worms were paralyzed and died more quickly. The crude extracts of Nerium indicum, Mill (Roots) exhibited the presence of phytoconstituents such protein, flavonoids, carbohydrates, tannins, and steroids, according to preliminary phytochemical screening. Nerium indicum, Mill. roots demonstrated strong anthelmintic action at concentrations of 10 mg/ml, 30 mg/ml, 50 mg/ml, and 100 mg/ml when compared to the common medication albendazole.[17]

Plant phenols such as flavonoids and tannins have been shown in numerous scientific investigations to have antibacterial, anti-inflammatory, anti-allergic, and free radical scavenging properties. These substances may be in charge of the successful treatment of skin conditions because they were discovered to be present in the oil extract of Nerium indicum leaves. The traditional medical system uses the oil extract of Nerium indicum leaves to treat skin conditions since it also contains heart active glycosides. Therefore, cardiac glycosides found in Nerium indicum leaf oil extract may also be in charge of skin disease recovery.

Numerous researches have discovered that Nerium indicum leaf alkaloidal extracts have anti-inflammatory, antibacterial, and pesticidal properties. According to current research, alkaloids found in oil extract of Nerium indicum leaves may also be in charge of curing skin conditions by reducing inflammation and bacteria.[18]

NEMATICID ACTIVIVTY

The extract from Nerium indicum Mill. exhibited the highest nematocidal activity against J2 of Meloidogyne incognita, with a death rate of 98.60% after 24 hours.[22]

In China and Southeast Asia, the white or pink flowered oleander Neriumindicum, often called Kaner, is frequently cultivated. It is a member of the Apocynaceae family. Neriumindicum's flowers and leaves were used in traditional Chinese medicine to reduce pain and stimulate the heart muscle. Numerous alkaloids, cardiac glycosides, and sugars have been discovered in their poisonous leaves, which also show encouraging inhibitory effects against COVID-19.[23]

Fig: *Nerium Indicum* Plant.

Summarizes an overview of the ethnopharmacological application of oleander against a range of ailments and verifiable pharmacological characteristics in in vivo preclinical models

Ethnomedicinal use

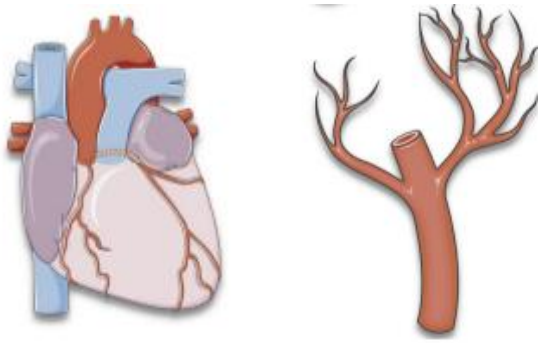
- Skin disease and inflammatory infections
- Leprosy
- Fever and allergic dermatitis
- Spondylolysis
- Cardiac abnormalities
- Wound healing
- Respiratory tract and intenstinal infections
- Ear pain
- Swelling and common cold
- Anti-diabetic
- Hypertension

Pharmacological Actions

- Anti-diabetic
- Hypolipidemic
- Anti-obesity
- Cardiotonic
- Anti-cancer
- Diabetic-cardiomyopathy
- Hapatoprotective
- Anti-inflammatory
- Immunostimulatory
- Anti-oxidant

The three varities of Nerium Indicum flowers

Effects of Oleander poisoning



- Inter fasicular edema Increase of mean corpuscular hemoglobin
- Congested vessels Iron and hepcidin increase; lower ferritin
- Focal vacuolar degeneration of cardiac muscle IL-1,IL-6,TNFalpha,CRP,LDH increase
- Myocyte granular degeneration, coagulative necrosis Creatine kinase myocardial band elevation
- Cardiac muscle fragmentation, loss of strations Mean platelet volume decrease
- Intra- sarcoplasmic vacuole generation Decreased white blood cells, including lymp
- Sinus arrhythmia and tachycardia -cytes

- Inflammatory edema
- Dilation and alveolar collapse
- Hemorrhage
- Bronchus mucosal folds disruption
- Interstitial pneumonia
- Loss of pulmonary alveolus
- Matrix thickening

HEPATOPROTECTIVE EFFECTS

Several pre-clinical investigations have used a variety of in vivo experimental models to show that oleander has hepatoprotective properties. For example, by lowering blood transaminases and restoring histological evidence of tissue damage, an oleander aqueous extract showed hepatoprotection against thioacetamide-induced liver injury.[30] By enhancing the liver's antioxidant defense, oleander pink flower extract shielded rats from the hepatotoxicity caused by carbon tetrachloride (CCL4).[31]

CONCLUSION

Nerium indicum, sometimes referred to as Nerium oleander, has a variety of therapeutic qualities, including as anti-inflammatory, anti-microbial, anti-cancer, cardiotonic, and wound-healing effects. Its pharmacological potential is supported by a variety of phytochemicals, including flavonoids, glycosides, saponins, alkaloids, and triterpenoids. The plant's inherent toxicity, mainly from cardiac glycosides like oleandrin, is well-known despite its medicinal uses in traditional medicine. As a result, even though Nerium indicum has potential for drug development and therapeutic formulations, thorough toxicological analyses and clinical research are necessary to guarantee its safe use. Standardizing extracts, separating bioactive substances, and creating tailored medication delivery methods that optimize effectiveness while reducing toxicity should be the main goals of future research.

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