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Oleaceae family-Bioactive Secoiridoids - A Report

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Abstract : The *Oleaceae* family has been a source of various traditionally useful and pharmacological active species. Many plants of this genus prominently feature white, yellow or pink flowers with sweet fragrance and others are unscented. The species are cultivated for flowers containing bioactive compounds especially iridoids, secoiridoids and essential oils. The pharmacological effects evaluated from the crude extracts or pure isolated compounds from these species have been antimicrobial, antifungal,antiviral, insecticidal, antioxidant, anti-inflammatory antioxidant, antimicrobial, anthelmintic, antiulcer, antidiarrhoea and analgesic activities. Secoiridoids are cyclopentane mono-terpene derivatives formed by cleavage of the cyclomethene oxime compounds at C-7 and C-8. Nearly 250 secoiridoids in the form of aglycones, dimers and derivatives have been identified from Oleaceae family. The secoiridoids from the genera- *Ligustrum, Faxinus, Syringa, Osmanthus and Jasminum* are studied in this report. The chemical compounds isolated from these species have been reported for their pharmacological effects. Although, few experimental studies validated their traditional claim, but uncharacterized crude extracts were employed in most of the activities. Such species need to be explored properly for their bioactive principle and exploited as potential drug.

IndexTerms - Ligustrum, Faxinus, Syringa, Osmanthus, Jasminum.

INTRODUCTION

Herbal plants are pioneer for new drug discovery and development, not only for plant constituents used directly as therapeutic agents, but also as precursor for half of the clinical drugs available in the market [1]. The herbal plants are used for the prevention and treatment of various ailments in the developing countries due to their availability to the native people and heavy cost factor of clinical drugs. Plants are potential source of therapeutic aids beside as food and shelter resources. The medicinal plants have been the raw base for preparation of medicines in all the pharmacopeias including Chinese, Ayurveda, Unani, Siddha and native and ethnic communities. However, among the 250,000-400,000 plant species only 6% have been screened for biological potential and 15 % for phytochemical exploration [2]. The lack of systematic research, effectiveness, efficacy, disease specific formulations and place of natural product in primary healthcare system are the primary concerns. Still, it is estimated that about 25% drugs prescribed in modern medicines are derived from plants. In the essential list of WHO, out of 252 drugs 11% have plants origin. Despite of advancement and treatment through modern medicines, 85 to 90% of world population consumes plants or plants derived medicines due to one reason or other [3]. The plants defense mechanism against the herbivorous animals and pathogens to biosynthesize defensive compounds particularly secondary metabolites have attracted the attention to isolate, characterize and lab scale formulation of these compounds for various biological effects.

Oleaceae is a family of dicotyledonous flowering plants which is widely distributed in the temperate and tropical regions. This family includes 25 genera with approximately 688 species [3]. The genera- *Ligustrum, Faxinus,Syringa, Osmanthus and Jasminum* of *Oleaceae* and an important group of flowering plants, commonly cultivated for their aromatic flowers. The species of these genera are rich in flavonoids, monoterpenoids, iridoids, secoirirdoids and phenyl ethanoid glycosides. The pharmacological reported reported from *Oleaceae* family are antimicrobial, antioxidant, anti-inflammatory, antifungal, antiviral, insecticidal, anthmintic, antiulcer, antidiarrhoa and analgesic. Secoiridoids are cyclopentane mono-terpene derivatives formed by cleavage of the cyclomethene oxime compounds at C-7 and C-8. Nearly 250 secoiridoids in the form of aglycones, dimers and derivatives have been identified from Oleaceae family. These compounds are mainly distributed in the genera- *Fontanesia, Fraxinus, Jasminum, Ligustrum, Olea, Osmanthus, Phillyrea, Picconia* and *Syringa* [4]. Secoiridoids have shown a variety of pharmacological effects including anti-diabetic, anti-inflammatory, immunosuppressive, neuroprotective, anti-cancer and anti-obesity. Keeping in view this work was undertaken for the structural and pharmacological aspects of secoiridoids from the genera- *Ligustrum, Faxinus, Syringa, Osmanthus and Jasminum.* The data was withdrawn from Google Scholar, PubMed, Science Direct, Scopus, Krishikosh and Shodhganga.

Chemistry of Secoiridoids: Secoiridoids are cyclopentane mono-terpene derivatives formed by cleavage of the cyclomethene oxime compounds at C-7 and C-8. Nearly 250 secoiridoids in the form of aglycones, dimers and derivatives have been identified from Oleaceae family. These compounds are mainly distributed in the genera- *Fontanesia, Fraxinus, Jasminum, Ligustrum, Olea, Osmanthus, Phillyrea, Picconia* and *Syringa* [4]. These secoiridoids were classified into 5 groups namely, simple secoiridoids, conjugated secoiridoids, 10-oxyderivative of oleoside secoiridoids, Z-secoiridoids, secologanosides [5,6]. The substitution at different position of basic skeleton derive diverse compounds. The structures of the secoiridoids in the order of classification is summarized as-(Fig-1)

a) Simple secoiridoids-Generally, in the simple secoiridoids (Table-1) positions C-7 and C-11 have either a free carboxylic acid group or a methyl ethyl ester derivative of the acid. In addition, the configurations of positions C-1 and C-5 are S. e.g. methylglucooleoside.

b) Conjugated secoiridoids- This group of compounds constitute the majority of secoiridoids isolated from the *Oleaceae* family and *Jasminum* . The name of the class stems from the type of compound that is linked or conjugated to the secoiridoid nucleus. The C-7 position is usually oxidized to a carboxylic acid and esterified with different groups. The double bond between the C-8 and C-9 positions and the hydrogen at the C-8 position is replaced by a methyl group. Also, most of the aromatic-conjugated secoiridoids are also oxidized to carboxylic acids at the C-11 which may either be free or esterified with either 1,2-dihydroxyphenylethanol or p-hydro-xyphenylethanol. e.g. ligustroside [4].

c) 10-Oxyderivative of oleoside secoiridoids- This class possesses the oleoside nucleus with distinct structural differences. The C-8 and C-9 positions exist as double bonds and the hydrogen at the C-8 position is replaced by a hydroxy group or an ester is

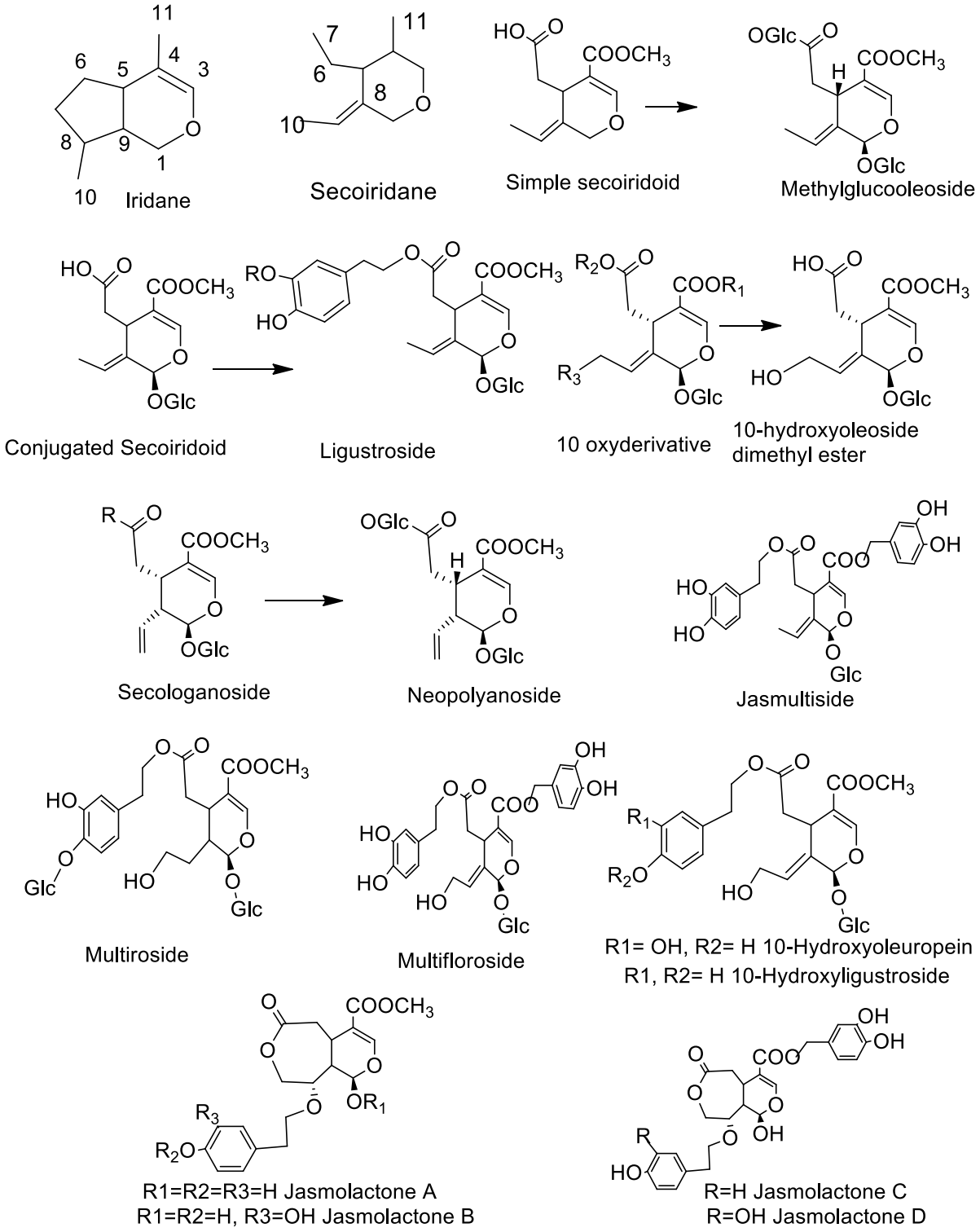

Fig. 1 Structures of Secoiridoids from Acanthaceae.

formed by an oxygen atom with different groups. These groups typically include an acetyl and phenolic moieties. A total of 40 10-oxyderivative of oleoside secoiridoids. e.g. 10-hydroxyoleoside dimethyl ester [4].

d) Secologanosides and oxidized secologanoside secoiridoids-Majority of compounds in this class are based on the secologanoside nucleus. The unique structural features of this class are the position of the carbon-carbon double bond is between C-8 and C-10 in most compounds and the level oxidation of C-10.Forty-four secologanosides and oxidized secologanoside glycosides have been isolated from the Oleaceae family and genus- *jasminum*. e.g. neopolyanthoside [4].

Secoiridoids from Oleaceae: Various secoiridoids of the skeletal formula -Simple secoiridoids, Conjugated secoiridoids, 10-Oxyderivative of oleoside secoiridoids, Secologanosides and oxidized secologanoside secoiridoids have been isolated from the species the genera- *Ligustrum, Faxinus, Syringa, Osmanthus and Jasminum* (Table-1).The vital species of genus *Ligustrum are L. Japonicum, lucidum,* genus *Syringa* are *S.afghanica, oblate,* genus *Fraxinus* are *F. americana, F. excelsior*, genus *Osmanthus* are *O. europaea, O. asiaticus*, and genus *Jasminum* are *J. polyanthum, J. nudiflorum , J. multiflorum.*

Genus Ligustrum- Oleoside 11-methyl ester, 7,11-Oleoside dimethyl ester, Methylglucooleoside, Ligstroside, 1‴-O-β-D-Glucosylformoside, 6‴-Acetylnicotiflorine, Oleuropein, (2″R)-2″-Methoxyoleuropein, Excelside B, 2″-Epifraxamoside, Fraxamoside, (8E)-Nuezhenide, Neonuezhenide, Specnuezhenide, Isonuezhenide, Oleonuezhenide, Hydroxyoleonuezhenide, Iso-oleonuzhenide, Obtusifoliside A, Liguside A, GI3, Nuezhenelenoliciside, 10-Hydroxyoleoside dimethyl ester, 10-Hydroxyoleuropein, 10-Hydroxyligustroside, (2”S)-10-Hydroxy-2″-methoxyoleuropein, (2”R)-10-Hydroxy-2″-methoxyoleuropein, Isojaslanceoside B, Obtusifoliside B, (8Z)-Nuezhenide A, (8Z)-Nuezhenide, Ligulucidumoside C, Secologanoside, 6′-O-trans-cinnamoyl-secologanoside, Liguluciside A, Liguluciside B, Ligulucinidoid A, p-Hydroxyphenethyl 7-β-D-glucosideelenolic ester, 6′-Elenolylnicotiflorine, Nuzhenal A, Nuzhenal B, Ligustrohemiacetal A, Ligustrohemiacetal B, Ligulucinidoid B, ,Ligustaloside A, Ligustaloside B, 4′, 5′-(2′-Hydroxy ligustrosidic acid) dimer, Ligulucidumoside B, Ligulucinside C, Oleuropeinic acid, Isoligustrosidic acid, Ligupurpuroside K, Ligujaponoside A, Ligujaponoside B,Lucidumoside A, Lucidumoside B, Nuezhenidic acid.

Genus *Fraxinus*- Oleoside 11-methyl ester, 7,11-Oleoside dimethyl ester, Methylglucooleoside, Excelside A, Demethylligstroside, Ligstroside, Angustifolioside B, Formoside, 1‴-O-β-D-Glucosylformoside, Oleuropein, Oleuropein-4″-methyl ether, Angustifolioside A, 2″S)-2″-Hydroxyoleuropein, (2″R)-2″-Hydroxyoleuropein, (2″S)-2″-Methoxyoleuropein, (2″R)-2″-Methoxyoleuropein, Isoligustrosidic acid, Isoligustroside, Butylisoligustrosidate, Framoside, Fraxiformoside, 1‴-O-β-D-Glucosylfraxiformoside, Hydroxyframoside A, Jasmultiside, Isooleuropein, Hydroxyframoside B, Insuloside, Excelside B, Insularoside-3’-O-β-D-glucoside, Insularoside-3′,6‴-di-O-β-D-glucoside, Insularoside, Hydroxyornoside, fraxuhdoside, Fraxamoside, Fraximalacoside, GI5, (8E)-Nuezhenide, Desrhamnosyloleoacteoside, Frameroside,, Escuside, Fraxisecoside, Isofraxisecoside, GI3, Uhdenoside, 10-Hydroxyoleoside dimethyl ester, 10-Hydroxyoleuropein, 10-Hydroxyligustroside, Fraxicarboside C, Fraxicarboside B, Fraxicarboside A, Uhdoside B, (8Z)-Nuezhenide, Angustifolioside C, Secologanoside, Secologanol, 5-Hydroxysecologanol, Fontanesioside, cis-7(p-coumaroyl)-5-hydroxysecologanol, trans-7(p-coumaroyl)-5-hydroxysecologanol, Swertiamarin, Secologanic acid, Ligstral.

Genus *Syringa*- Oleoside 11-methyl ester,7,11-Oleoside dimethyl ester, Demethyloleuropein, Ligstroside, Formoside, 1‴-O-β-D-Glucosylformoside, Oleuropein, (2″R)-2″-Methoxyoleuropein, Isoligustroside, Safghanoside C, Fraxiformoside, 1‴-O-β-D-Glucosylfraxiformoside, Hydroxyframoside A, Jasmultiside, Isooleuropein, Safghanoside D, Safghanoside E, Excelside B, Fraxamoside, Safghanoside G, Safghanoside H, Reticuloside, Safghanoside B, Safghanoside A, (8E)-Nuezhenide, Neonuezhenide, Safghanoside F, Isooleoacteoside, Oleoacetoside, Oleoechinacoside, Demethylhydroxyoleonuezhenide, Demethyloleonuezhenide, Oleonuezhenide, Oleoforsythoside B, Oleolipedoside A, Syringaoleoacteoside, 2″-epi-frameroside, Obtusifoliside A, Jaspolyanoside, Jaspolyoside 10-Hydroxyoleoside dimethyl ester, 10-Hydroxyoleuropein, (8Z)-Nuezhenide A, Secologanoside 7-methyl ester, Grandifloroside 11-methyl ester.

Genus Osmanthus- 7,11-Oleoside dimethyl ester, Demethyloleuropein, Ligstroside, Oleuropein, 3’-O-β-D-Glucopyranosyl oleuropein, 3’-O-β-D-Glucopyranosyl ligustroside, Fraxamoside, Ilicifolioside A, Ilicifolioside B, 10-Hydroxyoleoside-11-methyl ester, 10-Hydroxyoleoside dimethyl ester, 10-Hydroxyligustroside, 10-Acetoxyligustroside, 10-Acetoxyoleuropein, 3'-O-β-D-Glucopyranosyl 10-acetoxyligustroside, 3'-O-β-D-Glucopyranosyl 10-acetoxyoleuropein, 3'-O-β-D-Glucopyranosyl 10-hydroxyligustroside, Oleferrugine A, 6′-O-[(2E)-2,6-dimethyl-8-hydroxy-2-octenoyloxy]-secologanoside, 6′-E-p-coumaroyl-secologanoside, Oleuroside, Secologanoside 7-methyl ester, Secologanoside.

Genus *Jasminum*- Jaspolyside, Oleoside 11-methyl ester, Oleoside dimethyl ester, methylglucooleoside, Ligustroside, Angustifolioside B, Oleopein, GIS, Jaspolyoleoside A, Oleoacetoside, Jaspofoliamoside A, Jaspofoliamoside B, Jaspofoliamoside C, Jaspofoliamoside D, Jaspofoliamoside G, Jaspolinaloside, Jaspogeranoside A, Jaspogeranoside B, Isojaspolyoside A, Isojaspolyoside B, Isojaspolyoside C, Polyanoside, Jaspolyoleoside B, Jaspolyoleoside C,Jaspolyoside, Jaspofoliamoside E, Jaspofoliamoside F, Jaspolinloside B, 10-Hydroxyoleoside dimethyl ester, Oleopolyanthoside B, Oleopolyanthoside A, Jaspolyanthoside.

Pharmacological effects

Anti-diabetic effects- The secoiridoids hydroxyframoside A and fraxisecoside exhibited moderate PTP1B inhibition activity with IC_{50} 50 and 21 μM respectively Xiao et al. [27].

Anti-inflammatory effects- hydroxyframoside A and fraxisecoside Xiao et al. showed moderate PTP1B inhibition activity with IC_{50} of 50 and 21 μM respectively. Secoiridoids oleoechinacoside, demethylhydroxyoleonuezhenide, demethyloleonuezhenide and syringaoleoacteoside moderately suppressed the Lipopolysaccharide (LPS)-stimulated release of proinflammatory chemokine Interleukin −8 (IL-8) and Tumor necrosis factor α (TNF-α) from human neutrophils Dudek et al. [28]

Neuroprotective effects. Several secoiridoids have been reported to upregulate NGF without causing significant cell toxicity. Oleuropein , hydroxyframoside A ,fraxamoside and jaspolyoside exhibited potent stimulation of NGF release in a C6 rat glioma cell line, with stimulation levels of 201.58 ± 4.41, 205.64 ± 4.84, 207.48 ± 15.41 and171.64 ± 1.61%, respectively Park et al. [18]. 6-Hydroxydopamine is a selective neurotoxin that causes the death of dopaminergic neuronal cells in vivo and in vitro [29]. Several secoiridoids including (8E)-nuezhenide, oleonuezhenide, (8Z)-nuezhenide A, (8Z)-nuezhenide have demonstrated significant protection of SH-SY5Y cells from 6-hydroxydopamine induced neurotoxicity with percentage relative protection ranging from 23.6 ± 4.9 to 26.7 ± 3.1 and 40.3 ± 4.0 to 49.2 ± 4.3 at 1.0 μM and 10.0 μM respectively [30].

Anti-cancer effects

Oleuropein has been reported to modulate several oncogenic signaling pathways. Both in vivo and in vitro studies have demonstrated its anti-cancer potentials. Hypoxia inducible factor 1α (HIF1α) transcriptionally represses miR-519d in the nucleus. MiR-519d is involved in negative regulation of damage-regulated protein 1 in cancer cells. However, treatment of cancer cells

Table-1 Isolated Secoiridoids from the genus- *Ligustrum, Fraxinus, Syringa, Osmanthus and Jasminum*.

Genus	Secoiridoids	References
Ligustrum	Oleoside 11-methyl ester, 7,11-Oleoside dimethyl ester, Methylglucooleoside, Ligstroside, 1‴-O-β-D-Glucosylformoside, 6‴-Acetylnicotiflorine, Oleuropein, (2″R)-2″-Methoxyoleuropein, Excelside B, 2″-Epifraxamoside, Fraxamoside, (8E)-Nuezhenide, Neonuezhenide, Specnuezhenide, Isonuezhenide, Oleonuezhenide, Hydroxyoleonuezhenide, Iso-oleonuzhenide, Obtusifoliside A, Liguside A, GI3, Nuezhenelenoliciside, 10-Hydroxyoleoside dimethyl ester, 10-Hydroxyoleuropein, 10-Hydroxyligustroside, (2"S)-10-Hydroxy-2″-methoxyoleuropein, (2"R)-10-Hydroxy-2″-methoxyoleuropein, Isojaslanceoside B, Obtusifoliside B, (8Z)-Nuezhenide A, (8Z)-Nuezhenide, Ligulucidumoside C, Secologanoside, 6′-O-trans-cinnamoyl-secologanoside, Liguluciside A, Liguluciside B, Liguluciridoid A, p-Hydroxyphenethyl 7-β-D-glucosideelenolic ester, 6′-Elenolylnicotiflorine, Nuzhenal A, Nuzhenal B, Ligustrohemiacetal A, Ligustrohemiacetal B, Liguluciridoid B, ,Ligustaloside A, Ligustaloside B, 4′, 5′-(2′-Hydroxy ligustrosidic acid) dimer, Ligulucidumoside B, Liguluciside C, Oleuropeinic acid, Isoligustrosidic acid, Ligupurpuroside K, Ligujaponoside A, Ligujaponoside B,Lucidumoside A, Lucidumoside B, Nuezhenidic acid	[7,8,9,10]
Fraxinus	Oleoside 11-methyl ester, 7,11-Oleoside dimethyl ester, Methylglucooleoside, Excelside A, Demethylligstroside, Ligstroside, Angustifolioside B, Formoside, 1‴-O-β-D-Glucosylformoside, Oleuropein, Oleuropein-4″-methyl ether, Angustifolioside A, 2″S)-2″-Hydroxyoleuropein, (2″R)-2″-Hydroxyoleuropein, (2″S)-2″-Methoxyoleuropein, (2″R)-2″-Methoxyoleuropein, Isoligustrosidic acid, Isoligustroside, Butylisoligustrosidate, Framoside, Fraxiformoside, 1‴-O-β-D-Glucosylfraxiformoside, Hydroxyframoside A, Jasmultiside, Isooleuropein, Hydroxyframoside B, Insuloside, Excelside B, Insularoside-3'-O-β-D-glucoside, Insularoside-3′,6‴-di-O-β-D-glucoside, Insularoside, Hydroxyornoside, fraxuhdoside, Fraxamoside, Fraximalacoside, GI5, (8E)-Nuezhenide, Desrhamnosyloleoacteoside, Frameroside,, Escuside, Fraxisecoside, Isofraxisecoside, GI3, Uhdenoside, 10-Hydroxyoleoside dimethyl ester, 10-Hydroxyoleuropein, 10-Hydroxyligustroside, Fraxicarboside C, Fraxicarboside B, Fraxicarboside A, Uhdoside B, (8Z)-Nuezhenide, Angustifolioside C, Secologanoside, Secologanol, 5-Hydroxysecologanol, Fontanesioside, cis-7(p-coumaroyl)-5-hydroxysecologanol, trans-7(p-coumaroyl)-5-hydroxysecologanol, Swertiamarin, Secologanic acid, Ligstral,	[11,12,13,14]
Syringa	Oleoside 11-methyl ester,7,11-Oleoside dimethyl ester, Demethyloleuropein, Ligstroside, Formoside, 1‴-O-β-D-Glucosylformoside, Oleuropein, (2″R)-2″-Methoxyoleuropein, Isoligustroside, Safghanoside C, Fraxiformoside, 1‴-O-β-D-Glucosylfraxiformoside, Hydroxyframoside A, Jasmultiside, Isooleuropein, Safghanoside D, Safghanoside E, Excelside B, Fraxamoside, Safghanoside G, Safghanoside H, Reticuloside, Safghanoside B, Safghanoside A, (8E)-Nuezhenide, Neonuezhenide, Safghanoside F, Isooleoacteoside, Oleoacetoside, Oleoechinacoside, Demethylhydroxyoleonuezhenide, Demethyloleonuezhenide, Oleonuezhenide, Oleoforsythoside B, Oleolipedoside A, Syringaoleoacteoside, 2″-epi-frameroside, Obtusifoliside A, Jaspolyanoside, Jaspolyoside 10-Hydroxyoleoside dimethyl ester, 10-Hydroxyoleuropein, (8Z)-Nuezhenide A, Secologanoside 7-methyl ester, Grandifloroside 11-methyl ester	[15,16,17,18]
Osmanthus	7,11-Oleoside dimethyl ester, Demethyloleuropein, Ligstroside, Oleuropein, 3'-O-β-D-Glucopyranosyl oleuropein, 3'-O-β-D-Glucopyranosyl ligustroside, Fraxamoside, Ilicifolioside A, Ilicifolioside B, 10-Hydroxyoleoside-11-methyl ester, 10-Hydroxyoleoside dimethyl ester, 10-Hydroxyligustroside, 10-Acetoxyligustroside, 10-Acetoxyoleuropein, 3'-O-β-D-Glucopyranosyl 10-acetoxyligustroside, 3'-O-β-D-Glucopyranosyl 10-acetoxyoleuropein, 3'-O-β-D-Glucopyranosyl 10-hydroxyligustroside, Oleferrugine A, 6′-O-[(2E)-2,6-dimethyl-8-hydroxy-2-octenoyloxy]-secologanoside, 6′-E-p-coumaroyl-secologanoside, Oleuroside, Secologanoside 7-methyl ester, Secologanoside	[19,20,21,22]
Jasminum	Jaspolyside, Oleoside 11-methyl ester, Oleoside dimethyl ester, methylglucooleoside, Ligustroside, Angustifolioside B, Oleopein, GIS, Jaspolyoleoside A, Oleoacetoside, Jaspofoliamoside A, Jaspofoliamoside B, Jaspofoliamoside C, Jaspofoliamoside D, Jaspofoliamoside G, Jaspolinaloside, Jaspogeranoside A, Jaspogeranoside B, Isojaspolyoside A, Isojaspolyoside **B**, Isojaspolyoside C, Polyanoside, Jaspolyoleoside B, Jaspolyoleoside C,Jaspolyoside, Jaspofoliamoside E, Jaspofoliamoside F, Jaspolinloside B, 10-Hydroxyoleoside dimethyl ester, Oleopolyanthoside B, Oleopolyanthoside A, Jaspolyanthoside.	[23,24,25,26]

with oleuropein inhibits HIF1α-mediated transcriptional repression of miR-519d and consequently miR-519d quantitatively inhibits p53 and DNA PDRG1 [31]

Oleuropein demonstrated a dose-dependent induction of apoptosis in HepG2 human hepatoma cells Yan et al. [32]. Oleuropein is reportedly involved in induction of pro-survival signals in cancerous cells that overexpressed AKT/PKB. AKT/PKB inhibition was essential to maximize oleuropein-mediated apoptosis [32]. Additionally, the studies of Xu et al. [31] have indicated that, oleuropein (14) enhanced the radiosensitivity of Nasopharyngeal carcinoma (NPC) cells both in vitro and in vivo. Furthermore,

oleuropein, (2″R)-2″-methoxyoleuropein have shown antiproliferative activity against Human Melanoma Cell Line (SK-MEL-2 cells) with IC_{50} values of 10.86, 14.64 µM respectively [18].

Anti-obesity effects

The synthesis and accumulation of fatty acids are among the major causes of obesity. The work of Zhang et al. [33] has demonstrated secoiridoids possess significant triglyceride accumulation inhibitory effects. Ligulucidumosides A-C and nuzhenal C demonstrated a significant intracellular triglyceride inhibitory effects in HepG2 cells at concentrations of 10 µM.

Structure activity relationship (SAR) of secoiridoids.

From the literature available on the bioactivities of secoiridoids it could be inferred that, the presence of a carboxylic acid functionality at C-13, whether in the free acid form or the methyl ester form is critical for their activity. For example oleonuezhenide which has a methyl ester at C-13 possess neuroprotective effects and demethyloleonuezhenide which is a free acid derivative also possess antiinflammatory effects. Also, it is realized that, the cardio effects of these secoiridoids are associated with the presence of hydroxy at C-10. For instance, both 10-hydroxyoleuropein and multifloroside which are 10-hydroxy secoiridoids exhibit coronary dilating and cardiotropic activities. Furthermore, the presence of 1,2-dihydroxyphenylethanol or p-hydroxyphenylethanol moiety esterified to the carboxylic acid at C-7 and C-11 might be crucial for activity, and also the range of bioactivity increases when both C-7 and C-11 carboxylic groups are esterified. They effect is shown by the wide range of effects of Hydroxyframoside A which exhibits anti-diabetic, anti-inflammatory, immunesuppressive, and neuroprotective effects [4].

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