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Review article

A concise review on *Nerium oleander* L. - An important medicinal plant

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Abstract: *Nerium oleander*, commonly known as oleander, is an important medicinal plant in Indian folk medicine. It is one of the best pharmacognostic devices available in now-a-days. The modern as well as traditional uses make this plant much more valuable. Oleander is cultivated recently in pots and hence, large scale propagation of plant material for commercial use has great importance. This plant species also produces secondary metabolites such as alkaloids, flavonoids and steroids which have pharmacological applications. The important pharmacological activities are antibacterial, larvicidal, anticancer, antidiabetic activities. This review describes the evidence-based information regarding pharmacological activity as well as phytochemicals of this plant.

Keywords: Medicinal plant - Secondary metabolites - Antibacterial activity - Phytochemicals.

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INTRODUCTION

Nerium oleander L. is a small evergreen tree with 2–5 m in height and distributed in different geographical and ecological places (Fig. 1). In Bengali the common name is 'Karabi'. This plant is originated in the Mediterranean region and Indo-Pakistan subcontinent (Patel 2010). *Nerium oleander* is a drought-tolerant plant and belongs to the Family Apocynaceae. The leaves are 5 to 20 cm long, acuminate or acute, shortly petiolate, narrow, with a coriaceus dark-green blade. Flowers are produced in terminal cluster about 5 cm in diameter with five petals and different colours vary from lilac, salmon, carmine, deep to pale pink, purple, copper, apricot, orange, white and yellow. The fruit consists of a narrow follicle of 7.5 to 17.5 cm long and opens to disperse fluffy seeds. This plant can be propagated by seed (Pagen 1988) and shows great variability in seedling populations.

Nerium oleander is widely grown as an ornamental plant in tropical, subtropical and temperate regions due to its profuse flowering which are long lasting along with their moderate hardiness (Kingsbury 1964, Hardin & Arena 1974). It is used for screens, hedging along highways, planting along beaches. It is able to form attractive small trees by leaving just a few stems. In Northern regions it may be grown as an indoor or patio plant. Beside these all, the plant showed antibacterial (Mostaqul *et al.* 1999, Derwic *et al.* 2010), antimicrobial (Hussain *et al.* 2004), anti-inflammatory, antinociceptive (Erdemoglu *et al.* 2003) and antitumor (Ali *et al.* 2010) activity.

Systematic position of this plant

Kingdom:	Plantae
Division:	Angiosperms
Class:	Magnoliopsida
Subclass:	Asteridae
Order:	Gentianales
Family:	Apocynaceae
Genus:	*Nerium* L.
Species:	*oleander* L.

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Figure 1. *Nerium oleander* L. plant in flowering condition.

ETHNOMEDICINAL VALUE

Nerium oleander L. has been reported in ancient texts and folklore for many years. Literature survey shows that most of its plant parts such as flowers, leaf juice, bark and latex leaves are used for the treatment of microbial and fungal diseases. All parts of the plant are also used as therapeutic agent and have been used in folklore to treat variety of ailments. The leaves and bark are used as expectorant, heart tonic, diuretic, emetic and diaphoretic (Patel *et al.* 2010). Roots were boiled in water and helpful in skin complaints, herpes and also ringworm infection. Very small doses of leave juice are used in snake and other venomous bites. Juice of young leaves is effective in the cure of eye diseases. Root paste is administered in ulceration, haemorrhoids, various types of cancer and leprosy (Ahmed *et al.* 2006, Sikkarwar *et al.* 2009, Vinayagam & Sudha 2011, Chauhan *et al.* 2013). Oil obtained from the root is used in the treatment of leprosy and skin diseases (Saini 2010)**.** For the treatment of scabies and to reduce swellings, decoction of the leaves has been applied externally. The leaves and the flowers are emetic, diaphoretic, cardiotonic, diuretic, expectorant and sternutatory (Asha & Chakraborthy 2010). *N. oleander* is used in the treatment of ulcers and also causes abortion (Hseini & Kahouadji 2007). In some areas of Morocco, Africa the leaves are used in maceration and in external friction tale scabies, hair loss, lice, diabetes and toothache (Lahsissene *et al*. 2009).

BIOLOGICAL ACTIVITIES

Antimicrobial activity

The roots of *Nerium oleander* possessed a new cardenolide, 12β- hydroxy- 5β- carda-8, 14, 16, 20 (22) – tetraenolide which showed antibacterial and digoxin-like cardiac activities (Huq *et al.* 1999). Hussain & Gorsi (2011) showed that the ethanolic extract of the plant root and leaves was very effective against bacteria and fungi. Tannu *et al.* (2011) noted the anti-microbial activity of stem extracts of *Nerium oleander* on wistar strain albino rats against *Pseudomonas aeruginosa* and *Bacillus subtilis. N. oleander* showed effective against *Staphylococcus aureus* as observed by Wong *et al.* (2013). According to Jude (2013) *Nerium oleander*, showed the highest inhibitory zone against *Klebsiella pneumoniae Proteus vulgaris*, *Salmonella typhi* and *Escherichia*

coli. As per the observation of Jeyachandran *et al.* (2010) the methanolic extract of *Nerium oleander* showed maximum zone of inhibition (28 mm) against *S. typhi*. Swai *et al.* (2010) showed that *B. subtilis* was found to be more sensitive than Gram negative bacteria. The ethanolic extract of *Nerium oleander* leaves showed highest bactericidal activity at 900 mg.ml^{-1} concentration against *Pseudomonas aeruginosa* (Malik *et al.* 2015). The ethanolic flower extracts of *N. oleander* showed anti-fungal activity *in vitro* against four important plant pathogenic fungi *viz.*; *Fusarium oxysporum, Alternaria alternata, Fusarium solani* and *Rizoctonia solani* using agar dilution bioassay. Oleander exhibited the best inhibition against *F. oxysporum* and *F. solani* (Hadizadeh *et al.* 2009). Essential oil is obtained from the flowers of *N. oleander* and showed *in vitro* antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa* and *Staphylococcus aureus*. It also showed a very effective bactericidal activity with minimum inhibitory concentrations (MIC) ranging from 1.45 to 5.10 mg.ml^{-1} (Derwich *et al.* 2010).

Larvicidal activity

The bark, stem, leaves, flowers and roots of *Nerium oleander* possess insecticidal and anti-feedant property against *Plutella xylostella* (Gupta & Thorsteinson 1966, Jacobson 1975, Grainge *et al.* 1984). This plant has been also reported for larvicidal activity against *Aedes aegypti* by Komalamisra *et al.* (2005). Insect growth regulatory activity against *Anopheles stephensi* and *Culex quinquefasciatus* of this plant also recorded (Pushpalatha *et al*. 1995). The aqueous leaf extract of *Nerium oleander* were exhibited ovicidal and larvicidal properties (Kumar *et al.* 2012) and for ovicidal and adulticidal activity of this plant against *Anopheles stephensi* was also recorded (Roni *et al.* 2013). *Culex quinquefasciatus* larval mortality was tested against *Nerium oleander* crude hexane and aqueous flower extracts by Raveen *et al. (*2014). It was revealed that flower extract with hexane possessed high larvicidal activity when compared to aqueous extract with LC_{50} values of 102.54 and 61.11 ppm after 24 and 48 hours.

Antidiabetic activity

Shikkarwar *et al.* (2009) studied antidiabetic activity of this plant. Neither exact biologically active components responsible for anti-diabetic activity have not been reported nor, the exact mode of action was reported previously. They found that single dose of ethanolic extract (300 mg.kg^{-1} bw) of *Nerium indicum* has more significantly ($P<0.01$) reduced the blood glucose level as compared to seventh day of their study. The chloroform extract (500 mg.kg^{-1} bw) showed significant reduction of blood glucose after one hour while the ethanolic extract showed significant reduction after three hours. However, the water extract of this plant did not able to reduce glucose level at sub-acute level. The effects of various solvent extracts on glucose tolerance level in normal rats were done. After 30 minutes glucose administration, the blood glucose level peak increased rapidly from the fasting value and then subsequently decreased. Glibenclamide treated group prevented glucose induced hyperglycemia significantly at 30 min and 90 min (171.83±4.214 and 106.16±4.316) as compared to control (167.83±2.301 and 146.83±2.960) respectively. Highest glucose tolerance in *Nerium oleander* extracts was observed in chloroform extract (121.00±2.966) and lowest glucose tolerance was observed in aqueous extract (155.33 ±3.018) in 90 minutes. The activity of *Nerium oleander* observed in chloroform extract showed that the diabetic rats had lower body weights, high blood glucose level as compared to normal rats. Beside this orally administered *Nerium oleander* chloroform extract and ethanolic extract significantly increased the body weight and decreased blood glucose level in diabetic rats (Sikkarwar *et al.* 2009).

Anticancer activity

Ali and co-workers (2009) was able to extract essential oil from the flowers of the oleander. It showed antitumor activity on the cell lines, Ehrlich Ascites Carcinoma (EAC). Pathak *et al.* (2000) used different amount of Anvirzel (1.0 ng.ml^{-1} to 500 microgram.ml^{-1}) or Oleandrin (0.01 ng.ml^{-1} to 50 microgram.ml^{-1}) in both continuously treated and pulse-treated/recovery Cell cultures. Both Oleandrin and Anvirzel were able to induce cell killing in human cancer cells, but not in murine cancer cells.

PHYTOCHEMICALS

High quantity of polyphenols is present in the leaves of *Nerium oleander* as revealed by Siham *et al.* (2014). Thus, different fractions of the phenolic compound were shown by HPLC analysis. The cinnamic acid was the major component and other components were epicatechine, catechin and chlorogenic acid. The aqueous extract of leaves of *Nerium oleander* yielded 2.3% of crude polysaccharide. Major of the fractions was pectic

polysaccharide which is composed of arabinose, galacturonic acid, galactose, and rhamnose. Two new coumaryl oxy-triterpenoids, neriucoumaric and isoneriucoumaric acids have been isolated from fresh leaves of *Nerium oleander*. The preliminary phytochemical screening showed that the leaves of this plant possess carbohydrates, flavonoids, alkaloids, steroids, cardiac glycosides and tannins (Yadav *et al.* 2013). Siddiqui *et al.* (2012) reported oleanderocinoic acid, a pentacyclic triterpene, flavonoid glycosides,quercetin-5-O-[α-L-rhamnopyranosyl-(1→6)]-β-Dglucopyranoside and kaempferol-5-O-[α-L-rhamnopyranosyl- (1→6)]-β-D-glucopyranoside and a cardenolide, oleandigoside found in the leaves of Nerium oleander this compounds showed The growth inhibitory and cytotoxic acrivites against MCF-7, human breast cancer cell lines using sulforhodamine B assay. Two new compounds heptacosane-3-enyl-5- hydroxyhexanoate and 4-oxooctyl-2-hydroxyundecanoate were isolated by Sharma *et al.* (2012) from the stems of *Nerium oleander*. Polysaccharide fraction was isolated from the hot water extract of flowers of this plant using ethanol precipitation, cetyltrimethylammoniumbromide (CTAB) complexing, gel permeation chromatography and anion exchange chromatography. It has been found to contain L-rhamnose, L-galactose and D-galacturonic acid (Qun *et al.* 2010). Siddiqui *et al.* (1995) reported two novel cytotoxic pentacyclic triterpenoids ciskarenin (3-β-hydroxyphenoxy-28-Z-p-coumaroyloxy-urs-12-en- 27-oic acid) and trans-karenin(3-β-hydroxy-28-E-pcoumaroyloxy- urs-12-en-27-oic acid) from *N. oleander* leaves. A new labdane diterpene, oleanderoic acid and a new triterpene, oleanderen were isolated from the fresh, leaves of *Nerium oleander* (Siddiqui *et al.* 1987). Siddiqui *et al.* (1986) had been isolated Kaneroside and neriumoside,type of cardiac from the fresh, undried, winter leaves of *Nerium oleander* and their structures evaluated 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 by spectral and chemical studies.

CONCLUSION

From the review of the existing work it was concluded that *N. oleander* has been used in the treatment of skin diseases, cancer, diabetes, inflammation ,CNS depression and also any other microbial infection. Larvicidal activity also found. Various bioactive compounds isolated from different parts of this plants. So it is an utmost of importance to explore its potential in the field of medicinal and pharmaceutical sciences for novel application. As *N .oleander* is a popular remedy among the various ethnic groups, this plant is used in Ayurvedic and traditional medicine. So further or more work is needed to investigate the therapeutic potential of this plant.

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