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Review Article

REVIEW ON PHARMACOLOGICAL ACTIVITIES OF *LIGUSTRUM OVALIFOLIUM*

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ABSTRACT

The identification of privet in the middle southern United States can be difficult. Because most introduced species of privet can be invasive, and recent mapping projects seek location and species population data, proper identification is important. Ligustrum is currently marketed as a treatment for strengthening the immune system, R 3\05\ 9and on this basis is often recommended for use by people undergoing treatment for cancer or HIV. There is no meaningful scientific evidence that ligustrum provides any benefit for these, or any other, conditions. Very weak evidence from test-tube and animal studies hints that ligustrum might have anti-parasitic, 1 anti-viral, 2l iver-protective , 3immunomodulatory (this means "altering" immune function, rather than, as commonly misunderstood, "strengthening" it), 4,5 and cancer-preventive 6 effects. However, this evidence is too preliminary to rely upon at all. Ligustrum ovalifolium are used the activities of hypotensive activity, hypoglycemic activity, anti inflammatory activity and antioxidant activity.

Keywords: ligustrum ovalifolium , pharmacological study.

INTRODUCTION

Evergreen ligustrum shrubs and trees thrive throughout the state of Florida .They are widely used as landscape shrubs, hedges, and specimen trees [1]. The genus Ligustrum (privet) is part of the Oleaceae family and comprises about 20 species, subspecies and varieties. Of these, seven species are endemic to India [2], while the others grow naturally across Europe in narrow passes and mountains above 1000m (3); however, they are most frequently found in urban environments, since they are widely used as either ornamental trees or hedges in parks and gardens. In Spain three species are used most widely in gardening: Ligustrum japonicum, L. ovalifolium and L. Zucidum, the latter due to its reluctance to adapt to urban conditions and to clearance of cutting and pruning. They are usually found as small trees or shrubs but some specimens can reach a height of 10 m; they are deciduous or evergreen with entire, curvaceous, lance late or oval-shaped leaves. They contain a large amount of oleuropein, a phenolic secoiridoid glycoside (4).The small, white flowers are grouped in terminal clusters that bloom spectacularly. Flowering takes place during late -May, June and July, and pollination is entomophilies. This latter characteristic, together with the large size of its pollen grains (5), impedes long-distancen dispersion of the pollen.

3. PHARMACOLOGICAL PROPERTIES

3.1 *HYPOTENSIVE PROPERTY*

The structures have been elucidated by spectroscopic means including ^{1}H NMR ^{13}C, and DEPT), 2D NMR (COSY, HMQC and HMBC experiments), UV, IR and FAB-MS (positive mode). Both n-BuOH fraction and the isolated new compounds 1-5 were evaluated for their hypotensive activity on experimental animal. The n-BuOH fraction showed good activity; however, the activity of the isolated new compounds

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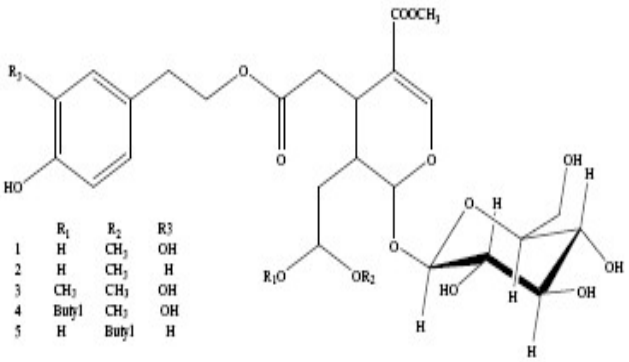
1-5 did not particularly strong. A dose dependent hyportensive effect in the normal anaesthetized cats was obtained by administration of gradually increasing doses (0.5, 1.0, 2.0, 4.0, 8.0, 16.0 mg/ml) of the aqueous n-BuOH fraction. Adrenaline (5 g/kg) was used for induction of hypertension of the anaesthetized cat which returned to normal level after 12 min A mild drop of the hypertension to about 50% in 1 min. was observed after administration of the n-BuOH fraction (50 mg/kg) on the top of the hypertension. After administration of another dose of the n-BuOH fraction (50 mg/kg) the hypertension returned to normal level with about 2 min .The prominent hypotensive effect of the n-BuOH fraction after blocking successively the α- and β- adrenergic and histaminergic receptors by injection of Regitine (2 mg/kg), propranolol (2 mg/kg) and pheniramine (1 mg/kg) and cimetidine (2 mg/kg) respectively before administration of the n-BuOH fraction in each case, and the antagonize hypotensive effect of the n-BuOH fraction after blocking muscarinic (cholinergic) receptors by injection of Atropine (1 mg/kg), clearly indicated that the hypotensive effect of the n-BuOH fraction was largely antagonized by anticholinergics and not affected by α- or β-adrenergic or histaminergic blocking agents. Therefore, the mechanism for the hypotensive effect of the n-BuOH fraction may be due to the cholinergic effect. Doses of (1.0, 2.0, 4.0, 8.0 mg/cat), of the new compounds 1-5 show a dose dependent hypotensive effect.

Structure elucidation **:** Compound 1, was obtained as a white amorphous powder. Its FAB mass spectrum showed a $[M+Na]^+$ peak at m/z 611, corresponding to the molecular formula $C_{26}H_{36}O_{15}$. It showed UV maxima at 235 and 284 nm and IR bands at 3375, 1715, 1625 and 1520 cm^{-1} . These spectral data suggested the presence of an enol-ether system conjugated with a carbonyl group that was typical of secoiridoid nucleus [14] , in addition to the presence of aromatic moiety. The ^{1}H NMR spectrum of **1** [Table 1], exhibited two hemiacetalic proton signals at δ 5.43 (d, J = 7.8 Hz, H1) and 4.69 (d, J = 7.8 Hz, H-1 '), proton signal of the carboxyenolic chromophore at δ 7.47 (brs, H-3) and a carbomethoxy group signal at δ 3.64 (s, OCH_3 -11) due to the secoiridoid glucoside moiety and an ABX-spin system at δ 6.67 (d, *J* = 1.8 Hz, H-4 ' '), 6.69 (d, *J*= 8.4 Hz, H-7 ' ') and 6.55 (dd, *J* = 8.4/1.8 Hz, H-8 ' ') together with a triplet at δ 2.77 (*J* = 7.2 Hz, H_2 -2 ' '), a doublet of doublet and a doublet of triplet at δ 4.14 and 4.20 (*J* of each = 10.2/7.2 Hz) for H-1 $_a$' ' and H1 $_b$' ' , respectively, due to the 3,4-dihydroxyphenylethyl moiety. The ^{1}H NMR spectrum of 1 was similar to that of ligustaloside A [5] except for the absence of signal due to an aldehydic function and the appearance of a new hemiacetalic proton signal at δ 4.75 (dd, *J* = 10.2/5.4 Hz) and one methxyl signal at δ 3.34. The hemiacetalic proton was attributed to H-10 which correlated with H-8 $_a$ (δ1.60, m) and H-8 $_b$) (δ1.80, m) as shown from the cross peaks in the COSY spectrum. Furthermore H-8 $_a$ and H-8 $_b$, was further correlated with H-9 (δ2.10, m) which in turn correlated with H-1 (δ 5.43) and H-5 (δ 3.22, m). HMBC spectrum of **1** indicates the position of the additional methoxyl group to be at C-10 from the long-range correlation observed between the methoxyl protons at δ 3.34 and C-10 at δ 104.20 and between H-10 and the carbon of the methoxyl at δ 54.00. These observations suggested that 1 differed from ligustaloside A only in the moiety consisting of C-8-C-10 and possessed a C-10 hemiacetalic group. Furthermore, the ^{13}C NMR spectrum of **1** [Table 2], showed signals of C-8 and C10 in the upper field in comparison with the corresponding signals of ligustaloside A [5] .This established the structure of **1** to be a methyl hemiacetal derivative of ligustaloside A.



Compound **2** , was obtained as a white amorphous powder. Its UV and IR spectra exhibited absorption bands similar to **1** . The FAB mass spectrum showed a pseudomolecular ion peak at *m/z* 595 $[M+Na]^+$, compatible with the molecular formula $C_{26}H_{36}O_{14}$. Its ^{1}H and ^{13}C NMR spectra were

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identical to those of **1** , except for the phenylethyl moiety protons and carbons. The ^{1}H NMR spectrum of 2 showed one triplet at δ 2.83 (2H, *J* = 7.2 Hz, H$_2$ -2 ' '), one doublet of doublet at δ 4.16 (1H, *J* = 10.2/ 7.2 Hz, H-1$_a$ ' '), one doublet of triplet at δ 4.20 (1H, *J* = 10.2/ 7.2 Hz, H-1$_b$ ' '), and the AA' BB' signal pattern at δ 6.72 (2H, d, *J* = 8.4 Hz, 5' ' , 7' ' - H) and δ 7.06 (2H, d, *J* = 8.4 Hz, 4' ',8' '- H), indicates the presence of a *p*-hydroxyphenylethyl moiety [5] . These data implied that the structural relationship between **1** and **2** was the same as that between ligustaloside A and ligustaloside B [5] . Therefore **2** was assumed to possess a p-hydroxyphenylethyl moiety instead of 3,4-dihydroxyphenylethyl moiety of **1** . This was established from FAB-MS which indicated that **2** was lower than **1** by 16 mass units. The ^{13} C NMR spectral data [Table 2] was assigned on the bases of comparison with those of **1** which revealed close correspondence in every aspect that the signals of 3, 4-dihydroxyphenylethyl moiety were missing for **2** . Thus the structure of **2** was established as ligustaloside B methyl hemiacetal.

3.2 ANTIOXIDANT PROPERTY

The free radical scavenging activities of extracts from Ligustrum ovalifolium H. leaves (LOH) as well as various antioxidant activities such as ferric reducing antioxidant power (FRAP) ,2,2'-azino-bis-(3-ethylbenzothiazoline-6-sulfonic acid)(ABTS) radical scavenging activity, reducing power and lipid peroxidation inhibition were evaluated by electron spin resonance (ESR). The total polyphenol and flavonoid contents of the water and ethanolic extracts from LOH were 105.5±1.31 and 102.1±1.82 mg gallic acid equivalent/g extract, espectively, and 84±1.72 and 82.8±1.65 mg catechin equivalent/g extract. In addition, IC\50 values for the 1, 1-diphenyl-2-picryldrazyl (DPPH), alkyl, and hydroxyl radical scavenging activities of the water and ethanolic extracts were 0.021±0.002 and 0.010±0.003 mg/mL, 0.011±0.003 and 0.012±0.002 mg/mL, and 0.395±0.002 and 0.443±0.002 mg/mL, respectively. The ABTS radical scavenging activities of the water and ethanolic extracts from LOH and BHT were 0.073±0.12, 0.130±0.06 and1.461±0.02 mM Trolox equivalent/mg extract, respectively. The FRAP values of the extracts from LOH were higher than those of BHT, which was used as a positive control. The LOH extracts showed strong inhibitory effects on lipid per oxidation as measured by ferric thiocyanate (FTC) and thio barbituric acid (TBA) assay compared to that of α-tocopherol. Using MTT assay on human liver cells (Chang), extracts from LOH showed no toxicity at a concentration of 0.5 mg/ml. These results indicate that the LOH extracts possessed antioxidant activity.

3.3 ANTIINFLAMMATORY EFFECT

This study investigated the anti-inflammatory effects of Ligustrum ovalifolium H. (LOH) leaf extracts on RAW264.7 macrophages. Cell toxicity was determined by MTT assay. We evaluated the anti-inflammatory effects of LOH extracts by measuring nitric oxide (NO), reactive oxygen species (ROS), inducible NOS (iNOS) production, and cyclooxygenase-2 (COX-2) expression by Western blotting. LOH ethanolic extracts (0.05, 0.1, and 0.2 mg/mL) significantly suppressed LPS-stimulated production of NO. The intracellular ROS level also significantly decreased. LOH ethanolic extracts reduced the expression of iNOS and COX-2 proteins. The present results show that LOH ethanol extract has potent anti-inflammatory effects on RAW264.7 macrophages. These results also suggest that the anti-inflammatory effects of LOH extracts may be related to the inhibition of LPS-stimulated ROS and NO production. Therefore, ethanolic extracts of LOH leaves may be utilized as a good source of functional foods for protection against inflammatory diseases.

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