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PHCOG REV.: Plant Review
Olea europaea: A Phyto-Pharmacological Review

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ABSTRACT –
Medicinal herbs are significant sources for treating various diseases. *Olea europaea* is used traditionally as diuretic, hypotensive, emollient, laxative, febrifuge, skin cleanser, cholagogue, and also used for the treatment of urinary infections, gallstones, bronchial asthma and diarrhoea. Several phytoconstituents have been isolated and identified from different parts of the plant belonging to the category glycosides, secoiridoid, flavonoids and poly-unsaturated fatty acids. Many studies have been conducted to prove its potential as anti-oxidant, anti-viral, anti-microbial, anti-diabetic and for cardiovascular disorders. The present review aims toward forming a bridge between traditional use and modern therapeutics of *Olea europaea*.

KEY WORDS - Olea europaea, oleuropein, Phytochemistry, Pharmacotherapeutics.

INTRODUCTION

Alternative systems of medicine viz. Ayurveda, Siddha, and Chinese Medicine have become more popular in recent years (1). Medicinal herb is a biosynthetic laboratory, for chemical compounds like glycosides, alkaloids, resins, oleoresins, etc. These exert physiological and therapeutic effect (2). The compounds that are responsible for medicinal property of the drug are usually secondary metabolites. *Olea europaea* preparations have been used widely in folk medicine in European Mediterranean area, Arabia peninsula, India and other tropical and subtropical regions, as diuretic, hypotensive, emollient and for urinary and bladder infections (3). Olive oil represents an important component of the Mediterranean diet whose intake is greatly growing in developed and developing countries for its known healing effects (4).

Olea europaea (syn. Zaytoun, Jetun) belonging to the family Oleaceae is a small evergreen tree, from 12 to 20 feet high, with hoary, rigid branches, and a grayish bark. The leaves are opposite, lanceolate, or ovate-lanceolate, mucronate, short-petioled, green above, and hoary on the underside. The flowers are small, in short, axillary, erect racemes, very much shorter than the leaves. The corolla is short, white, with 4 broad, ovate segments; the calyx short and 4-toothed. The fruit is a drupe about the size of a damson, smooth, purple, 2-celled, with a nauseous, bitter flesh, enclosing a sharp-pointed stone. Virgin olive oil is the only edible oil of great production obtained by physical methods from the fruit of *Olea europaea*. It shows sensory characteristics and nutritional properties that allows to distinguish it from the others (5). In the current review, we will highlight on the traditional uses and modern therapies of the *Olea europaea*.

TRADITIONAL MEDICINAL USES

Most of the plant parts of *Olea europaea* are used in traditional system of medicine in world. Oil is taken with lemon juice to treat gallstones (6). Leaves are taken orally for stomach and intestinal diseases and used as mouth cleanser (7). Decoctions of the dried fruit and of dried leaf are taken orally for diarrhoea and to treat respiratory and urinary tract infections (8). Hot water extract of the fresh leaves is taken orally to treat hypertension and to induce diuresis (9, 10). Seed oil is taken orally as a cholagogue, to remove gall stones, in nephritis associated with the lead intoxication. To prevent hair loss, oil is applied every night on the scalp then shampooed the next morning (11). Seed oil is taken orally as a laxative and applied externally as an emollient and pectoral (12). Decoction of dried leaves is taken orally for diabetes (13). Tincture of leaves is taken orally as a febrifuge (14). Fruit is applied externally to fractured limb (15). Fruit is used externally as a skin cleanser (16). Hot water extract of dried plant is taken orally for bronchial asthma (17). Infusion of the fresh leaf is taken orally for as an anti-inflammatory (18).


Fig: 1 Branch with ripe olives


Fig: 2 Flowering olive branch


Fig: 3 Olive flowers

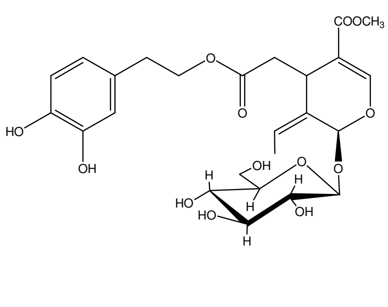
PHYTOCHEMISTRY

Glucoside components in the olive (leaves and fruits)

Among the different components which are already known in the olive plant, the first one is the oleuropein. This is the most important component of the glucosidic fraction of the *Olea europaea* from the quantitative point of view and from the historical point of view. In fact, the oleuropein is the first secoiridoid isolated from all over the world. In the oleuropein molecule, both a *mono*-terpenic and an *orhto*-diphenolic unit are present (19). Panizzi *et al*. (20) isolated oleuropein in the 50s. They determined its structure and established that this compound was one of the most important compounds responsible for the bitter taste of the fruits and the leaves of olive plant. It was the active compound responsible for the known hypotensive action of the extracts of the olive plant. Recently the accurate quantitative determination of oleuropein content in olive and olive oil was proposed by Sindona el al (21).

The oleuropein **1** is a secoiridoid glucoside that esterifies a dihydroxy-phenyl-ethyl alcohol. Two of its by-products are also present in the olive plant together with the oleuropein **1** and the mono-demethyl-derivatives **2** and **3**. Compound **2** is demethyl-oleuropein, which differs from oleuropein **1** in having a free carboxylic group on the pyranosic ring. Compound **3** is the oleoside methyl ester, known also as a glucoside of the elenolic acid, in which the carboxyl that esterifies the dihydroxy-phenyl-ethanol in the oleuropein **1** is here the free functionality. The two acid compounds **2** and **3** are two indicators of maturation of the olives. Their relative quantity, as regards to the oleuropein **1**, increases in fact as soon as the maturation proceeds, while the quantity of oleuropein decreases. This datum is in connection with the increase of the activity of the hydrolytic enzymes with the progress of the maturation, particularly to the activity of the esterases, responsible of the hydrolysis of the two ester bonds of the oleuropein (22). The ligstroside **4** (23) differs from the oleuropein **1** in the presence of a tyrosol residue instead of dihydroxy-phenyl-ethylic alcohol. The dimethylester of the oleoside **5**, also known as glucoside of the methylester of the elenolic acid, contains the two acidic functions of the oleuropein esterified with a residue of methanol (24). The oleuroside **6** is an isomer of the oleuropein, differing (25) from **1** in the exocyclic double bond position. Then several glucosidic compounds are present in connection with the dihydroxy-phenyl-ethanol. The first one is the cornoside **7**, a glucoside of a hemiquinoid isomer of the dihydroxy-phenyl-ethyl alcohol (26). The others are the β-glucopyranosyl-derivatives of dihydroxy-phenyl-ethanol **8a**, **8b** and **8c**. The structure of compound **8a** has been demonstrated by spectroscopic analysis by Bianco et al (27). Compounds **8b** and **8c** were previously described in *O.europaea*. Another new compound isolated from the olive plant is the product **9**, the di-galactoside of a poly-unsaturated diester of the glycerol (28). The particularly interesting datum of this structure is that the poly-unsaturated acid that esterifies the glycerine is α-linolenic acid. The product **9** is the principal component of a group of glycosides of poly-unsaturated di-esters of glycerine, present in the leaves and in the olives and whose concentration seems to decrease with the maturation, even if in a not marked way. In the end, two new esters of tyrosol **10** (29) and of hydroxyl-tyrosol **11** (30) have been isolated from olives. Both compounds indicate the interesting metabolic activity of *O.europaea*. Compound **10** is the oleic ester of tyrosol and it appears to be present mainly in olives. Compound **11** is the malic ester of hydroxy-tyrosol and is another of ester of tyrosol derivatives present in *O.europaea*.

Structure of isolated phytoconstituents



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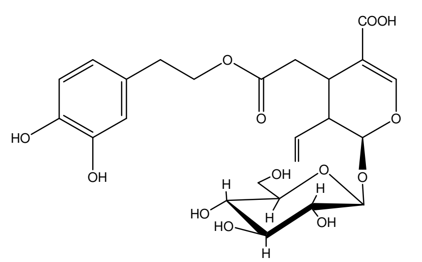

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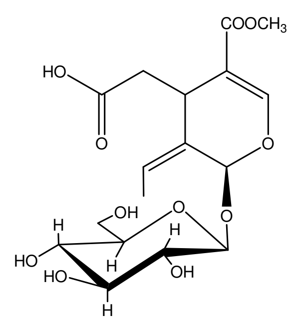

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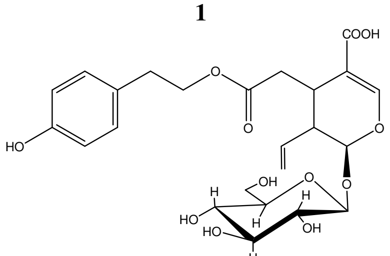

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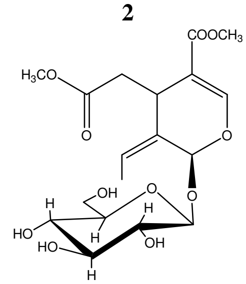

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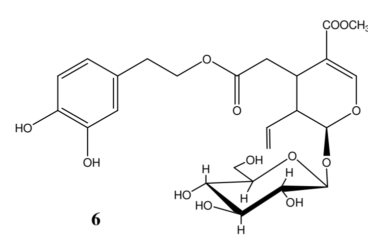

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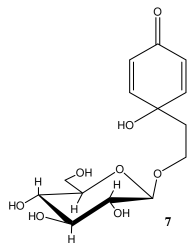

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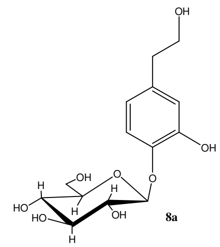
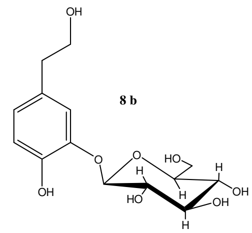
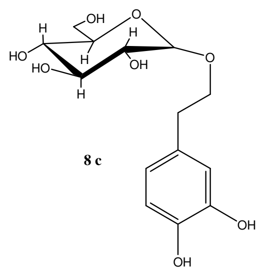


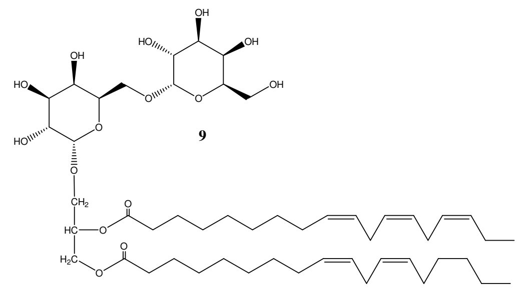
8a



8b



8c



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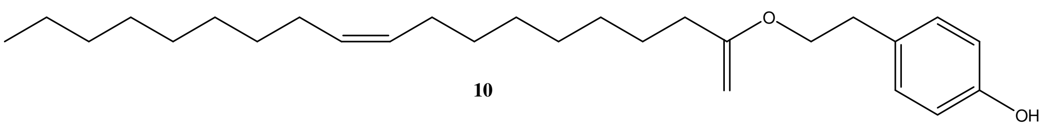

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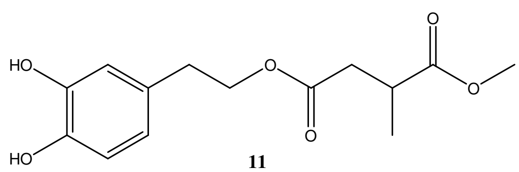

11

PHARMACOLOGY

Cardiovascular disorders

Epidemiological data obtained from clinical studies have consistently demonstrated that the Mediterranean diet, rich in olive oil, fruits, vegetables, and grains is correlated with a lower than average risk of coronary heart disease (31). The natural antioxidants, including oleuropein, from the olive tree may play a role in the prevention of cardiovascular diseases through a decreased formation of atherosclerotic plaques by inhibiting LDL oxidation (32). An olive leaf extract was reported in a laboratory study to have vasodilating effects, seemingly independent of vascular endothelial integrity (33). Traditional uses support olive leaf and olive oil in cardiovascular disease prevention (34, 35). Animal experiments in rabbit and rat preparations found a hypotensive effect of oleuropein, possibly via direct action on smooth muscle. Oleuropeoside also may exert vasodilator activity. Additionally, olive leaf extracts may possess antispasmodic, vasodilator, and anti-arrhythmic properties (36, 37).

Anti-viral activities

Olive leaf extract has reported antiviral activity, reportedly caused by the constituent calcium elenolate, a derivative of elenolic acid (38, 39). The isolated calcium salt of elenolic acid was tested as a broad-spectrum antiviral agent active against all viruses tested (40). Some viruses inhibited by calcium elenolate *in vitro* include rhinovirus, myxoviruses, Herpes simplex type I, Herpes simplex type II, Herpes zoster, Encephalomyocarditis, Polio 1, 2, and 3, two strains of leukemia virus, many strains of influenza and para-influenza viruses (41,42 ,43). The mechanism of action of the antiviral activity is reported to include (44):

- An ability to interfere with critical amino acid production essential for viruses.
- An ability to contain viral infection and/or spread by inactivating viruses or by preventing virus shedding, budding, or assembly at the cell membrane.
- Ability to directly penetrate infected cells and stop viral replication.
- In the case of retroviruses, it is able to neutralize the production of reverse transcriptase and protease.

- Stimulation of phagocytosis.

Anti-microbial activities

Olive leaves are known to resist insect and microbial attack, and *in-vitro* studies have been conducted to establish the range of activity of olive leaf extracts (45,46).Olive leaf extract has been reported to be an effective antimicrobial agent against a variety of pathogens, including *Salmonella typhi*, *Vibrio parahaemolyticus*, and *Staphylococcus aureus* (including penicillin-resistant strains); and *Klebsiella pneumonia*, and *Escherichia coli*, causal agents of intestinal or respiratory tract infections in humans (47). Olive leaf could be considered a potentially effective antimicrobial agent for the treatment of intestinal or respiratory tract infections. The component usually associated with olive leaf's antimicrobial properties is oleuropein (48, 49). Oleuropein has also been reported to directly stimulate macrophage activation in laboratory studies (50). Hydroxytyrosol demonstrated broader antimicrobial activity than oleuropein and is comparable to ampicillin and erythromycin in spectrum and potency (51).

Anti-oxidant activities

Olive leaf has antioxidant properties associated with oleuropein. Caffeic acid was also reported to have antioxidant activity through the scavenging of superoxide anion (52). Olive leaf has been reported to have anti-complement *in vitro*, and is a proposed mechanism for its anti-inflammatory effects (53). Oleuropein, an antioxidant, has been reported to decrease the oxidation of LDL cholesterol (54). Oxidized LDL is the most damaging form of cholesterol and can initiate damage to arterial tissues, thereby promoting atherosclerosis. Olive leaf has been reported to inhibit platelet aggregation and production of thromboxane A_2 (a stimulator of platelet aggregation with vasodilatory effects) (55). Also of interest, is a recent study reporting that olive leaf extract inhibited both angiotensin converting enzymes (56). *In-vitro* and animal experiments have been conducted to demonstrate the antioxidant activity of olive leaf extracts. In rat epithelial cells stimulated with cytokines, a concentrated polyphenol extract reduced nitrite concentration and free radical production (57). Rabbits with induced diabetes showed a decrease in oxidative stress markers when treated with oleuropein (58). Other experiments support the antioxidant activity of the phenols oleuropein and hydroxytyrosol (59-62).

Hypolipedemic activities

Studies in laboratory animals have reported hypoglycemic and hypolipidemic activity of olive leaf (63, 64). The active constituent was reported to be oleuropein, with a proposed mechanism of action of potentiation of glucose-induced insulin release, and an increase in peripheral blood glucose uptake.

Anti- diabetic activities

The hypoglycemic activity of olive leaf has been demonstrated in animals. In rabbits with induced diabetes, an ethanol extract of olive leaf decreased blood glucose. Suggested mechanisms include potentiation of glucose-induced insulin release and increased peripheral uptake of glucose (65, 66).

Thyroid activities

An aqueous extract of olive leaf administered to rats for 14 days increased T_3 levels and reduced circulating thyroid-stimulating hormone levels, possibly via a feedback mechanism (67).

CONCLUSION

Plants have been used as medicines since the time of immemorial, among which is *Olea europaea* whose products are widely available in the market for the treatment of various ailments. It has proved it efficacy in the management of various complex diseases including diabetes, cardiovascular disorders, viral and microbial infections but still a lot of work is to be done for exploring the evidences for other traditional uses of the plant.

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