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Review Article

A Review on: *Nerium oleander* Linn. (Kaner)

*Chaudhary Kiran[1], Prasad D.N.[2]

[1]*K.C. Institute of Pharmaceutical Sciences, Pandoga, Distt.Una (H.P.)*
[2]*Shivalik College of Pharmacy, Naya Nangal, Distt.Ropar, Punjab*

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ABSTRACT
Nerium oleander is an evergreen shrub or small tree in the dogbane family Apocyanaceae. It is commonly known as oleander but has many other names like *Nerium indicum* mill. and *Nerium odorum* soland. It bears flowers in clusters with white, pink, yellow and red colours. It contains plumericin, alpha-amyrin, beta-sitosterol, kaempferol, cardioactive glycosides named Odorosides A-H obtained from the root bark. Leaves contain the cardiac glycosides kaneroside, neriumoside, digitoxigenin, alpha –L-olendroside -5α-adynerin and other glycosides. Odorosides are cardioactive glycosides. Gentiobiosyl –oleandrin, Odoroside A and Oleandrin were the main glycosides identified. It has potent cardiotonic activity, digitalis like effect on heart. It has been reported to have effective against skin diseases,wound infections, cancer, diabetes, inflammation and CNS depression. All parts of the plant are poisonous in nature which can be treated by the use of activated charcoal.Topical preparation containing *Nerium* extract can be used as antiageing cream.

Keywords : *Nerium oleander*, *Nerium indicum*, Oleander, Cardiotonic, Odorosides , Antibacterial, Antiageing

INTRODUCTION

Taxonomic classification
Phyllum- Plantae
Class/ Subphyllum- Angiosperms
Series – Eudicots
Order – Gentianales
Family – Apocyanaceae
Genus – Nerium
Species- Oleander

General Description- *Nerium oleander* is an evergreen shrub or small tree in the dogbane family Apocyanaceae. It is known as oleander from its superficial resemblance to the unrelated plant *Olive olea* but has many other names like *Nerium indicum* mill. and *Nerium odorum* soland. The white and red flowered variety is equated with *Nerium indicum*[1].

Botanical Description – Oleander grows to 2–6 m (6.6–20 ft) tall, with erect stems that splay outward as they mature; first year stems have a glaucous bloom, while mature stems have a grayish bark. The leaves are in pairs or whorls of three, thick and leathery, dark-green, narrow lanceolate, 5–21 cm (2.0–8.3 in) long and 1–3.5 cm (0.39–1.4 in) broad, and with an entire margin. The flowers grow in clusters at the end of each branch; they are white, pink to red, 2.5–5 cm (0.98–2.0 in) diameter, with a deeply 5-lobed fringed corolla round the central corolla tube. They are often, but not always, sweet-scented. The fruit is a long narrow capsule 5–23 cm (2.0–9.1 in) long, which splits open at maturity to release numerous downy seeds.

Distribution – *N. oleander* is distributed in Mediterranean region and subtropical Asia, is indigenous to India–Pakistan subcontinent. Distributed in the Himalayas from Nepal westwards to Kashmir upto 1950m, extending to Baluchistan, Afghanistan and found throughout India in gardens .The white and red flowered variety is equated with *Nerium indicum*.

Classical uses – Charka prescribed the leaves of white flowered variety externally in chronic and obstinate skin diseases of serious nature including leprosy. Sushruta used karavira in medicinal paste for application in alopecia . Root powdered with water was applied to alleviate venereal diseases. The powder of leaves was used as a snuff for treating epilepsy. All parts of plant especially roots were known to be highly poisonous when taken internally.

Tincture of flowers exhibited cardiotonic, root CNS-active and spasmolytic activity. Externally, root exhibited healing properties for haemorrhoids and ulcers. Oil of rootbark gave good results in leprosy.

Nerium oleander Linn.

**Author for correspondence: Email: kiranchaudhary1998@gmail.com*

In Homoeopathy, tincture of *Nerium oleander* (red laurel) leaves is used in diseases of nervous system, hemiplegia and paralytic conditions under strict medical supervision.

Roots give plumericin, alpha-amyrin, beta-sitosterol, kaempferol, cardioactive glycosides named Odorosides A-H obtained from the root bark. Leaves contained the cardiac glycosides kaneroside, neriumoside, digitoxigenin, alpha –L-olendroside -5α-adynerin and other glycosides. Odorosides are cardioactive glycosides. Gentiobiosyl – oleandrin, Odoroside A and Oleandrin were the main glycosides identified.

The whole plant exhibited potent cardiotonic activity, digitalis like effect on EKG and heart lung preparation. Tincture from the leaves is used and found two times more potent than tincture digitalis assayed on frogs. Pumieride, a glycoside did not possess cardiotonic activity but possess antistress activity .[2]

Phytochemical Constituents

- Siddiqui et al., 2012 reported a pentacyclic triterpene, oleanderocinoic acid, flavonoid glycosides,quercetin-5-O-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside and kaempferol-5-O-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside and a cardenolide, oleandigoside from the leaves of *Nerium oleander.* The growth inhibitory and cytotoxic activites of compounds were studied against MCF-7, human breast cancer cell lines using sulforhodamine B assay [3].
- Sharma et al., 2012 reported two new compounds heptacosane-3-enyl-5-hydroxyhexanoate and 4-oxooctyl-2-hydroxyundecanoate from the stems of *Nerium oleander* [4].
- Santhi et al., 2011 screened the ethanolic extract of the leaves of *N.oleander* and found to contain carbohydrates, proteins, amino acids, alkaloids and cardiac glycosides. Flavonoids and terpenpoids were absent [5.]
- Luay et al., 2011 reported that monoglycosidic cardenolides from *Nerium oleander* possessing the 3β,14β-dihydroxy-5β-card-20(22)-enolidestructure with or without an acetoxy group at C-16 exhibited significant anticancer activity.The results indicated that the cytotoxic effects are induced by the inhibition of plasma membrane bound Na+/K+-ATPase [6]
- Patel et al., 2010 collected the leaves and roots of *Nerium oleander* and treated with pet ether and methanol using soxhlet apparatus. The preliminary studies reported the presence of alkaloids, glycosides, tannins and phenolic compounds for methanolic extract of *N.indicum.* [7]
- Qun et al., 2010 reported a polysaccharide fraction from the hot water extract of flowers of *N.indicum* using ethanol precipitation, cetyltrimethylammoniumbromide (CTAB) complexing, anion exchange chromatography
- and gel permeation chromatography.It has been found to contain L-rhamnose, L-galactose and D-galacturonic acid.[8]
- Hasan et al., 2006 reported two aristolochic acid derivatives and 3-aristolactam derivatives in addition to one methylparaben from the *Nerium oleander* leaves aqueous and methanolic extract and identified by direct comparision of melting point,co-chromatography and spectral analysis with authentic samples.[9]
- Siddiqui et al., 1995 reported two novel cytotoxic pentacyclic triterpenoids cis-karenin (3-β-hydroxyphenoxy-28-Z-p-coumaroyloxy-urs-12-en-27-oic acid) and trans-karenin(3-β-hydroxy-28-E-p-coumaroyloxy-urs-12-en-27-oic acid) reported from the leaves of *N. oleander*.[10]
- Abe et al., 1992 examined polar glycosides from the air dried leaves and gentiobiosyl nerigoside and G.beaumontoside reported along with major triosides gentiobiosyl-oleandrin. Minor triosides also includes glycosides of 8-β-hydroxy and Δ^{16} -8-β-hydroxydigitoxigenin and Δ^{16}- neriagenin along with glycosides of known cardenolides, oleandragenin, digitoxigenin, adynerigenin, neriagenin and their Δ^{16} derivatives.[11]
- Siddiqui et al., 1989 reported two new triterpenes oleandrolic acid and kanerodione[16] from the fresh undried and uncrushed leaves of *Nerium oleander* and their structures established as 3-β-p-hydroxyphenoxy-11α-methoxy-12-α-hydroxy-20-ursene-28-oic acid and 28-hydroxy-20(29)-lupen-3, 7-dione respectively by means of chemical and spectral studies.[12]
- Siddiqui et al., 1987 reported two new cardiac glycosides kaneroside and neriumoside from the fresh undried, winter leaves of *N.Oleander* and their structures established as 3β-O-(D-diginosyl)-2α-hydroxy-8,14β-epoxy-5β-carda-16:17,20:22-dienolide and 3β-O-(D-diginosyl)-2α,14β-dihydroxy-5β-carda-16:17,20:22-dienolide respectively through chemical and structural studies.[13]
- Yamuchi et al., 1976 reported the β-D-digitaloside & β-D-glucosyl($1 \rightarrow 4$)- β-D-digtialoside from the root bark of *N.odorum*. Odoroside B obtained in high yield among the digitoxigenin and uzarigenin glycosides. With the help of Column Chromatography oleandrigenin β-gentiobiosyl-(1→4)-β-D-digitaloside was reported along with other oleanderigenin glycosides.[14]

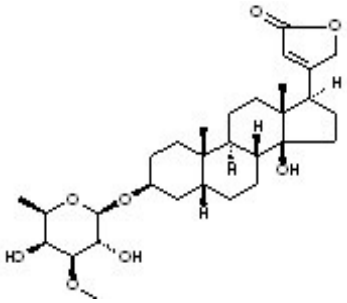
Pharmacological Activity

Antibacterial activity

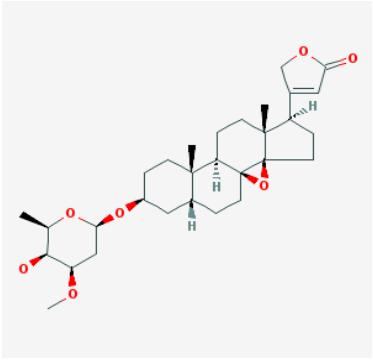
Classical names

Ayurvedic	Karavira,Viraka,Ashvamarka,Hayamaara, auripushpa, Siddhapushpa (white flower variety), Raktapushpa, Raktaprasava, Ravipriya (Red flowered variety)
Unani	Kaner, Diflaa, Samm-ul-maar, Khar-Zaharah
Sidha	Alari, Arabivaya
English	Indian Oleander

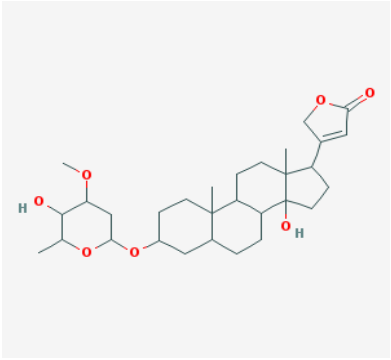
Parts used – leaves, roots, root bark



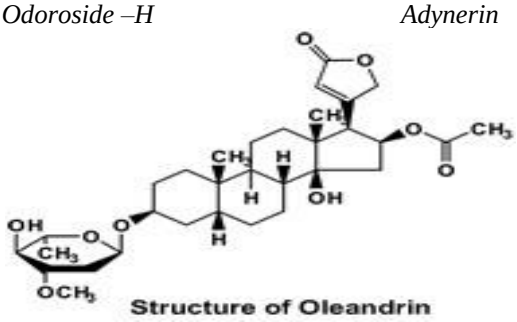
Odoroside –H



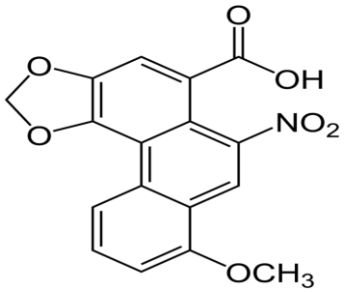
Adynerin



Odoroside -A



Structure of Oleandrin



Aristolochic acid

- Leaves of *Nerium indicum* possess antibacterial activity in selected extracts of benzene and ethanol against Gram positive micro-organism *Bacillus subtilis* but negligible activity against Gram positive micro-organism *E-coli*.
- Comparative study for antibacterial activity of both extracts with standard antibiotic Ofloxacin showed relatively higher zone of inhibition for ethanolic extract than benzene extract, therefore ethanolic extract possesses potential antibacterial activity over benzene extract against Bacillus subtilis.[15]
- Antibacterial activity of the plant extracts was studied against *Bacillus subtilis*, *Staphylococcus aureus*, *Clostridium perfringens* and *Streptococcus mutans*. According to results, methanolic extract was more effective than chloroform or hexane extract.[16]
- Hepatoprotective and antioxidant activity - Singhal and Gupta, 2012 reported hepatoprotective and antioxidant activity of methanolic extract of flowers of *Nerium oleander* against CCl_4 induced liver injury in rats.[17]
- Antiproliferative activity -Wong et al., 2011 carried out antiproliferative and phytochemical analysis of *N.oleander* leaf extracts and all the four extracts of *Nerium oleander* were effective against MCF-7 cell lines.The antiproliferative activities were carried out by using sulforhodamine B assay.[18]
- Antidiabetic activity -Sikarwar et al., 2009 studied the antidiabetic activity in alloxan induced diabetic albino rats and comparison was done with glibenclamide. The chloroform & ethanolic extract reported significant antidiabetic activity.These extracts also prevented body weight loss in diabetic rats. The antihyperglycemic action of the extracts may be due to improving the glycemic control mechanisms.[19]
- Anti-inflammatory activity - Nurgun et al., 2003 reported anti-inflammatory and antinociceptive activity invivo from the ethanolic extracts of dried and fresh flowers of *N.oleander against* carrageenan- induced hind paw oedema model in mice without inducing any gastric damage [20]
- CNS depressant effect - Begum et al., 1999 carried out a bioactive directed isolation from the extract of fresh uncrushed leaves of *N.oleander* and reported a CNS depressant effect in mice. As a result CNS depressant cardenolides including a new cardenolide, neridiginoside and odoroside-H have been reported which exhibited CNS depressant activity in mice at a dose of 25mg/kg.[21]
- Zia et al., 1995 studied two fractions with respect to their action on CNS & behavior pattern in mice. Both fractions have shown reduction in locomotor activity, rotarod performance and potentiation of hexobarbital sleeping time.These fractions also showed analgesic activity. When tested against picrotoxin induced convulsions two fractions showed protection against biculline induced convulsions.These findings suggest that both fractions possess a CNS depressant action.[22]
- Anticancer activity –Anvirzel™, an extract of *Nerium oleander*, induces cell death in human but not murine cancer cells. Study was done to examine the mechanism and differential killing effect of AnvirzelTM, an extract of oleander and its derivative compound oleandrin on human, canine and murine tumor cells. Cells received different concentrations of anvirzel(1.0ng/ml to 500ug/ml) or Oleandrin (0.01ng/ml to 50ug/ml) in both pulse treated/recovery cultures.The cytotoxicity of these compounds was determined. Both were able to induce cell killing in human cancer cells, but not in murine cells. The cell killing potency of oleandrin was greater than that of Anvirzel. Canine oral cancer cells treated with Anvirzel showed intermediate levels of response.[23]

Nerium in Cosmetics: Nerium AD Age defying treatment–skin care range is known for its antioxidant properties. Two products are in range Nerium AD night cream and Nerium AD day cream. Primary ingredient is *Nerium oleander* in these preparations.These preparations are used

for ageing and skin damage, hyperpigmentation, fine lines and wrinkles and uneven skin texture.[24]

Oleander Poisoning: *Nerium oleander* has historically been considered a poisonous plant because some of its compounds may exhibit toxicity, especially to animals, when consumed in high amounts. Among these compounds are oleandrin and oleandrigenin, known as cardiac glycosides, which are known to have a narrow therapeutic index and can be toxic when ingested.

Toxicity studies of animals administered oleander extract concluded that rodents and birds were observed to be relatively insensitive to oleander cardiac glycosides. Other mammals, however, such as dogs and humans, are relatively sensitive to the effects of cardiac glycosides and the clinical manifestations of "glycoside intoxication".

There is no toxicity or deaths reported from topical administration or contact with *Nerium oleander* or specific products derived from them.

Toxicity studies that have been conducted in dogs and rodents administered oleander extracts by intramuscular (IM) injection indicated that on an equivalent weight basis, doses of an oleander extract with glycosides ten times in excess of those likely to be administered therapeutically to humans are still safe and without any "severe toxicity observed".[1]

Nerium oleander is a potentially lethal plant after ingestion.All parts of the plant are toxic and contain a variety of cardiac glycosides. Ingestion of oleander results in nausea, vomiting, abdominal pain, diarrhea, dysrhythmias and hyperkalemia. In most cases management of poisoning involves administration of activated charcoal and supportive care. Digoxin specific Fab fragments are an effective treatment of acute intoxication.[25]

SUMMARY

The plant kingdom is a rich source of potential medicinally important plants. *Nerium oleander* is a popular remedy among the various ethnic groups, Ayurvedic and traditional practitioners for the treatment of various ailments like topical, diabetes, antibacterial, antioxidant etc. So there is need to explore the therapeutic potential of this plant as it has more therapeutic properties which are still not known.

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