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File: ■ Olive (*Olea europaea*)

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RE: Monograph on Olive Leaf Focuses on Pharmacological Studies

Monograph. Olive leaf. *Altern Med Rev.* 2009;14(1):62-66.

Olive (*Olea europaea*) leaf, the first botanical medicine mentioned in the Judeo-Christian *Bible*, was used by the ancient Greeks for fevers. In 1843, it was reported that a bitter substance in olive leaf tea was effective against malarial fever. Since the early 1900s, olive leaf extracts (OLEs) have been found to be antimicrobial, antioxidant, and hypoglycemic, and to have cardiovascular benefits in animals and humans. Primary constituents are secoiridoids (oleuropein and its derivatives), hydroxytyrosol, and various polyphenols, triterpenes, and flavonoids. Oleuropein is responsible for many of olive leaf's effects. Also found in olive fruits and oil, it is more concentrated in the leaves.

Olive leaf components in vitro inhibit many viruses, e.g. pseudorabies, some forms of polio, cold and influenza viruses, and human immunodeficiency virus (HIV). One constituent, calcium elenolate, inhibited nearly every virus studied, including coxsackie, encephalitis, and two strains of leukemia. Olive leaf inhibits assembly of the cell membrane and stops viral shedding. Anecdotal reports suggest that gargling with olive leaf tea may relieve sore throat, and taking OLE at the first sign of colds or flu may shorten symptom duration. Calcium elenolate given to hamsters with influenza cured infection. Anecdotal reports of benefits to HIV-positive individuals date to 1996. OLE is widely used in this population to strengthen the immune system, reduce viral load, relieve chronic fatigue, treat Kaposi's sarcoma and *Herpes simplex*, and reduce adverse side effects of antiretrovirals. Some patients have reported reversal of HIV status. Treating HIV-1-infected cells with OLE upregulated apoptosis inhibitor proteins, calcium and protein kinase C pathway signaling HIV-1 infected cells treated with OLE ornithine suppressed cell-to-cell HIV transmission. No clinical trials have been conducted on OLE as a viral treatment.

OLE inhibits many gram-negative and gram-positive bacteria, yeasts, and parasites, including malaria-causing *Plasmodium falciparum*. It may inactivate cellular enzymes needed for replication, or directly attack bacterial cell walls. Clinical trials have not

evaluated olive leaf against bacterial pathogens. It inhibits food-borne *Bacillus cereus* in vitro and in humans, altering germinating spores to delay growth. In vivo, in multi-drug resistant *Pseudomonas aeruginosa*, oleuropein reduced oxidative stress and prolonged survival.

OLE was reported to be hypotensive in 1951. It suppresses the L-type calcium channel directly and indirectly, causing vasodilation and reducing blood pressure. Oleuropein individually is also a vasodilator. OLE is antioxidant and anti-inflammatory. It had the highest radical-scavenging ability of 55 medicinal herbs in one study, more than twice that of green tea (*Camellia sinensis*) or milk thistle (*Silybum marianum*). Oleuropein reduces oxidation of low-density lipoprotein (LDL) in vitro and in vivo. OLE inhibits platelet aggregation and thromboxane A₂ production. All of these effects contribute to olive leaf's cardiovascular benefits, as do its hypoglycemic effects. Given to rats with induced diabetes, it reduced blood glucose levels significantly, raised insulin levels, and increased peripheral glucose uptake dose-dependently. OLE components luteolin and oleanolic acid inhibited postprandial glucose increase in vivo. OLE given to hypertensive rats at 100-1000 mg/kg for 2-6 weeks significantly lowered mean arterial pressure and heart rate. Given to salt-sensitive, genetically hypertensive rats at 60 mg/kg, it prevented severe hypertension and atherosclerosis (most likely by suppressing inflammation) and improved insulin resistance.

A human clinical trial studied OLE's effects on blood pressure in 40 borderline hypertensive pairs of identical twins. Twins from each pair were assigned to control or to one of two groups receiving 500 or 1000 mg/d OLE for six weeks. Mean blood pressure was unchanged for control and 500 mg groups, but the 1000 mg group had a significant decrease in mean systolic blood pressure (from 137 +/- 10 to 126 +/- 6; P<0.01). Another clinical trial (n=30) reported significant decreases in blood pressure in hypertensive patients given 400 mg aqueous OLE four times/d for three months. In vitro, olive leaf polyphenols significantly suppressed platelet-ATP release and platelet aggregation in a dose-dependent manner.

In vivo, OLE in doses of 100, 250, and 500 mcg/d increased T3 levels dose-dependently and significantly reduced circulating thyroid stimulating hormone after 14 days, suggesting a possible use in hypothyroidism.

Due to OLE's hypotensive and antiplatelet aggregation effects, caution should be used if also using blood pressure lowering or blood thinning medicines. In vivo studies report no toxicity even at high doses; studies in human cell lines likewise have found no toxicity. No studies have been undertaken in pregnancy or lactation. OLE is best taken with food to avoid gastrointestinal irritation.

—Mariann Garner-Wizard

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