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BOTANICAL MEDICINE

Olive-leaf extract

A current buzzword among CM users is seen as a cure-all for anything from the common cold to arthritis, asthma and eczema. Lesley Braun **attempts to discern efficacy behind the popularity.**

Australian consumers are spending approximately a million dollars every month on olive-leaf extract (OLE).[1] Over 16,000 bottles of OLE are sold each month by Australia's largest olive-leaf supplier, chiefly to the Australian market, but increasingly to countries such as Taiwan and Korea, where it is used as a medicinal agent, an ingredient in functional foods (such as enriched tofu; see *JCM* 2004;3(3):50) and in cosmetics.[1]

The plant *Olea europaea* (Oleaceae) has been used widely as a folk medicine in countries such as Spain, Italy, France, Greece, Israel, Morocco, Tunisia and Turkey, and the Mediterranean islands. Over 200 Biblical references to olive suggest its medicinal use dates back to ancient times.[2] As a folk remedy, the plant is used as a diuretic, hypotensive, emollient, febrifuge and tonic, for urinary and bladder infections and for headaches.[3] The leaves are described as astringent and antiseptic by Grieve in the traditional text *A Modern Herbal*, and are boiled in water to create a decoction used to treat obstinate fevers.

Today, the olive plant is most well known for its fruit crop and oil. The Mediterranean region produces approximately 98 per cent of the world's total olive crop (approximately 11 million tons)[4], although the plant is also widespread in the Arabian peninsula, the Indian subcontinent and Asia. More recently, olive plantations have been developed in Australia and research is now being undertaken to identify the best varieties suited to the subtropical climate.

The good oil

Olives and olive oil are important components of the Mediterranean diet and have been scientifically investigated for their health-giving effects. Olive oil, in particular, has health benefits that include reduction of risk factors for coronary heart disease, prevention of several varieties of cancers, and modification of immune and inflammatory responses. It has been investigated as both part of the Mediterranean diet and as a stand-alone supplement. Olive oil is a typical functional food, with varied components and mechanisms of action that contribute to its overall therapeutic characteristics. It is known for its high levels of monounsaturated fatty acids and is also a source of phytochemicals such as polyphenolic compounds, flavonoids, squalene, beta-carotene and α–tocopherol.[5] Extra-virgin olive oil is particularly rich in phenolic anti-oxidants.[6]

The extract even better?

For many growers, OLE is considered a by-product from the plant. It contains various trace elements vital to good health, such as selenium, chromium, iron, zinc, vitamin C, beta-carotene and a wide range of amino acids. Most importantly, it contains numerous phenolic compounds, such as oleuropein (thought to be identical to oleuropeoside[7]), hydroxytyrosol, tyrosol, rutin, luteolin, catechin and apigenin[8], which are responsible for most of the leaf's pharmacological effects. Unlike the olive fruit, olive leaf does not contain significant amounts of monounsaturated fatty acids, oleic acid or squalene.[9]

Olive phenolics have strong free-radical scavenging capacity and show a synergistic behaviour when combined, as occurs naturally in the olive leaf and hence OLE. The most active flavonoids — rutin, catechin and luteolin — exert anti-oxidant effects almost to 2.5 times more than those of vitamins C and E and are comparable to lycopene, according to *in-vitro* tests.[10] In addition, the anti-oxidant effect produced by OLE is higher due to the synergy of flavonoids, phenols and the high oleuropein content.[10]

It is important to note that not all olive products contain the same concentration of phenolic compounds. Only OLE

OLIVE PRODUCTS AUSTRALIA

Factfile

Indications	hypertension, cough, fever, oedema, asthma, eczema, psoriasis, cold and flu
Pharmacology	anti-oxidant, antihypertensive, anti-arrhythmic, diuretic, emmenagogue, febrifuge, hypoglycaemic, hypoinsulinaemic, hypocholesterolaemic, vasodilatory, possibly antimicrobial
Constituents	iridoid glycosides (oleuropein 6–9%, believed to be identical to oleuropeoside), flavonoids, elenolic acid, hydroxytyrosol
Products	dried leaf, liquid extract, tea infusion
Therapeutic dosage	5 mL 1:2 liquid extract tid
Precautions	none known
Interactions	none known

and olive oil marketed as extra-virgin olive oil (acidity <1%) are considered superior sources.[11] Of the two, OLE is the most concentrated. According to one test, total phenol levels ranging from 6360–8190 mg/L were identified in OLE (samples from Olive Products Australia) compared to 200–800 mg/L for extra-virgin olive oil (Department of Primary Industries Laboratory, Wagga Wagga).

Oleuropein – the pungent principal

For several decades, studies conducted on active constituents in olive leaf have found that many exert significant biochemical effects. In particular, oleuropein and its derivatives have received much attention. Originally isolated in 1908 by Bourquelot and Vintilesco, oleuropein is the phenolic constituent responsible for the typically bitter and pungent aroma associated with olives and olive oil and leaf.[12]

Oleuropein and its derivatives have a variety of roles including anti-inflammatory and anti-thrombotic activities.[13] More specifically, oleuropein and one of its catechol derivatives, hydroxytyrosol, inhibit leukotriene B4 generation, which is involved in a wide range of pro-inflammatory pathways.[14] These polyphenols are able to prevent LDL oxidation and platelet aggregation and to inhibit lipoxygenases and eicosanoid production.[15,16] Oleuropein has antimicrobial activity against a variety of viruses, bacteria, yeasts and fungi; however, one study suggests that hydroxytyrosol has stronger broad-spectrum effects.[17–24] Hypotensive, anti-arrhythmic, coronary-dilating and antispasmodic effects have also been reported for oleuropein.[25]

Luteolin is another key constituent that exhibits anti-inflammatory activity in animal models and anti-allergy effects in test-tube studies.[26,27] It has been found to possess antimutagenic and antitumorigenic properties.[28] Apigenin, also in the leaf, inhibits the inflammatory mediators nitric oxide and prostaglandin E2. More recently, significant calcium-antagonist activity was identified for hydroxytyrosol, another olive-leaf constituent.[29]

Considering that the olive leaf contains numerous active constituents, it is no surprise that a number of *in-vivo* studies have identified significant effects.

Effects on blood pressure and glucose

The hypotensive effect of olive leaves from *O. europaea* has been well documented *in vivo*.[30–33] One of the more recent studies tested a specially prepared OLE (EFLA 943) and confirmed dose-dependent hypotensive activity when given orally to animals.[34] To date, only one small clinical study has been published, which examined whether the effects are clinically significant. The study was conducted by the Service de Cardiologie, Hopital Militaire in Tunis, and tested OLE in 30 patients with essential hypertension.[35] OLE was given every four hours for three months after 15 days' treatment with a placebo. Active treatment resulted in a statistically significant decrease of blood pressure ($P<0.001$) in all patients and was considered well tolerated.

Olive-leaf extract has also demonstrated hypoglycaemic activity in animal models.[33,36] One of the compounds responsible for this activity is oleuropein, which produced anti-diabetic activity in animals with alloxan-induced diabetes. Researchers have suggested potentiation of glucose-induced insulin release and increased peripheral uptake of glucose as the most likely mechanisms of action. Clinical studies are not yet available, however anecdotal evidence suggests people are using it as an adjunct to dietary modification in diabetes type 2. One report from Morocco found that 80 per cent of people surveyed used herbal medicines for diabetes, hypertension and cardiac disease, and olive leaf was one of the most popular treatments.[37]

Anecdote outweighs scientific evidence

Overall, a review of the literature reveals that the number of published clinical trials is sparse; however, the amount of anecdotal evidence is constantly building. Ray Archer, founder

of Olive Products Australia Pty Ltd, receives dozens of letters each week from people claiming that OLE has prevented or treated their cold quickly and effectively, improved their sense of well-being and energy levels in general, or improved the management of various chronic diseases.[38]

Anecdotal reports suggest people are also taking OLE to help manage conditions characterised by inflammation, such as asthma and musculoskeletal pain, and are using it as a gargle for relief of sore throat. The anti-inflammatory effects demonstrated by several key components in olive leaf provide a theoretical basis for its use in this way. Interestingly, *in-vivo* tests report that OLE has a hypouricaemic effect in treated animals, suggesting a possible use in gout.[33]

In practice, some practitioners consider recommending it for its anti-oxidant properties, as adjunctive treatment for patients with mild hypertension or type-2 diabetes, and as both prevention and acute treatment for upper respiratory infections.

Clearly, there is much we still do not know about OLE and, at this stage, *in-vitro* and animal studies, together with traditional and anecdotal evidence, are driving its popularity. Considering that preliminary research suggests some of its uses may be justified, it is certainly time for the clinical testing to begin.

Pharmacists – dosage

The dose used is 5 mL three times a day, taken with or after meals, of a liquid extract containing approximately 4mg/mL oleuropein. Currently, drug interactions and adverse effects are unknown. ◗

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