

Pharmacognostical study and Biological potential of *Nerium oleander* Linn

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Abstract: Medicinal plants are used all over the world in traditional and ethnological medicine. Medicinal plants include various types of plants used in herbal medicine, some of which have medicinal properties. These medicinal plants are rich source of materials that can be used in drug development and synthesis. Sushruta Samhita and Charaka Samhita form the basis of the Ayurvedic medical system, in which thousands of plants are used therapeutically. *Nerium oleander* is an important medicinal plant in traditional Indian medicine. It is commonly known as Kanner. In Sanskrit medical literature, the plant is described as spicy and poisonous. Two powerful cardiac glycosides, oleanderin and nerium, are toxic compounds isolated from all parts of the plant. The leaves, stems, bark, roots and flowers of the oleander plant are used to treat various ailments such as heart disease and asthma, corns, epilepsy, cancer, painful catamenial periods, leprosy, malaria, ringworm, upset stomach, and genital disease; and to cause abortions. *Nerium Oleander* has many secondary metabolites with important pharmacological uses such as flavonoids, alkaloids, steroids, cardiac glycosides, etc., which have significant pharmacological applications. This review describes the pharmacognostic study, phytochemical screening and biological potential of *Nerium oleander*.

Keywords: *Nerium Oleander*, Phytochemicals, Pharmacognosy, Pharmacological Activities.

I. INTRODUCTION

Nerium Oleander is an evergreen shrub or little tree with white latex reaching up to 2-5 m in height within the dogbane family Apocynaceae. It is a crucial medicinal plant in Indian folk medicine. It is known as oleander from its superficial likeness to the unrelated plant Olive olea¹.

Nerium oleander is native to Mediterranean regions. Distributed within the Himalayas from Aisan country westwards to Kashmir up to 1950m, extending to Baluchistan, Afghanistan and located throughout Indian gardens². *Nerium oleander* is widely grown as an ornamental plant in tropical, subtropical and temperate regions because of its exuberant flowering which are long lasting along with their moderate hardiness^{3,4}.

Nerium oleander (pink, red, white) and *Thevetia peruviana juss* (yellow) these are two common oleander are found⁵. All parts of the *Nerium*, especially roots, were known to be highly poisonous when taken internally. The most significant toxic principle is that the 2 potent cardiac glycosides (oleanderin and neriine) which can be isolated from all parts of the *Nerium oleander* are similar in activity to digitalis⁶. There are a large number of secondary metabolites found in plants such as flavonoids, alkaloids, steroids, cardiac glycosides which have significant pharmacological applications.

Oleander was used by primitive folks as arrow and dart poisons. Despite its well-recognized toxic potential, oleander has been used for centuries in traditional medicine for numerous ailments such as heart conditions, asthma, corns, epilepsy, cancer, painful menstrual periods, leprosy, malaria, ringworm, indigestion, and venereal disease; and to cause abortions⁷. Roots of *Nerium oleander* shows healing properties for haemorrhoids and ulcers. Tincture of flowers used as cardiotonic and roots acts as a CNS- depressant and spasmolytic².

II. PLANT PROFILE



Figure: *Nerium Oleander*



Figure: Dried roots *Nerium oleander*

Botanical name: *Nerium oleander*

Family: Apocynaceae

Marathi name: Kanher

Hindi name: Kaner, kanail

English name: Indian oleander

Synonyms: Soland, lorier bol, rosebay, rose laurel, kaner, Karavira, Viraka, Ashvamarka, Hayamaara, auripushpa, Siddhapushpa (white flower variety), Raktapushpa, Raktaprasava, Ravipriya (Red flowered variety).

III. MORPHOLOGY

The leaves are 5-23 cm long and 1-3.9 cm broad, simple, lanceolate, with an entire margin, narrow, acute in the apex, short-stalked and dark or grey-green in colour. Flowers are produced in terminal clusters about 5 cm in diameter with five petals and different colours vary from red, pink, white and yellow. The fruit consists of a narrow follicle of 7.5-17.5 cm long and opens to disperse fluffy seeds. Plants can be propagated by seeds and show great variability in the seedling population. Stem is erect, woody, solid, branched, green or grey with latex. Roots are 0.5- 3.9 cm in diameter, crooked in shape, prominent, usually branched and tuberous with grey colour^{8,9}.

3.1 Phytoconstituents

The entire *Nerium oleander* plant contains various phytochemicals. Oleanderin and neriine are the main cardiac glycosides found in all parts of plants. The leaves of *N. oleander* are the cardiac glycosides kaneroside, neriumoside, digitoxigenin, alpha-L-olendroside-5 α -adenerin, and other glycosides. Odoroside is a cardioactive glycoside. Gentiobiosyl-oleandrin, odoroside A and oleandrin were the main glycosides identified. Root contains cardioactive glycosides called flumerizin, alpha-amirin, beta-sitosterol, kaempferol, and ododosides A-H, which are extracted from the root bark². In addition many other pharmacologically active compounds have been identified in plants, including folinerin, rosagenin, rutin and oleandomycin have been identified in the plant¹⁰. The bark contains scopoletin and scopoli^{11,12}. The seeds contain glucosides (oleandrine, odorosides, adigoside). There are also moderately active cardenolides (adenergic heterosides) and inactive cardenolides (adenergic heterosides, foxglove), triterpenoids, a resin, tannins, glucose, a paraffin, ursolic acid, vitamin C and an essential oil. Active cardenolides (heterosides of adynergenine) and inactive cardenolides (heteroside of adynergenine, of digitalose), triterpenoids, a resin, tannins, glucose, a paraffin, ursolic acid, vitamin C and an essential oil. Hydromethanolic leaf extract of *Nerium oleander* with potent anti-diabetic activity

is reported to contain high concentration of p-coumaric acid, jasmonic acid, gallic acid, vanillic acid, 4-hydroxybenzoic acid and rutin¹³. The leaves contain the most saponins, riboflavin, thiamine and tannins, while the roots contain a lot of alkaloids and ascorbic acid. An in vitro study examining the antioxidant activity and free radicals of oleander showed that oleander root has the highest total leaf content and the highest total phenol content (87.38 ± 0.16 mg/mL gallic acid equivalent per 100 mg plant extract). Phenolic flavonoids (93.06 ± 0.03 mg/mL, corresponding to quercetin per 100 mg plant extract).¹⁴.

3.2 Phytochemical Screening

Phytochemical screening disclose *Nerium Oleander* leaf, stem and roots to contains tannin, phlobatannin, cholesterol, terpinoid, glycoside, phenolics, flavonoid, steroid, anthraquinone, saponin, carbohydrate, alkaloid and protein.

A. Alkaloids

Alkaloids are a class of natural products containing nitrogen. Many of them are used in medicinal purpose such as vinblastine and vincristine as antitumor agents, reserpine as antihypertensive and quinine as antimalarial. *N. Oleander* has been claimed to have anti-tumor activity from hundreds of years and also been tested successfully for anti-cancer activity¹⁵. Quite a high percentage of alkaloid has been detected in all the parts of the plant among which the root (67.86 ± 1.54 g/100g) and leaves (63.28 ± 2.38 g/100g) contain the highest amount¹⁶.

B. Flavonoids

Flavonoids, contains benzopyrone, are polyphenolic plant secondary metabolites which act as antioxidants and also have cardio protective role¹⁷. Flavonoids suppress the progression of cancer by inhibiting estrogen producing enzymes. For example, estrogen synthase which couples estrogen to its receptor is inhibited by flavonoids¹⁸. The percentage of total flavonoids estimated in leaf, stem and root were 8.05 ± 0.19 mg/g, 7.48 ± 0.87 mg/g and 8.11 ± 0.88 mg/g respectively and the total plant had a yield of 7.77 ± 0.61 mg/g¹⁶.

C. Saponins

Saponins are natural anticancer agents¹⁹. Belongs to the class of glycosides. They possess hemolytic activity and cholesterol binding property and also inhibit microbial proliferation^{20,21}. In *N. Oleander*, very high amount of saponin content has been found in the underground part. Overall saponin content in the whole plant is high (10.57 ± 0.37 g/100 g). The leaf, stem and root have been estimated to contain 12.56 ± 0.67 g/100 g, 9.06 ± 0.75 g/100 g and 12.4 ± 0.45 g/100 g of saponin,¹⁶.

D. Tannins

Pharmacologically tannins shows antiviral activity. Presence of high level of tannins Various enteric viruses, polio virus and herpes simplex virus have been found to get inactivated. They also acts against antimicrobial agents²². The leaf contain more tannin (22.53 ± 0.86 mg/100g) compared to stem (16.65 ± 0.87 mg/100g) and root (18.12 ± 0.44 mg/100g)¹⁶.

E. Phenolic Compounds

Natural phenols are present in varying concentrations in all plants, primarily for their medicinal value. They are potent vasodilators²³ and also having active antioxidants property having hydroxyl groups possessing potent scavenging activity²⁴. Very high quantity of total phenolic compound has been detected in all the parts of *N. Oleander*. The green stem contains a cream-colored, sticky, viscous, resinous sap which is traditionally used as antiinflammatory agent. The whole plant had a very high phenol content (74.70 ± 3.39 mg/g). Roots are the most abundant (82.53 ± 2.41 mg/g), followed by stems (76.31 ± 1.63 mg/g) and leaves (69.86 ± 2.32 mg/g)¹⁶.

F. Proteins

The whole plant possesses a very high quantity of protein (39.21 ± 0.65 mg/g) leaf contains the highest amount (43.76 ± 1.60 mg/g). With rich in protein, *N. Oleander* showed to possess a high quantity of lipid substances which adds to its energy content. Oleander leaves contain the highest amount of lipids compared to other parts (25.61 ± 0.07 mg/g)¹⁶. Vitamin B2 or riboflavin has anti-jaundice, anti-migraine and pain relieving effect. Riboflavin in combination with ultraviolet ray has been proved to kill harmful pathogens found in blood which cause disease. *N. Oleander* contain satisfactory amount of riboflavin. Leaf possesses the highest quantity (0.42 ± 0.04 mg/100g). Thiamine is also estimated in *N. Oleander*. The leaf contains the highest amount (0.48 ± 0.05 mg/100g) followed by stem (0.43 ± 0.06 mg/100g) and root (0.40 ± 0.06 mg/100g). Ascorbic acid or vitamin C is a potent antioxidant and terminate the chain radical reactions by electron transfer and scavenges free radicals. *N. Oleander* extracts may prove to be a good antioxidant due to the presence of high concentration of ascorbic acid. The roots contain highest amount of ascorbic acid (1.01 ± 0.06 mg/100g) followed by the leaves (0.88 ± 0.02 mg/100g)¹⁶.

Secondary Metabolites	<i>Nerium oleander</i> root
Tannins	+
Phlobatannin	+
Cholesterol	-
Terpenoid	+
Glycoside	+
Phenolics	+
Flavonoid	+
Steroid	-
Anthraquinone	+
Saponin	+
Carbohydrate	+
Protein	+
Alkaloid	+

Table 1: Phytochemical screening of Nerium Indicum

3.3 Ethanomedicinal Uses

Neium oleander L. is an important medicinal plant, traditional as well as modern uses make this plant more valuable. Oil obtained from the roots used to treat skin diseases and leprosy. To treat microbial and fungal diseases leaf juice, flowers, bark and latex of the leaves were used. Leaves juice is used in snake bites and very effective in the cure of eye diseases. Root paste is effective in various cancers, ulceration and haemorrhoids. Leaves and bark are used as heart tonic, diuretic, expectorant, emetic and diaphoretic. *Nerium oleander* used to induce abortion. Decoction of the leaves applied externally to treat scabies and to reduce swellings²⁵. Root rubbed with water, is used to alleviate sexually transmitted diseases. The paste of *Nerium oleander* used in alopecia². Green dye extracted from the oleander flowers is used to treat skin diseases and also has a healing and anti- inflammatory effect. The juice extracted from the peel is used to treat ear pain²⁶.

IV. PHARMACOLOGICAL ACTIVITIES

4.1 Anti- Caner Activity

The essential oil obtained from oleander flowers has shown antitumor effects on the Ehrlich ascites cancer cell line when the oil concentration is increased²⁷. *Nerium oleander* leaf, stem and root extracts were tested against the leukemic cell lines HL60 and K562. The leaf and root extracts were more cytotoxic than the stem extracts. It has also been shown that cytotoxic effects are mediated by inhibition of the P-glycoprotein pump in leukemic cells²⁸. Dichloromethane extracts from leaves and flowers showed high cytotoxic effects against T47D, HepG-2 and K562 cell lines²⁹. The

cardenolide-containing fraction of the cold water extract of oleander leaves showed antitumor effect (IC₅₀ 0.85 µg / ml) against 36 human tumor cell lines ³⁰. Anvirzel, an extract of *Nerium oleander* (1.0 ng/ml to 500 microg/ml and oleandrin (0.01 ng/ml to 50 microg/ml) were able to treat human cancer cells but not mouse cancer cells, resulting in apoptosis. The lethality of oleandrin is greater than that of anvirzel ³¹.

4.2 Antimicrobial Activity

The antibacterial effect of root, bark and leaf extracts of *Nerium oleander* against *Bacillus pumilus*, *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Aspergillus niger* was studied. Chloroform, methanol and ethanol extracts of *Nerium oleander* showed high activity against all tested bacteria (growth inhibition zone 20-23 mm after 24 hours of incubation) ³². Ethanol leaf extract showed bactericidal activity against *Pseudomonas aeruginosa*. The methanol extract showed maximum inhibition of *S. typhi*. The oil extracted from oleander flowers has shown antibacterial action against *E. coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. *Nerium oleander* stem extract showed antibacterial activity in albino mice against *Pseudomonas aeruginosa* and *Bacillus subtilis*. From the root of *Nerium oleander* 12β-hydroxy-5β-carda-8,14, 16, 20 (22) - Tetraenolide is a new cardenolide with antibacterial action and digoxin-like cardiac activity ²⁵.

4.3 Cardiotonic Activity

Evidence for the cardiac effects of crude ethanol extract of dried leaves on contraction force, heart rate, and cardiac flow was investigated in isolated guinea pig hearts. Under the influence of 100 mg / ml of the extract, the heart rate increased from 28 beats / min to 41 beats / min, blood flow increased from 0.4 ml / min to 1.9 ml / min, and the amplitude of myocardial contraction decreased 22 to 49 mm ³³.

4.4 Antidiabetic Activity

Hydromethanolic leaf extract (50 and 200mg/kg bw, for 20 days) of *Nerium oleander* was studied in alloxan induced diabetes in mice. The extract possessed antihyperglycemic activity, it reduced blood glucose level by 73.79% after 20 days of treatment. Oral glucose tolerance test revealed increase in glucose tolerance as evident by 65.72% decrease in blood glucose in 3h post treatment. Percentage decrease in numerous liver marker enzymes were important in conjugation with decrease in triglyceride and cholesterol levels, displaying potent antihyperlipidemic activity ¹³. We studied the effects of oleander extract (250 mg/kg bw/day for 4 weeks) on insulin, glucose levels, and the activity of several liver enzymes compared with a sulfonylurea (glimepiride) in streptozotocin-induced diabetic rats. The diabetic mice showed hypoinsulinemia and hyperglycemia compared to the control group. The results showed that glimepiride and herbal extracts increased insulin and glucose levels. Treatment of diabetic rats with glimepiride or oleander extract also increased the activity of liver enzymes ³⁴.

4.5 Anti- Inflammatory Activity

Anti- inflammatory activity of 500 mg/ kg dose of ethanolic and aqueous extract of the *Nerium oleander* was studied on carrageenan – induced paw edema model. Ethanolic extract of dried leaves shows least amount of inflammatory reaction ³⁵.

4.6 Antinociceptive Activity

Dried as well as fresh flowers and leaves of *Nerium oleander L.*, were shown to possess valuable antinociceptive activity against p- benzoquinone- induced abdominal contractions in mice ³⁶.

4.7 Larvicidal Activity

The aqueous extract of *Nerium oleander* were showed ovicidal and larvicidal properties ³⁸. Whole plant of *Nerium oleander* possess insecticidal and anti- feedant activity against *Plutella xylostella* ^{39,40}. Ovicidal and adulticidal activity of *Nerium oleander* against *Anopheles stephensi* was also done . *Culex quinquefasciatus* larval activity was done against

Nerium oleander with crude hexane and aqueous extract. Flower extract with hexane showed significant larvicidal activity than aqueous extract ²⁵.

4.8 Hepatoprotective Activity

The methanolic flower extract of *Nerium oleander* was investigated against CCl₄ mediated hepatotoxicity in rats. The revealed that the flower extract improves the damaged liver of rats by reducing the levels of glutamic transaminase, glutamic- pyruvic transaminase, alkaline phosphatase, bilirubin and increasing the level of superoxide dismutase which gives maximum hepatotoxic protection at the high dose of *Nerium oleander* extract at 400 mg/kg dose level ^{26,41}.

4.9 Antioxidant Activity

The leaves and flower extract of *Nerium oleander* for antioxidant effect were evaluated by DPPH assay. The methanolic extract of the leaves and flowers shows high antioxidant activity ⁴². The antioxidant activity of water, methanol, water: methanol, and acetone extracts of *Nerium oleander* was studied by employing various in-vitro assay (DPPH free radical scavenging, reducing power and total antioxidant capacity). The methanolic and aqueous methanolic extracts were the most potent antioxidant extract ⁴³.

V. CONCLUSION

Nerium oleander is one of the important medicinal plant known for its curative effects in various diseases. *Nerium oleander* acts as a antidiabetic, anti- inflammatory, hepatoprotective, cardiogenic, antioxidant, antibacterial, antiviral, etc., The present review discusses the pharmacognostic study, phytochemical screening, ethnomedicinal uses, and biological potential of *Nerium oleander*.

REFERENCES

- [1]. Taxonomic and Botanical description from http://en.wikipedia.org/wiki/Nerium_oleander accessed on 24, 10, 2011.
- [2]. Khare CP. Encyclopedia of Indian Medicinal Plants, Springer-Verlag-Heidelberg, 2004, 328-330.
- [3]. Kingsbury JM (1964) Poisonous plants of the United States and Canada. Soil Science 98(5): 349
- [4]. Hardin JW & Arena JM (1974) Human Poisoning from Native and Cultivated Plants. 2nd eds. Duke University Press, Kingsport, Tennessee.
- [5]. Langford, S.D. and Boor, P.J: Oleander toxicity: an examination of human and animal toxic exposures. Toxicology 1996; 109, 1–13
- [6]. Shumaik G.M., W.U. A.W., Ping A.C. (1988). Oleander poisoning: Treatment with digoxin- specific Fab antibody fragments. Ann Emerg Med. 17:732–5.
- [7]. Radford DJ, Gillies AD, Hinds JA, Duffy P. Naturally occurring cardiac glycosides. *Med J Aust.* 1986;144(10):540-544.3086679.
- [8]. Pagen FJJ (1988) Series of revisions of Apocynaceae. XX. Oleanders: *Nerium* L. and the oleander cultivars. Agricultural University Wageningen Papers 87(2): 1–113.
- [9]. Rashmi Runa and Trivedi M.P. (2014). Effect of various growth hormone concentration and combination on callus induction, mature of callus and callogenic responses of *N. odorum*. J. Apply Biochem and Biotech. 172(5): 2562-2570.
- [10]. Siddiqui BS, Sultana R, Begum S, Zia A, Suria A. Cardenolides from the methanolic extract of *Nerium oleander* leaves possessing central nervous system depressant activity in mice. *J Nat Prod* 1997;60:540-4.
- [11]. Rangaswami S, Reichstein T. *Helv. Chim. Acta.* 1949; 32: 939.
- [12]. Hafeez F. Studies in the chemical constituents of *Nerium oleander* (Kaner). 1987.
- [13]. P. Dey, M.R. Saha, S.R. Chowdhuri, A. Sen, M.P. Sarkar, B. Haldar, T.K. Chaudhuri, Assessment of anti-diabetic activity of an ethnopharmacological plant *Nerium oleander* through alloxan induced diabetes in mice, *J. Ethnopharmacol.* 161 (2015) 128–137.

- [14]. Chaudhuri Dey, Mandal Chaudhuri, Comparative assessment of the antioxidant activity and free radical scavenging potential of different parts of *Nerium indicum*, *Med. Plants Int. J. Phytomedicines Relat. Ind.* 4 (1) (2012) 54–69.
- [15]. Pathak S, Multani AS, Narayan S, Kumar V, Newman RA. Anvirzel™, an extract of *Nerium oleander*, induces cell death in human but not murine cancer cells. *Anticancer Drugs*, vol. 11, 2000 pp. 455-463.
- [16]. Priyanka Dey, Subhrajyoti Roy, Tapas Kumar Chaudhuri A quantitative assessment of bioactive phytochemicals of *Nerium indicum*: An ethnopharmacological herb. 2012, 3(4), 579-587.
- [17]. Hertog MG, Feskens EJ, Hollman PC, Katan MB, Kromhout D. Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. *Lancet*, vol. 342, no. 8878, 1993 pp. 1007-11.
- [18]. Okwu DE, Omodamiro OD. Effects of hexane extract and phytochemical content of *Xylopia aethiopia* and *Ocimum gratissimum* on the uterus of guinea pig. *Biol Res*, vol. 3, no. 2, 2005 pp. 40-44.
- [19]. Rao AV, Sung MK. Saponins as anticarcinogens. *Jn nutrition*, vol. 125, no. 3, 1995 pp. 717S-724S.
- [20]. Asl MN, Hosseinzadeh H. Review of pharmacological effects of *Glycyrrhiza* sp. and its bioactive compounds. *Phytother Res*, vol. 22, no. 6, 2008 pp. 709–24.
- [21]. Xu R., Zhao W, Xu J, Shao B, Qin G. Studies on bioactive saponins from Chinese medicinal plants. *AdvExp Med Biol*, vol. 404, 1996 pp. 371–82.
- [22]. Bajaj YPS. Medicinal and aromatic plants (Biotechnology in agriculture and forestry). Berlin: Springer, 1993. ISBN-13: 978-3540560081.
- [23]. Padilla E, Ruiz E, Redondo S, Gordillo-Moscoso A, Slowing K, Tejerina T. Relationship between vasodilation capacity and phenolic content of Spanish wines. *Eur J Pharmacol*, vol. 517, no. 1-2, 2005 pp. 84–91.
- [24]. Dimitrios B. Sources of natural phenolic antioxidants. *Trends Food Sci Tech*, vol. 17, 2006 pp 505–512.
- [25]. Sankar Narayan Sinha and Karabi Biswas, A concise review on *Nerium oleander* L. -An important medicinal plant, 3(2): 408–412, 2016.
- [26]. Priyanka Dey, Tapas Kumar Chaudhuri, Pharmacological aspects of *Nerium Indicum* Mill:A comprehensive review, 2014; 8(16) :156- 162.
- [27]. Ali HFM, El-Ella FMA and Nasr NF. Screening of chemical analysis, antioxidant, antimicrobial and antitumor activity of essential oil of oleander (*Nerium oleander*) flower. *Intern J of Biolog Chem* 2010; 4(4):190-202.
- [28]. Turan N, Akgün-Dar K, Kuruca SE, Kiliçaslan-Ayna T, Seyhan VG, Atasever B, Meriçli F and Carin M. Cytotoxic effects of leaf, stem and root extracts of *Nerium oleander* on leukemia cell lines and role of the p-glycoprotein in this effect. *J Exp Ther Oncol* 2006; 6(1):31-38.
- [29]. Namian P, Talebi T, Gerami KG et al. Screening of biological activities (antioxidant, antibacterial and antitumor) of *Nerium oleander* leaf and flower extracts. *American J of Phytomed and Clinical Therap* 2013; 1(4): 378-384.
- [30]. Rashan LJ, Franke K, Khine MM, Kelter G, Fiebig HH, Neumann J and Wessjohann LA. Characterization of the anticancer properties of monoglycosidic cardenolides isolated from *Nerium oleander* and *Streptocaulon tomentosum*. *J Ethnopharmacol* 2011; 134(3):781-788.
- [31]. Pathak S, Multani AS, Narayan S, Kumar V and Newman RA. Anvirzel, an extract of *Nerium oleander*, induces cell death in human but not murine cancer cells. *Anticancer Drugs* 2000;11(6):455-463.
- [32]. Hussain MA and Gorski MS. Antimicrobial activity of *Nerium oleander* Linn. *Asian Journal of Plant Sciences* 2004; 3(2):177-180.
- [33]. Adome RO, Gachihi JW, Onegi B, Tamale J, Apio SO. The cardiotoxic effect of the crude ethanolic extract of *Nerium oleander* in the isolated guinea pig hearts. *Afr Health Sci* 2003;3:77–82.
- [34]. Mwafy SN and Yassin MM. Antidiabetic activity evaluation of glimepiride and *Nerium oleander* extract on insulin, glucose levels and some liver enzymes activities in experimental diabetic rat model. *Pak J Biol Sci* 2011; 14(21): 984-990.
- [35]. Erdemoglu N, Küpeli E, Yeşilada E. Anti-inflammatory and antinociceptive activity assessment of plants used as remedy in Turkish folk medicine. *J Ethnopharmacol* 2003;89:123–9.

- [36]. Zia A, Siddiqui BS, Begum S, Siddiqui S, Suria A. Studies on the constituents of the leaves of Nerium oleander on behavior pattern in mice. J Ethnopharmacol 1995;49:33–9.
- [37]. Kumar G, Karthik L, Rao KVB, Kirthi AV & Rahuman AA (2012) Phytochemical composition and mosquito controlling property of Nerium oleander leaves (Apocynaceae) against Culex tritaeniorhynchus and Culex gelidus (Diptera: Culicidae). Asian Pacific Journal of Tropical Biomedicine 2: 1–6.
- [38]. Gupta PD & Thorsteinson AJ (1960) Food plant relationships of the diamondback moth (Plutella maculipennis (Curt)). I. Gustation and olfaction in relation to botanical specificity of the larva. Entomologia Experimentalis et Applicata 3: 241–250.
- [39]. Jacobson M (1975) Insecticides from plants a review of the literature, 1954–1971. Agriculture Handbook 461, USDA, Washington, DC, 138 p.
- [40]. Singhal KG and Gupta GD. Hepatoprotective and antioxidant activity of methanolic extract of flowers of Nerium oleander against CCl₄-induced liver injury in rats. Asian Pac J Trop Med 2012; 5(9):677-685.
- [41]. Namian P, Talebi T, Germi KG et al. Screening of biological activities (antioxidant, antibacterial and antitumor) of Nerium oleander leaf and flower extracts. American J of Phytomed and Clinical Therap 2013; 1(4): 378-384.
- [42]. Al-Snai AE, Mousa HM, Majid WJ. Medicinal plants possessed hepatoprotective activity. IOSR Journal of Pharmacy 2019; 9(8): 26-56.