International Journal of
Life Sciences
International Peer Reviewed Open Access Refereed Journal

Int. J. of Life Sciences, 2021; 9 (1):7-20
ISSN:2320-7817(p) | 2320-964X(o)

Review Article Open Access

Nerium oleander L.: Phytochemical and pharmacological profile

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Manuscript details:

Received: 20.01.2020
Accepted: 08.02.2021
Published: 31.03.2021

Cite this article as:
Ashima Gakhar (2021) *Nerium oleander* L.: Phytochemical and pharmacological profile, *Int. J. of Life Sciences*, 9 (1):7-20.

Available online on http://www.ijlsci.in
ISSN: 2320-964X (Online)
ISSN: 2320-7817 (Print)

ABSTRACT

Nerium oleander linn. (Apocynaceae) is a beautiful flowering shrub bearing white and crimson flowers especially suited to dry and sunny locations. The plant is commonly called kaner. In view of its therapeutic activities, different parts of the plant have been subjected to chemical studies by various groups of workers, and several cardiac glycosides, pregnane derivatives and polysaccharides have been isolated. *N.oleander* is a good cardioprotective, anticancer, antidiabetic and antifungal agent. The present review summarizes traditional uses, pharmacological properties of extracts and phytoconstituents of *N.oleander*.

Keywords: *N.oleander*, Phytoconstituents, Pharmacological activity, Toxicity.

INTRODUCTION

Nerium oleander linn. (Apocynaceae) is native to a broad area from Morocco and Portugal eastward through the Mediterranean region and southern Asia to Yunnan in southern parts of China (Huxley *et al*., 1992). Nerium oleander is an important medicinal plant in Indian folk medicine and is commonly called kaner. It is the only species currently classified in the genus Nerium (Farooqui and Tyagi, 2018).

It is a beautiful flowering shrub bearing white and crimson flowers especially suited to dry and sunny locations (fig1). It typically occurs around dry stream beds. It grows to 2-6 m tall, with spreading to erect branches. Oleander grows well in warm subtropical regions, where it is extensively used as an ornamental plant in landscapes, parks, and along roadsides. It is drought tolerant and will tolerate occasional light frost down to -10°C, 14F (Chopra *et al*., 1956).

The leaves are in pairs or whorls of three, thick and leathery, dark green, narrow lanceolate, 5-21 cm long and 1-3.5 cm broad, and with an entire margin. The flowers grow in clusters at the end of each branch; they are white, pink, red or yellow, 2.5-5 cm diameter, with a deeply 5-lobed corolla with a fringe round the central corolla tube. They are often, but not

always, sweetly scented. The fruit is a long narrow capsule 5-23 cm long, which splits open at maturity to release numerous downy seeds (Satyanarayan *et al*., 1975) Major phytoconstituents present in plant are cardiac glycosides, pregnane derivatives and polysaccharides. Among them the major one is oleandrin. They are mainly responsible for anticancer, antidiabetic and antifungal properties (Abe *et al*., 1976).

Figure 1: *Nerium oleander* L. Plant in a flowering condition

Traditional uses of *N.oleander:*

Traditionally *N.oleander* has been used worldwide for the treatment of a number of diseases. In India it has been used as an antibacterial agent. It has been also used to provoke menstruation, as an abortifacient and as an antispasmodic in the treatment of angina pectoris. It is also used in treatment of skin diseases like rash, scabies, ringworm, lice, leprosy and boils. Flowers, leaf and leaf use have been used against warts, carcinoma, cancerous ulcers or hard tumors. In Tanzania hot water extract of its fresh leaves is used for antibacterial action; in Iran dried leaf extract has been used as a cardiotonic and diuretic in edema; in South Africa it has been used as abortifacient; in Cuba it is a folkloric medicine (Adome *et al*., 2003).

A few compounds of Nerium oleander exhibit toxic properties when tested in animals, especially when consumed in higher amounts. To name a few, it has an effect on the gastrointestinal system, heart, and the central nervous system. Though, some invertebrates are reported to be unaffected by oleander toxins and feed on the plant; caterpillars of the polka-dot wasp moth (Syntomeida epilais) survive by eating only the pulp surrounding the leaf-veins, avoiding the fibres, larvae of the common crow butterfly (Euploea core) also feed on oleanders, and they retain or modify toxins, making them unpalatable to would-be predators such as birds, but not to other invertebrates such as spiders and wasps. Despite the toxins, Nerium oleander is of great medicinal importance. It is useful for managing heart conditions, asthma, epilepsy, cancer, painful menstrual periods, leprosy, malaria, ringworm, indigestion, and venereal disease; and to cause abortions, as well as drugs derived from this plant, are used in treatment of cancer and the research is ongoing for its future implementation. (Farooqui *et al*, 2018).

Chemical constituents

The compounds like terpenes, steroids, polyphenols and flavonoids has been identified from the various parts of the plant. (Hase *et al.*, 2016). The plant revealed the presence of medically active metabolites. NO plant parts leaves reported carbohydrates, proteins, alkaloids, flavonoids, terpenoids, cardiac glycosides, tannins and saponins. In vitro methanolic extract of NO contained the highest amount of phenolic compounds and exhibited the maximum antioxidant activity. The chemical constituent of leaves present pectic polysaccharide mainly galactomeric acid besides rhamnose, arabinose and galactose. The four new cardenolides aminoglycosides, three new pregnanes, 21- hydroxy pregna-4,6-diene-3,12,20-trione, 20R-hydroxy pregna 4,6diene,3,12-dione and 16β,17β –epoxy-12β hydroxy pregna-4,6-diene-3,20-dione are found in plant. Two new coumaryloxy triterpenoids, nericomaric and isoneriu-coumaric acids isolated from leaves of plant.

The main glycosides are oleandrin, neriine, Cardenolides, gentiobiose, oleandrin and odoroside are also present In addition, a variety of other pharmacologically active compounds, including folinerin, rosagenin, rutin and oleandomycin have been identified in the plant. In leaves, two new cardenolides, 3 beta-O-(D-2-O-methyl digitalosyl)-14. (Farooqui *et al*, 2018).

Pharmacological studies on *N.oleander* extracts:

N.oleander is a plant that contains a number of cardiac glycosides. Glycosides in *N.oleander* include oleandrin, oleandrigenin and nerioside, etc (Rahman and Ishtiaq,1997) Earlier it was mentioned only to treat cardiac disorders but further clinical evidences shows that extracts of *N.oleander* possesses anticancer, anti-inflammatory, antifungal and antidiabetic properties.

Cardiovascular effects

The body needs constant nourishment to ensure that the cardiovascular system operates efficiently. However, 60 millions Americans suffer from cardiovascular disorders which include a wide range of diseases of heart and blood vessels such as chronic venous insufficiency and high blood pressure. These can lead to events such as heart attack and stroke (Jain *et al*., 2009) many herbal drugs are used to cure cardiovascular disorders the most common one of which is *N.oleander*.

Pharmacological activities of cardiac glycosides have increased significantly since the discovery of their effectiveness for treatment of congestive heart failure and also in proliferative disease. Development of such clinically targeted, antiproliferative cardiac glycosides could be developed as formulation. Chemical variants in compounds such as Oleandrtin (a lipid soluble cardiac glycoside) could be of help. Nerium oleander L. is an important Chinese folk medicine having well proven cardio protective and cytotoxic effects.

A study shows that the whole plant exhibits potent cardiotonic activity, digitalis like effect on electro-cardiogram and heart lung preparation. Tincture obtained from the leaves was found two times more potent than tincture from digitalis, when assayed on frogs. Another glycoside, Pumieride, exhibited antistress activity only and no cardiotonic activity. (Chaudhary and Prasad, 2014).

Crude ethanolic extract of *N.oleander* leaves showed a dose dependent increase in heart rate, force of contraction and cardiac flow in isolated guinea pig heart as compared with graded dose of digoxin the effects closely match the activities in dose dependent manner. Thus all three parameters prove that *N.oleander* is a good cardiovascular agent (Adome *et al*., 2003).

There are some chemical substances present in plants that may act as anticarcinogens or antimutagens by blocking or trapping ultimate carcinogen electrophile in a nucleophilic chemical reaction to form innocuous products. *N.oleander* extracts are effective to treat many forms of cancer. Stem extract was found to be cytotoxic according to LC_{50} value in MTT assay. It was observed that concentration of 1000, 500 and 50 µg/ml of the extract possess marked antileukemic effect (Tarun *et al*., 2006)

Anti-inflammatory effect

Inflammation is a common spectacle and it is a reaction of living issues towards damage. Physiological or acute inflammation is a beneficial host response to tissue damage; it may lead to immune associated disorders like rheumatoid arthritis, inflammatory bowel disease and cancer. Chronic inflammation may lead to early changes associated with the development of cancer through attraction of soluble proinflammatory mediators TNF-α, Interleukins (IL-6 and IL-8), Transcription activation factors (NF-KB) and bioactive lipids such as Eicosanoids (Balkwill *et al*., 2003) Elucidation of these complex mechanisms suggests new therapeutic strategies, with *N.oleander* a comparable complex and intriguing potential source for the strategic agents. *N.oleander* dried leaf and flower extract exhibited potential anti-inflammatory activity against carrageenan- induced hind paw edema model in mice without producing any gastric damage (Nurgun *et al*., 2003).

Atay *et al*. (2018), states the traditional use of the oily or alcohol extracts of N. oleander flowers to treat inflammatory diseases. The sub extracts obtained from the ethanolic extract of the oleander flowers were found to exert significant in vitro anti-inflammatory activity. The active components in this sub extract were determined to be kaempferol, kaempferol-3-O-β-D-glucoside and chlorogenic acid.

Another study involving a primary phytochemical investigation of the leaf extracts showed the occurrence of alkaloids, tannin, saponins, glycosides, anthraquinones, terpenoids and sterol etc. The plant has exhibited prominent effects on in vitro anti-arthritic assay protein denaturation method. Chloroform extracts of *N. oleander* leaves showed significant results in in-vitro anti-inflammatory models. Thus, it can be concluded that N. oleander has considerable anti-inflammatory potency.

Effect on Central nervous system

Methanol fractions of fresh, undried and uncrushed leaves of *N.oleander* were found to produce reduction in locomotor activity, Rota rod performance and potentiation of hexobarbital sleeping time in mice. One fraction also exhibited 60% protection against bicuculline induced convulsions these findings shows that *N.oleander* possesses CNS depressant effect (Atiya *et al*., 1995).

In a study, the extract (at doses of 100 and 200 mg/kg) significantly reduced ($p< 0.01$) spontaneous locomotor activity and also potentiated pentobarbital-induced sleep. At the higher dose (200 mg/kg) the extract showed 66 % protection against electroshock-induced convulsions while the lower dose (100 mg/kg) produced a significant reduction ($p<0.01$) in pentylenetetrazol (PTZ)-induced convulsions (Singhal and Gupta, 2011).

One more study investigated the effects of the different extracts of leaves of Nerium oleander on the central nervous system (CNS) in rats and mice. The CNS effects were evaluated by general behaviour, exploratory behaviour, muscle relaxant activity and phenobarbitone sodium–induced sleeping time using standard procedures in experimental animal models. The results revealed that the different extracts at 100 and 200 mg/kg dose levels, caused a significant reduction in the spontaneous activity (general behavioural profile), exploratory behavioural pattern (head dip test), muscle relaxant activity (rotarod), and significantly potentiated phenobarbitone sodium–induced sleeping time. The results conclude that the extract exhibits CNS depressant activity in tested animal models (Sushant *et al*, 2017).

Anti diabetic effect

Diabetes is a major threat to global public health that is rapidly getting worse and has the biggest impact on adults of working age in developing countries. At least 171 million people worldwide are diabetic. This figure is likely to be more than double by 2030 to reach 366 million (WHO, 2006) *N.oleander* extract has protective potential on lipid profile, body growth and renal function in streptozotocin induced diabetic rats. Streptozocin induced diabetic rats showed increase in level of serum triglycerides and cholesterol registering increase of 27.3% and 25.6%. *N.oleander* extract treatment lowered serum triglycerides in diabetic rats to increase of 10.1% and 14.5% respectively. *N.oleander* extract also shows decrease in growth rate as compared to control (Maged and Saley, 2007).

Another study showed that treatment of diabetic rats with glimepiride or Nerium oleander extract improved insulin, glucose levels and liver enzyme activities. However, the effect of glimepiride was higher (Mwafy and Yassin, 2011).

Antimicrobial effect

The antifungal property of plant extract from *N.oleander* was determined when it was used as a wood preservative. Ethanolic extract of leaves and flowers of oleander has ability to protect Turkish wood blocks (*Fagus orientalis*) and Scots pine (*Pinus sylvestris*) against attack of *Postia placenta* (Brown rot) and *Trametes versicolor* (White rot) (Osman *et al*., 2007)

A study reported antimicrobial activity of aqueous ethanolic extract of both Nerium oleander L. and Nicotiana tabacum L. from Multan district. The activity was studied against were checked, against three pathogenic bacteria viz: Staphylococcus aureus (gram positive), Escherichia coli and Pseudomonas aeruginosa; (gram negative), and disc diffusion technique was used to check the antimicrobial activity. The bacterial strains were found susceptible to plant extracts. The ethanolic extract of Nerium oleander leaves showed highest antibacterial action against Pseudomonas aeruginosa at 900mg/ml concentration (Malik *et al*, 2015).

Phytoconstituents isolated from *N.oleander* and their pharmacological activity

Many useful phytoconstituents have been isolated from *N.oleander* major phytoconstituents are glycosides, pregnane derivatives and polysaccharides.

Cardiovascular effects

Various pharmacological studies have shown *N.oleander* as a good cardiotonic agent. A number of secondary metabolites isolated from this plant has been reported to be effective in treatment of cardiac disorders. They are listed in Table No. 1.

Anticancer activity

N.oleander is a toxic plant. Oleandrin isolated from leaves of *N.oleander* has been shown to induce cell death through induction of apoptosis. There are many clinical studies that show that oleandrin is a very good anticancer agent and it is helpful in treatment of various types of cancer.

Oleandrin at low nanomolar concentration potently inhibited cell proliferation associated with induction of a profound G2/M cell cycle arrest. Subcellular changes within PANC-1 (Human pancreatic carcinoma cell line) cells induced mitochondrial condensation and translocation to a perinuclear position accompanied

by vacuoles. This shows that lipid soluble cardiac glycoside oleandrin is also effective in control of human pancreatic cancer proliferation (Newman *et al*., 2007).

Oleandrin also inhibited FGF-2 (Fibroblast growth factor) export in vitro from PC-3 and DU-145 prostate cancer cell lines in concentration and time dependent fashion and may, therefore contribute to the antitumor activity of this novel treatment for cancer. Oleandrin 0.1 ng/ml produces a 45.7% inhibition of FGF-2 release from PC-3 cells and 49.9 % inhibition from DU-145 cells (Judith *et al*., 2001).

Topical application of oleandrin before TPA (12-O-Tetradecanoylphorbol-13-acetate) application to mouse skin resulted in significant reduction in TPA induced expression of PI3K (Phosphoinositide 3-kinases) and phosphorylation of Akt and inhibition of NF-kB activation. So oleandrin can be use as a emollient or patch for chemoprevention of skin cancer (Farrukh *et al*., 2004).

Neridienone A isolated from leaves of *N.oleander* showed significant cell growth inhibition of malignant tumor cells VA-13 and human liver cancer cell lines HepG2 (Bai *et al*., 2007). Methanolic extracts of N. oleander possess considerable antiproliferative activity, as per a study. Odoroside A, was found to be the most potent compound in comparison to oleandrin and doxorubicin (Qamar *et al*, 2017).

Anti-inflammatory activity

The anti-inflammatory property of a substance or treatment is the one that reduces inflammation or swelling. Plants have a potential to heal and have their own antimicrobial characteristics (Ayyachamy, 2020).

Neridienone A isolated from leaves of *N.oleander* showed good anti-inflammatory activity. Its activity was examined on basis of inhibitory action against the induction of ICAM-I (Intercellular adhesion molecule-1) (Shan *et al*., 2007).

Another study involved a primary phytochemical investigation of the leaf extracts and showed the occurrence of alkaloids, tannin, saponins, glycosides, anthraquinones, terpenoids and sterol etc. It has exhibited prominent effects in vitro anti-arthritic assay protein denaturation method. Also, chloroform extracts of *N. oleander* leaves showed significant results in in-vitro anti-inflammatory models. Thus, it can be concluded that N. oleander has considerable potency as an anti-inflammatory. (Ayyachamy, 2020).

Effect on central nervous system

In an experimental animal study, the ethanolic extract of Nerium oleander flowers showed anticonvulsant activity. The activity of 50 % hydro alcohol flower extract of Nerium oleander Linn. on the central nervous system (CNS) of mice was evaluated.

The extract significantly reduced spontaneous locomotor activity and also potentiated pentobarbital-induced sleep. At the higher dose (200 mg/kg) the extract showed 66 % protection against electroshock-induced convulsions while the lower dose (100mg/kg) produced a significant reduction in pentylenetetrazol (PTZ)-induced convulsions (Singhal and Gupta, 2011).

Polysaccharides isolated from flowers of *N.oleander* exert partial protection in cortical neurons stressed by beta-amyloid peptides or deprivation of nutrition from serum. It can be serving as a potential neuroprotective agent against neuronal death in Alzheimer's disease and neuroprotective mechanism may primarily rely on inactivation of JNK signaling pathways (Sabira *et al*., 1999).

Neridiginoside isolated from methanolic extract of the leaves of *N.oleander* shows significant CNS depressant activity in mice at a dose of 25mg/kg (Siddiqui *et al*., 1997).

3β-*O*-(D-2-*O*-methyl-digitalosyl)-14β-hydroxy-5β-carda- 16, 20(22)-dienolide, 3β-*O*-(D-digitalosyl)-16β-acetoxy-5β-carda-20(22)-enolide,3β-*O*-(D-digitalosyl)-14β-hydroxy-5βcarda-20(22)-enolide have been isolated from leaves of *N.oleander* were found to exhibit sedation in mice at a dosage of 25mg/kg (Siddiqui *et al*., 1997).

Polysaccharide isolated from flowers of *N.oleander* shows neuroprotective activity on neurons against serum deprivation and β- amyloid peptide toxicity in primary rat cortical neuronal cultures. Polysaccharide could also cause decrease the activity of caspase-3 triggered by beta- amyloid peptides (Yu *et al*., 2004)

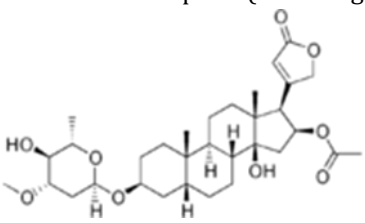
Antibacterial effect

A new cardinolide 12β-hydroxy-5β-*O*-carda-8, 14, 16, 20(22)-tetraenolide isolated from roots of *N.oleander*

shows antibacterial activity (Jabbar *et al*., 1999). A phytochemical analysis of N. oleander, exhibited the presence of alkaloids, terpenoids, cardiac glycosides, saponins, tannins and carbohydrates in all the solvents used. Disc Diffusion Method was employed to screen the extracts for antibacterial activity. Staphylococcus aureus, Pseudomonas aeruginosa and Salmonella typhimurium showed considerable zones of inhibition. (Bhuvaneshwari, 2007).

Toxicity of Nerium oleander

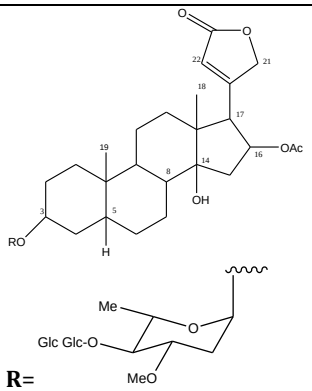
Oleander is one of the most poisonous plants in the world and contains numerous toxic compounds, many of which can be deadly to people, especially young children. The toxicity of Oleander is considered extremely high and it has been reported that in some cases only a small amount had lethal or near lethal effects. The most significant of these toxins are oleandrin (fig2) and neriine, which are cardiac glycosides. these toxins are oleandrin and neriine, which are cardiac glycosides. 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 or un-researched compounds that may have dangerous effects. Oleander bark contains rosagenin which is known for its strychnine-like effects. Boiling or drying the plant does not inactivate the toxins (Karawa *et al*., 1973). It is thought that a handful or 10-20 leaves consumed by an adult can cause an adverse reaction, and a single leaf could be lethal to an infant or child (Kingsbury, 1964) There are innumerable reported suicidal cases of consuming mashed oleander seeds in southern India. In animals, around 0.5 mg per kilogram of body weight is lethal to many animals, and various other doses will affect other animals. Most animals can suffer a reaction or death from this plant (Yarbrough *et al*., 1983).

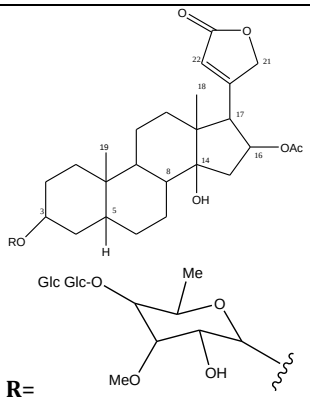
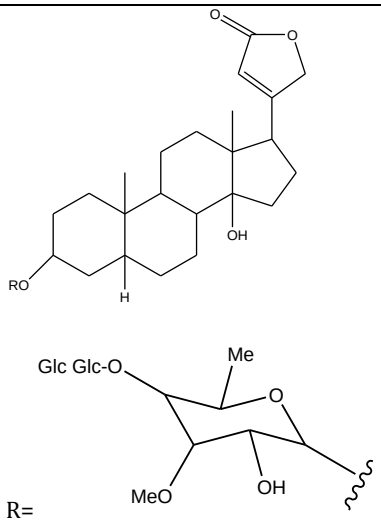
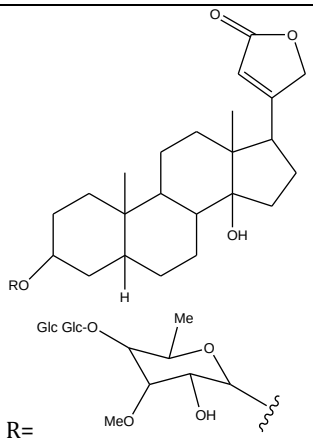
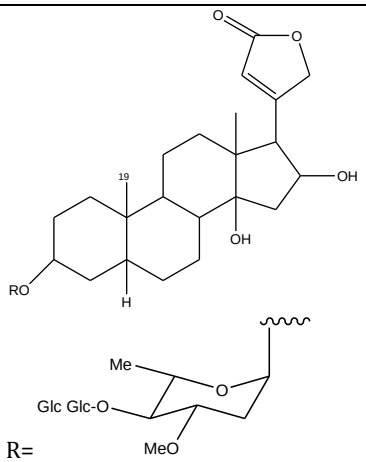


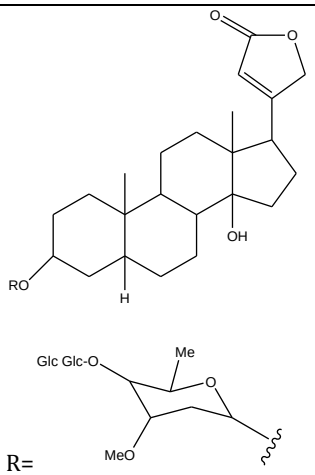
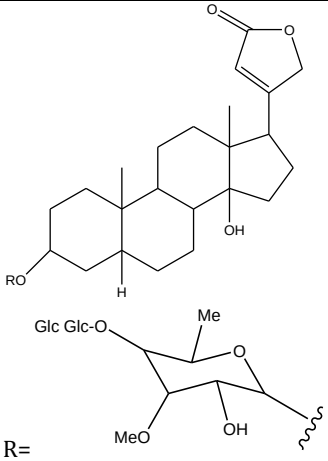
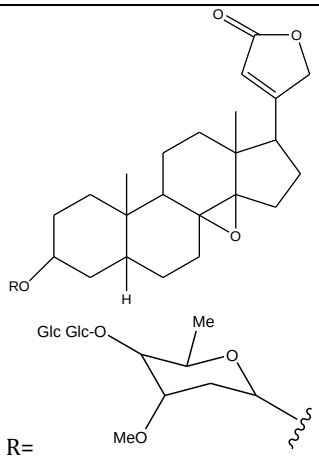
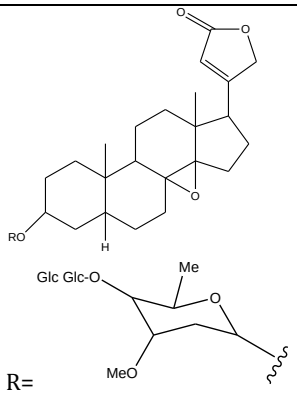
Effect of poisoning

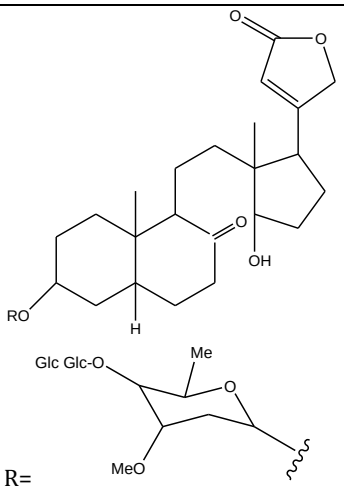
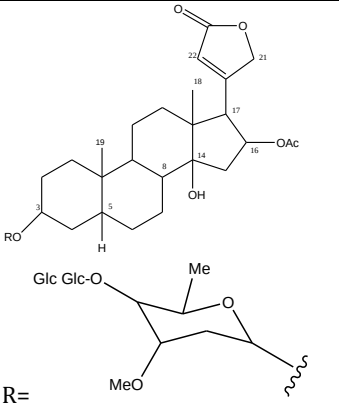
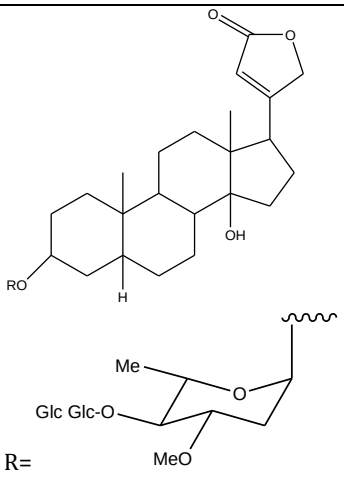
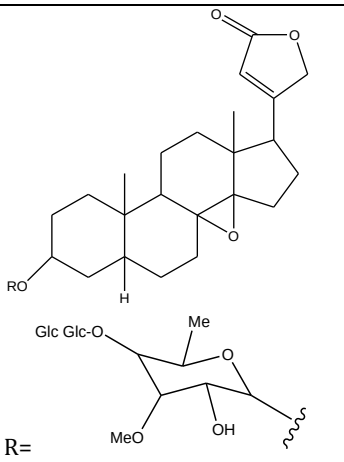
Ingestion can cause both gastrointestinal and cardiac effects. The gastrointestinal effects can consist of nausea and vomiting, excess salivation, abdominal pain, diarrhea that may or may not contain blood, and especially in horses, colic (Shaw and Pearn ,1979) Cardiac reactions consist of irregular heart rate, sometimes characterized by a racing heart at first that then slows to below normal further along in the reaction. The heart may also beat erratically with no sign of a specific rhythm. Extremities may become pale and cold due to poor or irregular circulation. Reactions to poisonings from this plant can also affect the central nervous system. These symptoms can include drowsiness, tremors or shaking of the muscles, seizures, collapse, and even coma that can lead to death. Oleander sap can cause skin irritations, severe eye inflammation and irritation, and allergy reactions characterized by dermatitis (Ansford and Morris, 1981).

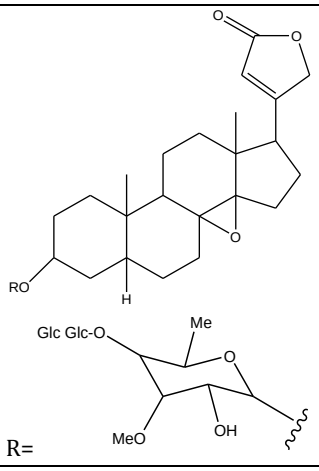
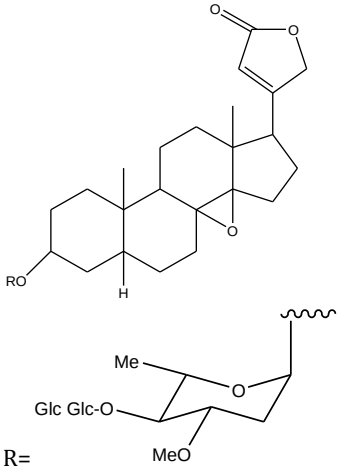
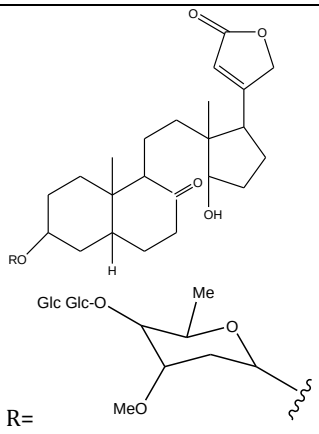
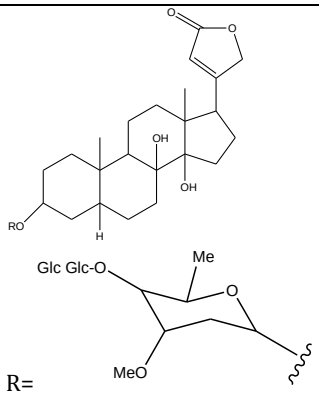
Table 1: Secondary metabolites isolated from Nerium oleander

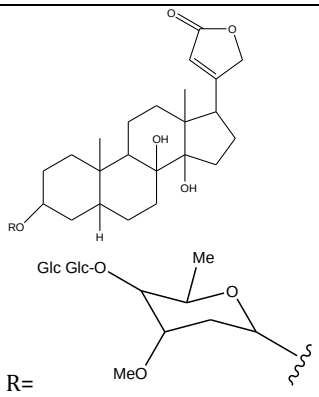
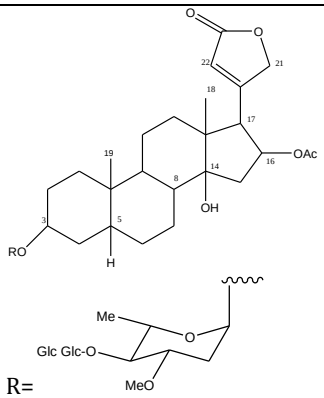
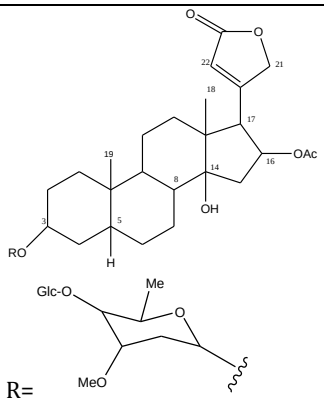
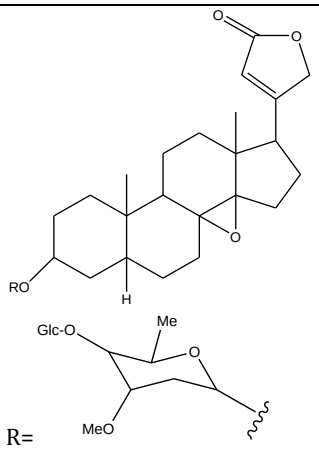
S.No.	Compound name	Chemical class	Part	Structure	Reference
1.	Oleandrigenin α-oleatrioside	Trioside	Air dried leaves	 **R=**	(Yamauchi and Ehara,, 1972, Yamauchi *et al*., 1975)

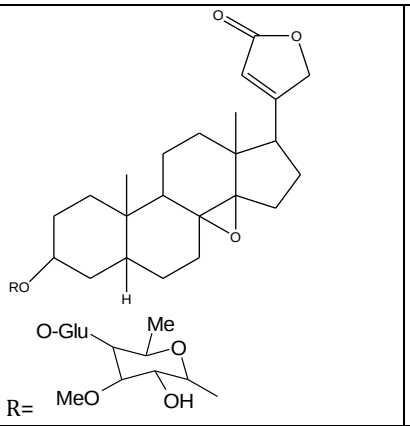
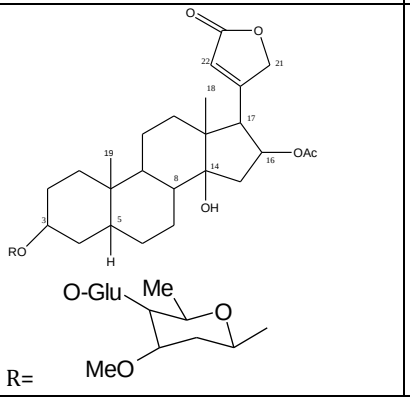
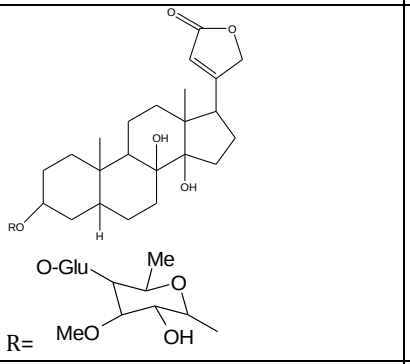
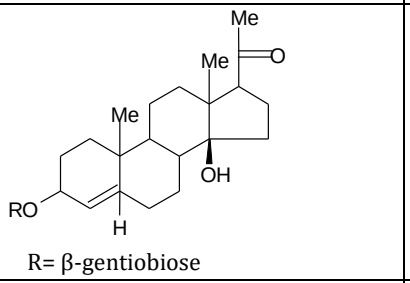
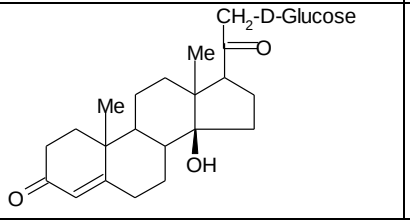
2.	Oleandrigenin β-odorotriside	Trioside	Air dried leaves	 **R=**	(Yamauchi and Ehara,, 1972, Yamauchi *et al*., 1975
3.	Δ^{16} -digitoxigenin β-neritrioside	Trioside	Air dried leaves	 R=	(Yamauchi and Ehara,, 1972, Yamauchi *et al*., 1975
4.	Δ^{16}-digitoxigenin β-odorotrioside	Trioside	Air dried leaves	 R=	(Yamauchi and Ehara,, 1972, Yamauchi *et al*., 1975
5.	Gitoxigenin α-oleatrioside	Trioside	Air dried leaves	 R=	(Yamauchi and Ehara,, 1972, Yamauchi *et al*., 1975

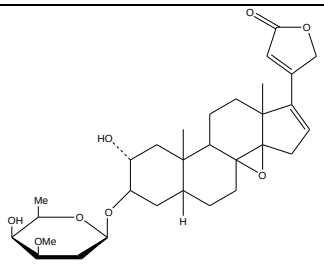
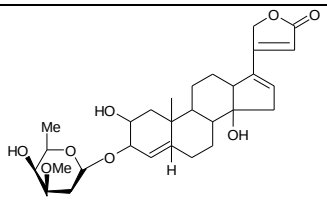
6.	Digitoxigenin β-neritrioside	Trioside	Air dried leaves		(Yamauchi and Ehara,, 1972, Yamauchi *et al*., 1975
7.	Odoroside G	Trioside	Bark		(Rheiner *et al*., 1952, Yamauchi *et al*., 1976)
8.	Adynerigenin β-neritrioside	Trioside	Air dried leaves		(Yamauchi and Ehara,, 1972, Yamauchi *et al*., 1975
9.	Δ^{16}- Adynerigenin β-neritrioside	Trioside	Air dried leaves		(Yamauchi and Ehara,, 1972, Yamauchi *et al*., 1975

10.	Neriagenin β-neritrioside	Trioside	Air dried leaves		(Yamauchi and Ehara,, 1972, Yamauchi *et al*., 1975
11.	Oleandrigenin β-neritrioside	Trioside	Air dried leaves		(Abe and Yamauchi. 1992)
12.	Digitoxigenin α-oleatrioside	Trioside	Air dried leaves		(Abe and Yamauchi. 1992)
13.	Adynerigenin β-odorotrioside	Trioside	Air dried leaves		(Abe and Yamauchi. 1992)

14.	Δ^{16}- Adynerigenin β-odorotrioside	Trioside	Air dried leaves		(Abe and Yamauchi. 1992)
15.	Δ^{16}- Adynerigenin β-gentiobiosyl- β-D-sarmentoside	Trioside	Air dried leaves		(Abe and Yamauchi. 1992)
16.	Δ^{16}- Nerigenin β-neritrioside	Trioside	Air dried leaves		(Abe and Yamauchi. 1992)
17.	8β-Hydroxydigitoxigenin β- neritrioside	Trioside	Air dried leaves		(Abe and Yamauchi. 1992)

18.	Δ^{16}-8β-Hydroxydigitoxigenin β- neritrioside	Trioside	Air dried leaves		(Abe and Yamauchi. 1992)
19.	Oleandrigenin α-oleabioside	Bioside	Air dried leaves		(Abe and Yamauchi. 1992)
20.	Oleandrigenin β-neribioside	Bioside	Air dried leaves		(Abe and Yamauchi. 1992)
21.	Δ^{16}- Adynerigenin β-neribioside	Bioside	Air dried leaves		(Abe and Yamauchi. 1992)

22.	Δ^{16}- Adynerigenin β-odorobioside	Bioside	Air dried leaves		(Abe and Yamauchi. 1992)
23.	Oleandrigenin β-D-glucosyl-β-D-sarmentoside	Bioside	Air dried leaves		(Abe and Yamauchi. 1992)
24.	Δ^{16}-8β-Hydroxydigetoxigenin β-odoroside	Bioside	Air dried leaves		(Abe and Yamauchi. 1992)
25.	3-*O*-β-gentiobiosyl-3 β, 14-dihydroxy-5α, 14β-pregnan-20-one.	Pregnane Glycoside	Leaves		(Yamauchi *et al*., 1992)
26.	21-*O*-β-D-glucosyl-14, 21-dihydroxy-14β-pregn-4-ene-3, 20-dione.	Pregnane Glycoside	Leaves		(Yamauchi *et al*., 1992

27.	Kaneroside	Glycosides	Fresh, undried leaves		(Siddhiqui *et al*., 1987)
28.	Neriumoside	Glycosides	Fresh, undried leaves		(Siddhiqui *et al*., 1987)

CONCLUSION

People have been using herbal medicines for centuries for safety, efficacy, and lesser side effects. By and large, the pharmaceutical industry is focused towards design and development of new innovative/indigenous plant based drugs through investigation leads from traditional systems of medicine.The industry is always in search of new molecules for management of various diseases. This paper is focussed on screening of the literature available on Nerium oleander. The plant possesses various therapeutic properties. Future research needs to be targeted in exploring all its therapeutic benefits along with coping up with the undesirable toxic effects.

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