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MINI REVIEW ON BIOLOGICAL ACTIVITIES OF PHENOLIC COMPOUNDS IN OLIVE LEAF

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Abstract
In our review we deals with the many activities of phenolic compounds in olive leaf and compound extracted which have antioxidant activity more than vitamin C, also phenolic compounds possess anti-inflammatory and antithrombotic activity, olive leaf depresses the blood pressure, so it have antihypertensive effect.

Introduction
Olive leaves are a source of many phytochemicals as phenolics and flavonoids which possess many activities e.g. antioxidant, antibacterial, antifungal. **[I].**The main characteristic of antioxidant compounds is their ability to trick free radicals such as peroxide, hydroperoxide or lipid peroxyl and thus prevent the oxidative mechanisms that lead to degenerative diseases **[II].**
Olive leaf extracts are of vested interest for their therapeutic effects. These extracts have different classes of biophenols counting phenolic acids, phenolic alcohols (hydroxytyrosol and tyrosol), flavonoids (luteolin 7-O-glucoside, rutin, apigenin 7-O-glucoside, luteolin 4-O-glucoside), and secoiridoids (oleuropein)**[III,IV].** Oleuropein is the most plentiful of all the constituents of olive leaf extract, having antioxidative, antimicrobial, antiviral**[V]** (even against the HIV virus),**[VI]**anti-atherogenic,and cardioprotective (by protecting membrane lipid oxidation acting on coronary dilation and by antiarythmic action**,[VII]**antihypertensive and anti-inflammatory properties**[VIII]**.Additionally, it has hypocholesterolaemic and hypoglycaemic activities **[IX]**it is also known to advance lipid metabolism to a dvanceobesityproblems**[X].**
The antioxidant compounds from olive leaves can increase the shelf life of food products by retarding the process of lipid peroxidation **[XI-XII].** Therefore; olive leaf extracts have been investigated as an additive supplement to improve the quality and stability of meat products **[XIII-XIV]** and vegetable oils **[XV- XV].**
The leaves of olive tree Olea europaea, comprise secoiridoids (oleuropein, ligstroside, dimethyloleuropein, and oleoside), flavonoids (apigenin, kaempferol, luteolin), in addition to phenolic compounds (caffeic acid, tyrosol, hydroxytyrosol). The leaves transmit the highest content of these compounds among other different plant organs of the tree. For example,

percentage of oleuropein (as an olive biophenol model) in olive oil, alperujo and olive leaves arrays between 0.005-0.12%; 0.87 and 1-14% respectively **[XVII - XVIII].**Confirmed that olive leaf extracts exercise a considerable foraging activity on DPPH. In addition, on enhancement of some oils (olive oil, sunflower oil, palm oil, as well as a vegetable shortening) with polyphenols of olive leaf extract secured protective effect against oxidation **[XX]**. In another study **[XIX]** it was shown that hydrolysate and Chemlali olive leaf extracts are excellent antioxidants and can serve as substitutes for synthetic antioxidants in advanced olive and in husk oils.

Result and Discussion

Antioxidant activity

Many phenolic components in olive leaf have a strong radical searching activity **[XXI, XXII, and XXIII–XXVI].** Additionally, extracts may be more beneficial than isolated constituents, since a bioactive individual constituent can **convert** its properties in the existence of other compounds existing in the extracts. Flavonoids, rutin, catechin and luteolin have nearly two and a half times more antioxidant activity than vitamins C and E**[XXVII]** Antioxidant activities of Oleuropein and hydroxytrosol were found to have alike with those of vitamins C and E [**XXVIII**] In added report, there was an order of radical scavenging capacity as rutin > catechin >≈luteolin > olive leaf extract ≈ hydroxytrosol > diosmetin > caffeic acid > verbascoside > oleuropein > luteolin -7-glucoside ≈ vanillic acid ≈ diosmetin-7-glucoside>apigenin-7-glucoside>tyrosol>vanillin. The most outstanding point is that olive leaf extract displays more antioxidant activity than vitamins C and E, due to the interaction among flavonoids, oleuropeosids and phenols [**XXIX].** A study of antioxidant capacity change by leaf maturation demonstrations that developed leaves have more antioxidant activity than young leaves [**XXX].**

Anti-inflammatory and anti-thrombotic activity

In particular, alongside the antioxidant activity, vasodilatatory, anti-platelet combination and anti-inflammatory effects have been allocated to the biophenols for example oleuropein and hydroxytyrosol in preclinical experimental models. They have been confirmed to prevent copper sulfate-encouraged oxidation of low-density lipoproteins [**XXXI].**

Antimicrobial activity

It is appealed that olive leaf might help in the management of a broad array of infectious diseases produced by bacteria, viruses, yeasts and fungi [**XXX]**. Olive leaf extract is intended for treatment of bacterial infections such as bronchitis and tonsillitis, fungal infections which happen in the vagina and viral infections like fever blister[**XXXII, XXVII, XXXIII].** In an in vitro study, tyrosol was found to be the greatest antifungal composite, subsequently catechin and oleuropein. Extracts may be more beneficial than isolated composites, since a bioactive individual constituent can change its features in the existence of other components existing in the extracts. Consequently, the most effective olive leaf products on the market today are made directly from fresh-picked leaves supplying the whole spectrum of natural biophenols, affecting them to work together in normal synergy to maximize the health benefits[**XXXIV, XXII, XXXV].**

The usage of OLE in the food industry can donate beneficially to a better food protection because of its high antimicrobial features [XXXVI- XXXVIII]. This normal antimicrobial action can decrease the damage microbiota and increase the shelf life of the product, [XXXIX] in addition to from a food safety point of view by preventing foodborne pathogens, [XL, XLI] or providing useful health effects in the gut microbiota of customers[XLII, XLIII]. The antimicrobial activity of OLE has been studied by numerous

authors to increase the shelf life of foodstuffs, such as inhibition of lactic acid bacteria and enterobacteria in refrigerated turkeys; [XXXIX] dipping S. enterica in leafy greens [XL] or against L. monocytogenes in cold-smoked salmon [XLIV] but no association was made with any specific compound.

Antihypertensive effect.

In vivo tries verify that olive leaf depresses the blood pressure. A prophylactic blood pressure dropping achievement of the olive leaf extract has been revealed in a preclinical study with rats treated with L-NAME [**XLV**]. Antihypertensive and cholesterol-lowering actions of the olive leaf extract have been confirmed in humans **[XLVI].**

Hypoglycaemic activity

Maximum hypoglycaemic activity was gained from samples collected in the winter months [**XLVII].** One of the compounds responsible for this activity was oleuropeoside, which showed activity at a dose of 0.16g kg^{-1}. This compound too established antidiabetic activity in animals with alloxan-persuaded diabetes. The hypoglycaemic action of this compound may result from two ways: (1) potentiation of glucose-induced insulin release, and (2) increased peripheral up take of glucose.

Streptozotocin (STZ)-diabetic rats exhibited raised fast blood glucose **(FBG)** level and decreased insulin level, which are revealing of hyperglycemia. However, treatment with olive leaves extract (OLE) enhanced the altered FBG and insulin levels in the diabetic rats [XLVIII]. This indicates that OLE is able to increase the ability of insulin to lower serum glucose, approving its anti-diabetic activity. These results are consistent with other studies [XLIX, L].

The significant drop of malondialdehyde (MDA) and increased levels of SOD, GPx, CAT and GSH in testicular tissues of diabetic rats in response to OLE treatment shown beneficial effect of the extract against oxidative stress. Phytochemicals such as polyphenols are essential non-toxic sources of antioxidants [LI]. The high stages of polyphenolic compounds in OLE; principally Oleuropein and hydroxytyrosol propose its protective ability in contrast to oxidative stress and cellular damage [XLIX]. Polyphenols too has an anti-hyperglycemic activity, which may destroy glucose production in the liver and advance glucose uptake in peripheral tissues [LII]. The improvement of blood glucose level in OLE-treated diabetic rats and the antioxidant property of OLE reduced reactiveoxygen species **(ROS)** generation and consequently decreases the **lipid peroxidation(LPO**) [LIII]. In another model, OLE treatment protected rats against cisplatin-induced testicular toxicity owing to its antioxidant and antiapoptotic properties [LIV]. [LV] added that the obvious increase in the serum testosterone of diabetic rats treated with OLE is due to the androgen releasing activity of the extract. This finding is alike to that gotten by [LV]. They stated that consuming of virgin olive oil improved blood levels of testosterone and LH among adult men. Moreover, the enhancement in serum testosterone level in diabetic rats treated with OLE may be associated to the antioxidant influence of polyphenols content of OLE that can respond free radicals.

Anti-candidiasis effect

In the study by **[LVI]**, the inhibitory effect of aqueous extract of Olive leaves on growth of a fluconazole resistant strain of C. albicans and stated MIC and MFC for the aqueous extract of this plant to be 24 and 48 µg/mL, respectively [**LVI**]. However, in the present study, considerably higher amounts of hydroalcoholic extract of this plant were established as MIC and MFC.**[LVII]** in a study showed that MIC for Oleuropein as one of the products of Olive against C. albicans was found to be at least 12.5 mg / mL. They also demonstrated that exposure of yeast to this compound caused morphological changes in the fungal cell nucleus

and cellular death process (apoptosis) of the fungus is detected when exposed to different concentrations of this compound. Yeast bond to epithelial surfaces has also been reduced, which has been shown to reduce some important fungal virulence factors, including yeast hydrophobic power, as well as reduction of secretory aspartate proteinases (SAPs) as another pathogenicity factor. Lastly, it has been recommended in the study that exposure of yeast to Oleuropein reduces the amount of sterols in the cytoplasmic membrane of the fungus, and consequently it is likely that the antifungal property of this compound is also related to preventing the membrane sterol synthesis pathway **[LVIII]**. It needs to be noted that the MIC value gained from the study of **[LVII]** in preventing yeast growth by only one of the polyphenolic derivatives of the Olive tree, produced higher values than MIC when exposed to total hydroalcoholic extract of this plant in this study. This might be attributed to a synergistic effect between the compounds in the total hydroalcoholic extract of the Olive plant. In the study by **[LIX]**, a mixture of honey and Olive oil was capable of inhibiting the growth of C. albicans and S. aureus. Olive oil alone reduces fungal growth, but combining it with a concentration of %66 of honey prevents fungal growth and creates a no-growth region of 3.5 mm. The results of a study also reveal that Olive oil has anti C. albicans effects **[LIX]**. Research shows that the polyphenolic compounds in the plant and fruit of Olive do not only affect the growth of fungi, but also affect the growth of other microbial groups. In the study by **[LX],** did a broad study of the impacts of some polyphenolic compounds in Olive, including Oleuropein, on reduction of multi-strain growth from Escherichia coli. Not only did they demonstrate the inhibitory effects of these compounds on the growth of the bacteria, but they also shown their mechanism of action which is affecting the vital enzyme ATP synthase.

Anxiolytic effect

In the study by [LXI] stated that, anxiety produces stress which causes increase production of adrenal hormones in addition to increase in the use of vitamin C, E and other micronutrients which improve metabolism of fats, carbohydrates and proteins to yield energy to overcome stress [LXII]. Biochemical alterations are induced because of stresses which are normally overcome by body's biological anti-oxidant system, comprising enzymatic anti-oxidants such as glutathione peroxidase and superoxide dismutase etc. Non-enzymatic anti-oxidants such as vitamin C, E and trace minerals provide secondary defense [LXIII].
Oleuropein possesses potent antioxidant and anti-inflammatory properties. Chelation of metal ions such as Cu and Fe with Oleuropein avoids free radical creation [LXIV]. Also, it prevents several inflammatory enzymes [LXV]. Both Oleuropein and hydroxytyrosol have been revealed to be scavengers of superoxide anion, contributing to its anti-oxidant nature [LXVI].
Oleuropein (OLE) advances various physiological functions, products multiple pharmacological actions in the central nervous system, and has in vitro and in vivo neuro protective effects [LXVII, LXVIII]. In the literature study on an animal model of anxiety, involving raised plus maze OLE administration potentially decreased anxiety-like behavior by more entries and exploratory activities, and less open arm avoidance, resulting in reduced index of anxiety [LXIX].

Conclusion

Phenolic compounds oliveleaf and compound extracted from olive leaf possess several activities like Antihypertensive effect, Anxiolytic effect,Hypoglycaemic activity,Anti-inflammatory and anti-thrombotic activity, and antioxidant activity .It has been found that they exhibit antioxidant activity more than Vitamin C.

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