Goraksh J.Hase. *et al.* / *International Journal of Phytopharmacology.* 7(2), 2016, 63-67.

e- ISSN 0975 – 9328
Print ISSN 2229 – 7472

International Journal of Phytopharmacology

Journal homepage: www.onlineijp.com

IJP

PHYTOPHARMACOLOGY OF *NERIUM OLEANDER* L.– A REVIEW

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ABSTRACT

In recent years, the attempts have been made to investigate the drugs against infectious diseases. The *Nerium oleander* has been widely studied for presence of pharmacological active constituents by the number of recent scientific literature. The compounds like terpenes, steroids, polyphenols and flavanoids has been identified from the various parts of the plant. The phytochemical review on *N. oleander* has anthologized from the electronic databases viz., SCOPUS, Google Scholar, PubMed, Springer, Elsevier, ACS, Medline Plus and Web of Science. The *N. oleander* shows the biological activities like antinociceptive, antiinflammatory, antioxidant, anti-asthmatic, anticancer, hepatoprotective and antibacterial, antidiarrhoeal, antimicrobial, diuretic, antileukemic, immunomodulatory, larvicidal, antibacterial, anti-diabetic, antiulcer and molluscicidal activities are supported by the literature.

Key words: *Nerium oleander*, Pharmacological, Phytochemical etc.

INTRODUCTION

There are many natural crude drugs which have the potential to treat many disorders and illnesses, one of them is a *Nerium oleander*. It is an evergreen shrub, belongs to the family Apocynacae. It is a tropical and subtropical plant, and most commonly known as oleander. The plant is native to a broad area from Mauritania, Morocco and Portugal, and also typically occurs around dry stream beds.In Sri Lanka this plant is grown as an ornamental in gardens. The plant has been reported to be the hepatoprotective (Singhal, 2012), anticancer (Montano, 2013), antidiarrhoeal and cytotoxic (Hassan, 2011), larvicidal (Raveen, 2014), antihelmintic (Native, 2014), antiulcer (Sabira, 1998) etc.

The plant shows these activities and it may due to the presence of various phytoconstituents in the plant. The major phytoconstituents reported in this plant are kanersoide, neriumoside, cis and trans karenin, oleandrin, folinrin, adenerin, nerine, digitoxigenin, cardenolides, bufadienolides, ouabain, proscillaridin, 4-oxooctyl-2-hydroxy-undecanoate, heptacosane-3-enyl-5-hydroxyhexanoate, betulin, betulinic acid, stigmasterol, quercetin-5-O-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside and kaempferol-5-O-[α-L-rhamnopyranosyl- (1→6)]-β-D-glucopyranoside

The aim of the present review is to be document the literature on phytopharmacological aspect of NO plant.

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PHARMACOLOGY

Hepatoprotective activity

Singhal et al. (2012) studied hepatoprotective activity of methanolic extract of flowers against CCl_4 in rats. The hepatoprotective effects of MENO-F on serum biochemical parameters in CCl_4-intoxicated rats are showed a significant increase in serum AST, ALT, ALP and total bilirubin levels compared to control animals

(Group I). Pretreatment with MENO-F at 100, 200 and 400 mg/kg for 7 days (Groups IV, V and VI) showed significant hepatoprotection in terms of serum AST, ALT, ALP and total bilirubin levels compared to the toxic control group (Group II). Pretreatment with the standard hepatoprotective agent-Silymarin (Groups III) also decreased all measured serum biochemical activities towards normalness.

Wound healing activity

Rout et al., investigated Collagen is a major protein of the extracellular matrix and is the component that ultimately contributes to wound strength tannins promote the wound healing through several cellular mechanism, chelation of the free radicals and reactive species of oxygen, promoting contraction of the wound and increasing the formation of capillary vessels and fibroblasts and including keratinocyte proliferation, but do not act on the differentiation towards cornified cells 36, 37. The collagen composed of amino acid (hydroxyproline) is the major component of extra cellular tissue, which gives strength and support.

Antimicrobial activity

Chauhan et al. reported antibacterial activity of ethanolic extract by agar well diffusion method and diameters zone inhibition study. All the extracts displayed broad spectrum of activity against gram +ve bacteria and fungus. The *Nerium indicum* extracts decrease the microbial growth; this suggests that it having microbiostatic effects. The results obtained are encouraging as the methanolic, chloroform; hexane extracts have shown considerable antimicrobial activity.

Antioxidant activity

Zibbu and Batra et al. and Mohadjerani et.al. reported the amount of total polyphenol was higher in vitro extract of methanol while lower amount was determined in *in vitro* aqueous solution.In that research the total amount of phenolic content termed as mg gallic acid equilvent per g of dried material ranged from 2.628 in the acetone extract to 9.402 in the aqueous methanol extract and 8.547 in the acetone extract to 36.690 in the methanol extract for the leaves and flowers.

In this plant Lipolytic, larvicidal, cytotoxic, antiulcer, anti-diabetic activities are reported.

Phytochemistry

Relevant literature releated to chemical constituents from the plant *Nerium oleander L.* adimmission were collected from different sources viz. pubMed, science direct and scifinder database. The plant revealed the presence of medically active metabolites NO plant parts leaves reported carbohydrates, proteins, alkaloids, flavanoids, terepenoids, cardiac glycosides, tannins and saponins (Suganya, 2012). In vitro methanolic extract of NO contained higest amount of phenolic compound and exihibited the maximum antioxidant activity (Garima, 2011). The chemical constituent of NO leaves present pectic polysaccharide mainly galactomeric acid besides rhamnose, arabinose and galactose. The four new cardenolides monoglycosides, three new pregnanes, 21- hydroxypregna-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 NO plant (Pegah, 2013).

Neridiqinoside (Yamaguchi *et al.*, 1970 and Sabira B *et al.*, 1998

Molecular formula:C_{30} $H_{46}O_{8,}$ M.P. : 195.8 ± 196.5, UV (nm):219

IR (KBR cm^{-1}):3450 (-OH), 1780,1740 (α,β unsaturated γ lactone).

^{1}H- NMR: dd (1H 4.98,4.80 δ) J=18 Hz,1.5 hz.and J=18 and1.5 Hz, t(1H 5.85 δ,J=1.5 Hz), s(1H 1.00 δ and s(1H 1.05 δ) ,dd (1H 2.74 δ) J=9.5 and 6Hz) bs(4.05 δ), $w_{1/2}$=7.0 Hz 1H.

^{13}C NMR: (26.89,27.01,72.20,35.03,74.50,32.04,17.60, 36.94,35.54,35.19,22.47,40.38,50.42, 85.90, 29.86, 27.38, 51.84, 18.42,25.36, 174.30,73.37, 117.90, 174.20 C^{1}-C^{23}), 97.80, 31.71, 78.03, 67.19, 70.40, 16.80,55.73 (55.73) – C_1'-C_6'.

MS: 390.2410 [M^{+}],373.2318, 355.2252, 337.2108, 208.1161, 181.0882,161.0850,145.0901.

Digitoxigenin (Torbjordnr A *et al.*, 1990)

Molecular formula: $C_{23}H_{34}O_4$, M.P.: 252-253^{0} C , UV (nm): 290

IR (cm^{-1}):1100 (c-o), 1750(α, β- unsaturated ester).

^{1}H-NMR: 1.50 (1 α-H)),1.50(1β-H),1.52 (2 α-H),1.57(2β-H),4.12(3H),1.34(4α-H),1.89(4β-H),1.78(5H), 1.87 (6α-H),1.22(6β-H),1.25(7α-H),1.68(7β- H),1.56(8H), 1.62 (9H), 1.43(11α-H,1.38(11β H),1.38(12αH), 1.52(12βH), 2.12(15αH), 1.70(15βH), 1.86(16αH), 2.15 (16βH), 2.77(17H), 0.87(18H), 0.95(19H), 4.81(21H), 4.98 (21H),5.87(22H).

^{13}CNMR: 29.69 (C-1),27.93(C-2),66.79(C-3),33.36(C-4),36.00(C-5),26.49(C-6),21.19(C-7),41.84(C-8),35.52(C-9),35.41(C-10),21.37C-11),40.06(C-12),49.62(C-13),85. 54(C-14),33.16(C-15),26.91(C-16), 50.95(C-17),15.79(C-18),23.72(C-19),174.49(C-20),73.44(C-21),117.63(C-22),174.42^{d}(C-23).

MS: m/z = 374

Ouabain (Adrienne AT *et al.*, 1993)

Molecular formula: $C_{29}H_{44}O_{12}$,M.P.:190^{0}C, UV (nm):226

IR (cm^{-1}):1130(c-o),1745(α, β- unsaturated ester) ^{1}H-NMR: 5.07(1-H),2.19,2.05(2-H),4.09(1-H),2.22,1.71 (2-H),1.41(6-H),1.83,1.26(7-H),1.81(8H),1.64(9H), 3.95 (11H) ,1.67, 1.42(12-H),2.12,1.71(15-H),2.15,1.77(16-H),2.84(17-H),0.86(18-H),4.05,3.79(19-H),4.93(21-H),5.90(22-H),4.75(H-1'),3.82(H-2'),3.72(H-3'),3.33(H-4'), 3.68(H-5'),1.19(H-6'). ^{13}C NMR: 71.3(C1), 32.1(C2), 71.5(C3), 34.1(C4), 76.2(C5), 33.7(C6), 23.2 (C7),39.9(C8),46.5(C9), 45.3(C10), 68.8(C11), 49.3(C12), 50.9(C13),86.0(C14),32.5(C15), 27.5(C16), 50.4(C17),17.1(C18),59.1(C19), 179.0(C20), 78.5(C21), 122.3(C22),178.9(C23),98.8(C1'), 71.2(C2'),71.1(C3'),73.1(C4'), 69.6(C5'), 7.5(C6'). MS: $[M+H]^+$ m/z= 555.1834.

Kaemferol 4'-O- α-L-rhamnopyranaoside (Amany I *et al.*, 2008)
Molecular formula:-$C_{20}H_{20}O_{10}$, M.P.:- 182-185^{o}C, UV (nm, MeOH):275(4.01) and 365(4.04).
IR (KBR cm^{-1}): 3398,1750,1677,1290,1190,1069.
^{1}H-NMR: 12.40 (5-OH)), 6.15(d,1.8), 6.41(d,1.2), 8.10(d,9.0), 7.17(d,9.0),7.17(d,9.0), 8.10(d,9.0), 5.51 (d,3.0),3.77(brs),3.77(brs),3.55(brs),3.83(m),1.02(d,6).
^{13}CNMR:146.7(C2),136.3(C3),176.5(C4),161.4(C5),99.0(C6),164.5(C7),94.2(C8),156.9(C9),103.6(C10),124.9(C1'),129.8(C2'),117.1(C3'),159.0(C4'),117.1(C5'),129.8(C6'),98.4(C1"),70.1(C2"),68.1(C3"),72.0(C4"),68.2(C5"),CH_3 17.1 ,MS- m/z = 431.1120 [M-H].

Ursolic Acid (Amany I *et al.*, 2008)
Molecular formula:C_{30} H_{48} O_3, M.P.: 284^{o}C,UV (**λ_{max}**, MeOH): 212.5
IR (KBr cm^{-1}):3427 cm^{-1} (-OH), 1689.53 (C=O) ,2650, 2358.7.
^{1}H NMR: (δ 300 MHz),3.43 (brs,H_3,5.50 (brs H_{12}),2.52 (d J=11 Hz H_{18}),1.24 (S,H_{23}),1.02 (S,H_{24}),0.93 (S, H_{25}),1.05 (S,H_{26}),1.22 (S H_{27}), 0.97(S H_{29}),0.99 (S,H_{30}).
^{13} C NMR : (δ 75 MHz) : 38.4 (C1),28.1(C2), 78.1(C3),38.4(C4), 55.8(C5),18.8(C6), 33.6(C7), 40.0 C8),48.3(C9),37.4(C10),23.6(C11),125.6(C12),139.7(C13),42.5(C14),28.7(C15),24.9(C16),48.0(C17),53.5(C18),39.5(C19),39.1(C20),31.1(C21),37.3(C22),28.8(C23),15.7(C24),16.6(C25),17.4(C26),23.8(C27)180.0(C28),17.5 (C29),21.4(C30)., MS: 455 M^+, 439,248,203,189,119.

Proscillaridin (Sujata R and Aelt B *et al*., 1966)
Molecular formula:C_{30} $H_{46}O_4$,M.P.:295^0 C,UV (nm):219
IR (KBR cm^{-1}):3550 (-OH),1765 (a five membered lactone) 1360 and 1380 (geminal dimethyl).
^{1}HNMR:1.90,1.65(2H),3.31(1H),1.70,1.45(2H),2.01,1.91(2H),1.41,1.16(2H),1.49,1.24(2H),1.52,1.27(2H),1.75,1.50 (2H),1.63,1.38(2H),2.17(1H),6.38(1H),7.56(1H),3.85(1H) ,3.40(1H),3.49(1H),3.73(1H),1.16(CH_3),-OH(2.0),1.21 (CH_3),2.0,2.0(2-OH),5.03(1H)1.44(1H),5.37 (1H),7.55 (1H). ^{13}C NMR: 27.6(-CH_2),74(CH),121.5(CH), 140.9(C),38.1(C),29.5(CH_2),33.7(CH_2),25.7(CH_2), 42.5 (CH),44.6(CH),90.2(-C),50.1(-C),31.2(CH_2),23.1 (CH_2), 34.6(CH_2),21.5(CH_2), 49.9(CH), 123(C),149.3(CH),162.6 (C),115.3(CH),147.7(CH),102.1(CH),70.5(CH),77.7(CH), 73.1(CH),74.2(CH),14.7(CH_3),23.2(CH_3),16.9(CH_3), MS: m/z = 470.

Oleandrigenin βneritrioside/gentiobiosyl nerigoside (Yamauchi T, Abe F *et al.*, 1990)
Molecular formula:C_{44} $H_{68}O_{19}$,M.P.: 182-185 ^{0}C, UV (nm): 226
IR (KBr cm^{-1}):1750(α, β- unsaturated ester), 1735(ester),1160(c-o)
^{1}H NMR: 0.89s, 1.09 s, 6.34 brs, 5.823 dd ,3.40 d, 5.70 1d ,4.68 dd, 3.42 brd ,3.52 brq, 1.66 d , 3.37 s , 5.o9 d, 5.16 d,4.35 dd,4.50 dd, 4.80 brd,1.87 O-AC.
^{13}C-NMR:30.7,27.1,73.5,30.4,37.0,26.9,21.7,41.9,35.8, 35.4,21.1,38.9,50.5,83.4,41.2, 74.9,56.8,16.3,23.8,170.2,76.2,121.6,174.1, (C^1-C^{23}) OAC ,169.7 ,20.6,98.8,33.2,80.11,73.1,70.8,18.1 C_1'-C_6' ,Ome- 56.1, 104.6,75.7,78.5,71.7,77.6,70.4 C_1''-C_6'' 105.5, 75.2,78.4,71.9,78.3,62.8.C_1'''-C_6'''
MS(m/z): 923.4247.

(3β, 7 β) 7-hydroxylup-20 (29)-en-3-yl hexadecanoate (Quan-Yu L *et al*., 2015)
Molecular formula:$C_{46}H_{18}O_3$, UV (nm):175
IR (KBR cm^{-1}):1650(C=C),3010(C=C-H),3000(C-H)
^{1}H-NMR:7S –me(0.79,0.84,0.85,0.86,1.06,1.41,1.68) –Me,td, 0.88, -OH (3.82 (dd J=10.8,4.8) 1H CH(2.37),dt (j=7.8,5.6 1H), ter-CH_3 0.88,s-CH_2 1.25,0.93-0.96 m ,1.66- 1.68 m, 1.27-1.29 m 4.47dd J=11.2 &4.4 , 0.86-0.88 (m), 1.30-1.32(m), 3.82(dd)J=10.8 & 4.8, 1.21-1.23 (m),1.42-1.44 (m),1.60-1.61 (m), 1.62-1.63 (m), 1.23-1.25 (m),1.37 (m),2.37 (dt, J=7.8,5.6),1.29-1.30 (m),1.17-1.19 (m),0.86(s),0.85 (s) ,0.84 (s) ,1.06 (s), 1.41 (s),0.79 (s), 4.57 (s), 4.68 (s) ,1.68 (s) ,2.28 (tJ=7.6),1.68-1.70 (m), 1.25 (brs),0.88 (t J=7.0 Hz.)
^{13} C NMR:38.2(t),23.7(t),80.8(d),37.5 (s),52.3 (d),29.0 (t),74.4 (d),44.2 (S),50.1(d),37.0 (s),20.8 (t),25.8 (t),38.3 (d), 42.6 (s),29.4 (t),35.9 (t), 46.7 (s),48.1 (d),47.1(d),150.9 (s),31.3 (t),40.0(t),27.8 (q),16.4 (q),15.7 (q),10.1 (q), 14.9 (q),17.8 (q),10.93 (t),19.3 (q),173.6 (s),34.8 (t), 25.0 (t),29.7 ,29.1(t),14.11 (q).
MS (m/z): 703.6010 $(M+ Na)^+$

CONCLUSION

Nerium oleander L. is a widely distributed shrub in Asia including India. Present review discusses the Phytochemistry and spectroscopic aspects. The plant is studied exhaustively last 60 years. It is demonstrated the huge medicinal potential of N. Oleander. The review describes analytical data for identified chemical compounds including different classes like terepenoids, steroids, flavoinds, and carbohydrates. The spectroscopic

data viz. UV, IR, mass and NMR data have been complied and represented. Nature is a unique source of structure of high phytochemical diversity, many of them possessing interesting biological activities and medicinal properties. Current reviews is extensively beneficial for modem ethanomedical practioners to assess it's potency scientifically with relevance to Phytochemistry. The review helps to many phytochemical scientists for bioassay guided fractionation and isolation of many compounds.

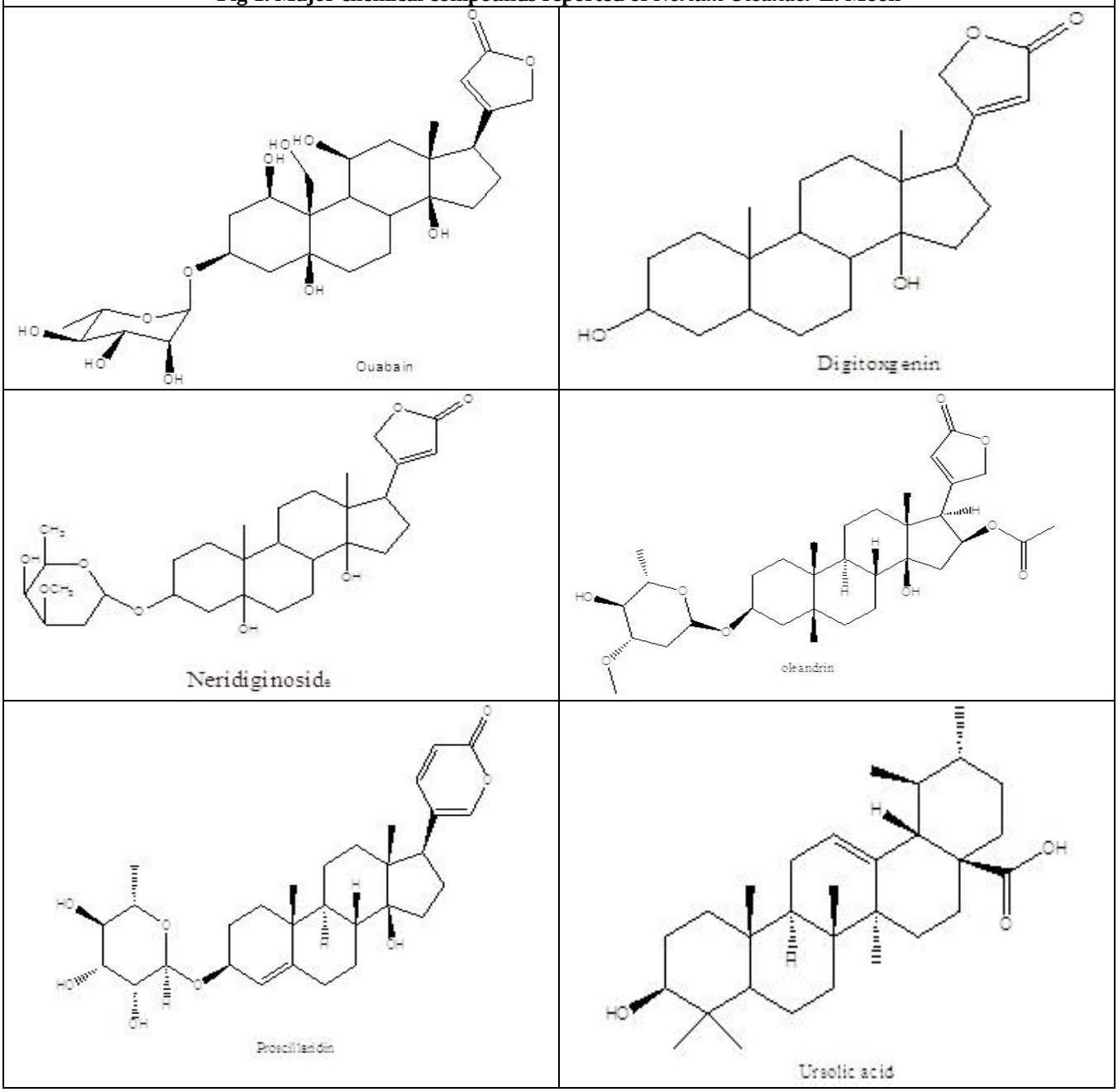
ACKNOWLEDGEMENTS

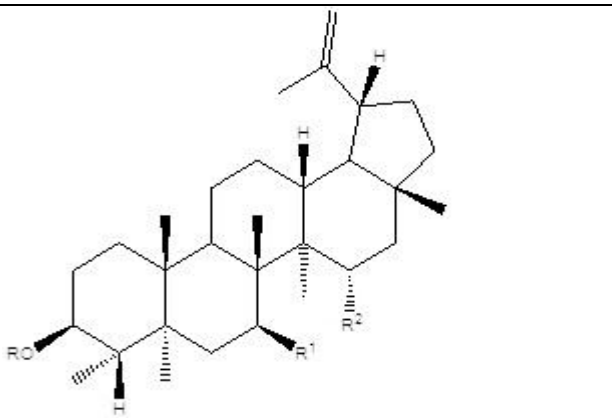
Authors are grateful to Dr. K. K. Deshmukh (Principal and Head, Department of Chemistry S. N. Art's, D.J. Malpani Commerce and B. N. Sarada Science College, Sangamner.)

CONFLICT OF INTEREST

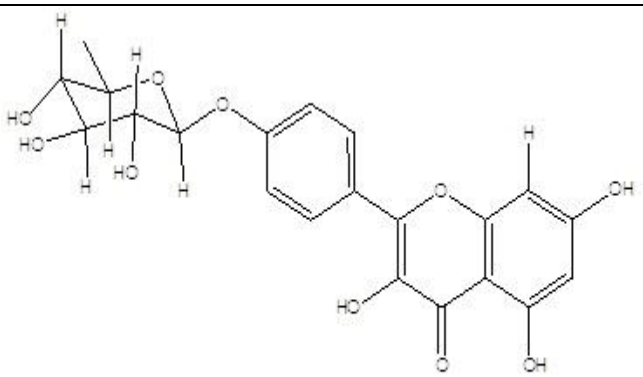
The authors declare no conflict of interest.

Fig 1. Major chemical compounds reported of *Nerium Oleander* L. Moon





(3β,7β)-7-hydroxylup-20(29)-en-3-yl hexadecanoate
R= me$(CH_2)_{14}$(co) ,R^1=OH , R^2= H



Kaempferol 4'-O-α-L-rhamnopyranoside

REFERENCES

Adrienne A. Physicochemical Characterization Of A Ouabain Isomer Isolated From Bovine Hypothalamus. *IJPR*, 1993(90), 8189-8193.

Amany I. Microbial Metabolism of Biologically Active Secondary Metabolites from Nerium oleander L. *Can J.*, 56(9), 2008, 1253-1258.

Garima Z. A Review on Chemistry and Pharmacological activity of Nerium oleander L. *J. Chem. Pharm. Res.*, 2(6), 2010, 351-358.

Garima Z. *In vitro* and *in vivo* determination of phenolic contents and antioxidant activity of desert plants of apocynaceae family. *Asian journal of pharmaceutical and clinical research*, 5(1), 2011, 0974-2441.

Hassan MM. Studies on the antidiarrhoeal, antimicrobial and cytotoxic activities of ethanol-extracted leaves of yellow oleander. *Open Veterinary Journal*, 1, 2011, 2218-6050.

Mohadjerani. Antioxidant Activity and Total Phenolic Content of Nerium oleander L. Grown in North of Iran. *Iranian Journal of Pharmaceutical Research*, 11(4), 2012, 1121-1126.

Montano A. Hydroalcoholic extract from the leaves from of Nerium oleander inhibits glycolysis and selective killing of lung cancer cells. *Cancer,* 2013, 0032-0943.

Native. Comparative evaluation of anthelmintic activity of nerium indicum, mill flower extract and punica Granatum Linn. Peel & seed extract 1:1 ratio & their phytochemical screening. *World journal of pharmacy and pharmaceutical sciences*, 3(6), 2014, 1438-1447.

Pegah N. Screening of Biological Activities (Antioxidant, Antibacterial and Antitumor) of Nerium oleander Leaf and Flower Extracts. *American Journal of Phytomedicine and Clinical Therapeutics*, 2013, 2321 – 2748.

Quan Y. A Hydroxylated Lupeol-based triterpenoid ester isolated from the Scurrul aparasitica parasitic on nerium indicum. *Verlag Helvetica Chimicaacta AG Zurich*, 2(98), 2015, 627-632.

Raveen R. Larvicidal activity of Nerium oleander L. (Apocynaceae) flower extracts against Culex quinquefasciatus Say (Diptera: Culicidae). *IJMR*, 1(1), 2014, 2348-5906.

Sabira B. Bio-active cardenolides from the leaves of Nerium Oleander. *Elsevier Science*, 2(98), 1998, 00523-8.

Shashi C. Antibacterial activity of nerium indicum against some gram positive bacterial species. *Int. J. Drug Res. Tech*, 3(1), 2013, 2277 – 1506.

Singhal. Hepatoprotective and antioxidant activity of methanolic extract of flowers of Nerium oleander against CCl4-induced liver injury in rats. *Asian Pacific Journal of Tropical Medicine*, 2012, 677-685.

Suganya RS. Phytochemical screening of and antibacterial activity of Nerium oleander and evaluative of their plant mediated nanoparticle synthesis. *IRJP*, 2012, 2230 - 8407.

Sujata R and Aelt B. Constitution of proceragenin A- A Trirepenoid Sapogenin from Albizzia Procera Brinth. *Tetrahedron letter*, 46, 1966, 5743-5750.

Torbjordnr A. Structural Studies Of Digitoxin And Related Cardenolides By Two-Dimensional. *Nmr. Can. J. Chem*, 1990, 68.

Vikas G. Phytochemical and pharmacological potential of nerium oleander: a review. *IJPSR*, 1(3), 2010, 0975-8232.

Yamauchi T. Cardiac glycosides and pregnanes from Adenium obesum. *Chemical and pharmaceutical Bulletin*, 38(3), 1990, 669-672.