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A Review on Chemistry and Pharmacological activity of *Nerium oleander* L.

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ABSTRACT

Nerium oleander L. is an important Chinese folk medicine. It is a vegetatively propagated ornamental plant, valued for its evergreen foliage and showy terminal flower clusters that are available in different colors. Oleander is cultivated recently as a flowering pot plant and therefore abundant propagation of plant material for commercial use is of great importance. This species also produces secondary metabolites, some of which are pharmacological interests. The important pharmacological activities are anti-inflammatory, antibacterial, anticancer, antinociceptive, and CNS depressant activity. This paper explains the evidence-based information regarding the phytochemistry and pharmacological activity of this plant.

Key words: *Nerium oleander*, Phytochemistry, Pharmacological activity, antinociceptive and secondary metabolites.

INTRODUCTION

In recent years, traditional system of medicine has become a topic of global importance. Many of the plant species that provide medicinal herbs have been scientifically evaluated for their possible medicinal applications. It has been mentioned that natural habitats for medicinal plants are disappearing at a faster rate and together with environmental and geopolitical instabilities; it is increasingly difficult to acquire plant derived compounds.

Nerium oleander L. is an evergreen shrub reaching up to four meters in height (Fig. A) . and belongs to the family – Apocynaceae, is a shrub or occasionally tree distributed in tropical Asia *Nerium oleander* L. is cultivated worldwide as an ornamental plant. It is native to the Mediterranean region [1, 2] and is also found in Southern Europe and Southwest Asia, but is naturalize very easily and in many areas the plant is sub-spontaneous.



Fig.A: The plant *Nerium oleander* L.

Fig.B: Inflorescence of *Nerium*

Fig.C: Immature pods-Seeds

Leaves are 10 to 22 cm. long, narrow, acute in the apex, shortly petiolate, with a coriaceous dark-green blade narrow, untoothed, short-stalked and dark or grey- green in color. Some cultivars have leaves variegated with white or yellow patches. All leaves have a prominent mid rib, are "leathery" in texture and usually arise in groups of three from the stem. The plant produces terminal flower heads, usually pink or white. Each flower is about 5 cm in diameter and five-petalled although some cultivators have double flowers. Oleander has flexible branches with green, smooth bark eventually turning to dark grey on maturity. Cut or broken branches exude a

thick, white sap. The fruit consists of a narrow follicle 7.5 to 17.5 cm long which opens to disperse fluffy seeds. Oleander can be propagated by seeds but, being allogamous and highly heterozygous, it shows great variability in seedling population. (Fig. B.)

Phytochemistry is the subject deals with chemicals derived from plants. There are large numbers of secondary metabolic compounds found in plants. Phytochemical technique mainly applies to the quality control of herbal medicine of various chemical components, such as saponins, alkaloids, flavanoids and anthraquinones. The entire plant, including the milky white sap, is toxic and any part of the plant can cause an adverse reaction, when applied to the living organisms.

Oleander is one of the most poisonous plants in the world and contains numerous toxic compounds, many of which can be deadly to people, especially young children. The toxicity of *Oleander* is considered extremely high and it has been reported that in some cases only a small amount had lethal or near lethal effects. The most significant of these toxins are oleandrin and nerine, which are cardiac glycosides [3]. They are present in all parts of the plant, but are most concentrated in the sap, which can block out receptors in the skin causing numbness. It is thought that *Oleander* may contain many other unknown compounds that may have dangerous effects. *Oleander* bark contains rosagenin which is known for its strychnine-like effects. The *Oleander* is also known to hold its toxicity even after drying. At the same time it is believed that a 10-20 leaves consumed by an adult can cause an adverse reaction, and a single leaf could be lethal to an infant or a child.

Economic importance:

The plant is used as a rat poison and an insecticide [5]. The pounded leaves and bark are used as an insecticide. A green dye is obtained from the flowers. The plant is commonly used for informal hedging in the Mediterranean. The leaves contain small amounts of latex that can be used to make rubber, though the amount is too small for commercial utilization. The plants have an extensive root system and are often used to stabilize soil in warmer areas.

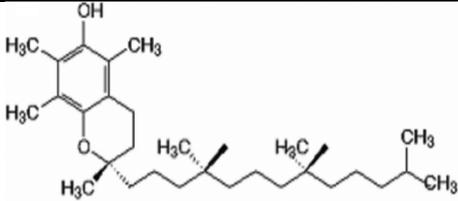
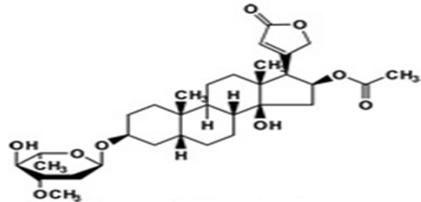
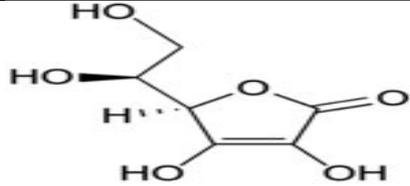
Medicinal Importance:

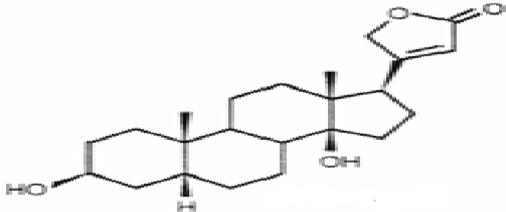
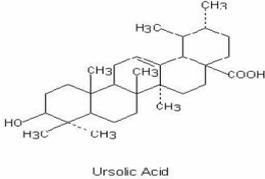
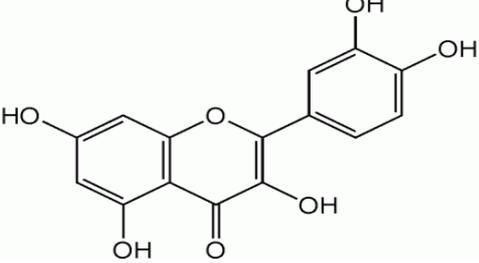
The leaves and the flowers are cardiogenic, diaphoretic, diuretic, anticancer, antibacterial [6], anti fungal [7] and expectorant. A decoction of the leaves has been applied externally in the treatment of scabies and to reduce swellings. This is a very poisonous plant, containing a powerful cardiac toxin and should only be used with extreme caution. The root is powerfully resolvent, is used in the form of plasters and is applied to tumors because of its poisonous nature it is only used externally. It is beaten into a paste with water and applied to lesion and ulcers on the penis. [8]. Bark is bitter and is used as cathartic, febrifuge and intermittent fever. Plants have an extensive root system and are often used to stabilize soil in warmer areas. Oil prepared from the root bark is used in the treatment of leprosy and skin diseases of a scaly nature. Seeds are Poisonous, abortifacient and alternative. They used as purgative in dropsy and rheumatism. The whole plant is said to have anticancer properties [9].

Nerium oleander has also been used in the treatment of cancer [10] the flowers, leaves, leaf juice or latex, bark and roots have been used against corns, warts, cancerous ulcers, carcinoma, ulcerating or hard tumors.

Chemical constituents:

The most well known effects of oleander are due to two glycosides, neriin and, and an alkaloid, oleandrin which have a cardiostimulatory action [11], and to the glycosides gentiobiosyl-oleandrin, gentiobiosyl-nerigoside and gentiobiosyl-beaumontoside extracted from the leaves [12]. Oleander is also diuretic and lentic on dermatosis and contusion [13]. In addition, its lymph is rich of minerals [14] and α -tocopherol, an important antioxidant [15]. Adyrogenin is a compound with no cardiac effect. There are also weakly active cardenolides (heterosides of uzarigenine) and inactive cardenolides (heteroside of adynergenine, of digitalose), triterpenoids, a resin, tannins, glucose, a paraffin, ursolic acid, vitamin C and an essential oil. The seeds contain glucosides (oleandrine, odorosides, adigoside). The bark also contains glucosides (rosaginoside, nerioside, corteneroside). The roots contain steroids.

Chemical Name	Chemical Structure
α -tocopherol	 <p>The word tocopherol comes from the Greek words tocos (childbirth) and pherein (to bring forth), after the essential role vitamin E plays in animal reproduction. The ending -ol is the standard chemical name ending for an alcohol. Tocopherol is used in many pharmaceutical products as a stabilizer. Some plastics, technical oils and greases contain alpha-Tocopherol as an antioxidant.</p>
Oleandrin	 <p>Oleandrin is a toxic cardiac glycoside. Ingestion of Oleander can cause both gastrointestinal and cardiac effects. The gastrointestinal effects can consist of nausea and vomiting, excess salivation, abdominal pain, diarrhea that may or may not contain blood, and especially in horses, colic.</p>
Vitamin C	 <p>Vitamin C is an essential, water-soluble vitamin. It cannot be synthesized by our bodies and must be ingested regularly. It is known as a coenzyme and as an antioxidant. It can prevent the oxidation of other compounds by being oxidized instead.</p>

Digitoxingenin	 <p>They are widely distributed in plants mainly as glycosides and are either toxic or insect deterrents. As potent cardiotonics, through their inhibition of Na/K-ATPases, these steroids were largely studied (digoxin and its derivative ouabain...). Monarch butterfly is well known to be highly toxic to birds because of cardenolides which come from the milkweed leaves eaten by its caterpillar.</p>
Ursolic acid	 <p>Ursolic acid has medicinally action, both topically and internally. Ursolic acid is used in many cosmetic preparations for its anti-inflammatory, antitumor and antimicrobial properties. Ursolic acid has antibacterial and antifungal activity.</p>
Quercetin	 <p>Quercetin has been the subject of numerous studies and appears to have many beneficial effects on human health, including cardiovascular protection, anti-cancer activity, anti-ulcer effects, anti-allergy activity, cataract prevention, antiviral activity and anti-inflammatory effects.</p>

Pharmacological action and toxicity

Oleandrine is anti inflammatory, anti tumoral and emollient and potentialises apoptosis. The hydro alcoholic and aqueous extract of the flowers is antinociceptive and cardiotoxic. The leaves and seeds provoke poisoning with nausea, vomiting, mental confusion, bradycardia and ventricular hyperkalaemia that can quickly end in death.

Antinociceptive activity: The aqueous and ethanol extracts of oleander leaves possess significant antinociceptive activity, but ethanolic extract was more pronounced. However both extract were shown to induce gastric, ulcerogenicity with mice. Flowers either dried or fresh also exhibit potent antinociceptive activity [16].

Anti-inflammatory activity: Anti-inflammatory activity assessment experiment has also verified that liposoluble components of flowers may have the activity, since only the ethanol extract were found active even then that of reference drug indomethacin [17]

Antimicrobial activity: The presence of antifungal and antibacterial substance in the higher plant is well established. Plant has provided a source of inspiration for novel drug compounds, as plants derived medicines have made significant contributions towards human wealth. At the same time Hussain and Gorski (2004) [18] reported the antimicrobial activity of leaves and roots of *Nerium oleander* against *Bacillus pumilus*, *B.subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Aspergillus niger*

Locomotor activity: Zia (1995) [18] reported that purified fractions obtained from the methanol extract of fresh oleander leaves possess a CNS depressant activity i.e., produced reduction in locomotor activity. They also showed significant analgesic activity as indicated by inhibitory effects on acetic acid- induced and increased reaction time to thermal test.

Anticancer activity: The aqueous extract of *Nerium oleander* L. has been undergoing clinical investigations as an anticancerous agent. Oleandrin and its aglycone oleandrogenin are the active compounds that are isolated from this plant which shown to have anticancerous properties. Anvirzel has also revealed cytotoxicity in human tumor cell lines with evidence of apoptosis as a principal mode of cell death [19].

Diuretic effect: The chief active principle oleandrin was found to stimulate the heart function and also had a diuretic effect. The effect of odorin on the heart of rabbits and dogs is identical with that of digitalis group whereas neriodin is twice as active as digitoxin in digitalis like action similar to that of oleandrin [20].

Antileukemic effects: Antitumor activity of this novel plant extract, the relative abilities of oleandrin and oleandrogenin to inhibit FGF-2 export from two human prostate cancer cell lines, DU145 and PC3, were examined [21]. Anvirzel and Oleandrin are extracts of oleander induce cell death in human cancer cells [22]. Toxicity of *Nerium oleander* [23] and *Calotropis procera* have an activity in the antitumor human cell line test with ED₅₀ varied in the range of 0.008 to 2.13 µg/ml, depending upon the cell line [24]. Used in chancres and ulcers on the penis, reduce swellings, powerful cardiac toxin [25].

Immunomodulating activity: CNS depressant activity: After the isolation of oleandrin a number of new chemical constituents have been isolated from this plant and their pharmacological properties have also been evaluated [26]. Experiments have been demonstrated that the crude alcoholic extract from the leaves has CNS depressant activity.

Nerium oleander contains at least 2% cardiac glycosides. Rosagenin may be extracted from the bark and has a strychnine-like action. Several flavones (0.5%) and volatile oils (unimportant amount), as well as rubber, fats, sugars and hydrocyanic acid, can be isolated from its leaves [27, 28, 29].

CONCLUSION

Today, our understanding of the interactions between drugs and herbs & food is still in its infancy. People are using herbal medicines from centuries for safety, efficacy, cultural acceptability and lesser side effects. Plant and plant products have utilized with varying success to cure and prevent diseases throughout history [30]. Major plunge by the pharmaceutical

industry is focused towards design and development of new innovative/indigenous plant based drugs through investigation leads from traditional system of medicine [31]. It is a best classical approach in the search of new molecules for management of various diseases. Though screening of literature is available on *Nerium oleander* depicted the fact that it is a popular therapy among the various racial groups, Ayurvedic and traditional practitioners for treatment of ailments. Researchers have been exploring the curative potential of this plant as it has more therapeutic properties which are still not known.

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