



Dynamic Chiropractic – July 14, 1997, Vol. 15, Issue 15

Herbal Health Report: Olive Leaf Extract Regains Interest as a Superb Anti-microbial Agent

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Headlines warning of antibiotic resistant bacteria, rare strains of flesh eating strep, rising HIV rates, and deadly outbreaks of viruses such as Ebola and Hanta are on the rise, prompting growing concerns amid the medical community and the population at large. Endeavors to slow the tide of increasingly virulent microorganisms has researchers clambering for new and more potent drugs. But while we may be winning some battles, the odds favor our much smaller opponents, which use sheer numbers and genetic variance to outwit our efforts, and which may ultimately be winning the war.

Interestingly, we are finding powerful allies in the plant world. From an evolutionary perspective, our bodies have relied on plants for maintenance and repair. Botanicals, which are the foundation of many pharmaceuticals, are now gaining new respect among researchers and practitioners of traditional medicine. Modern botanicals are produced by advanced extraction processes; they are highly concentrated substances yielding powerful weapons in the battle against disease, while promoting dynamic balance in the organism as a whole. Many herbal products possess a high degree of safety and efficacy without the toxic side effects seen in most pharmaceuticals.

The Mediterranean olive or *olea europaea* has recently rekindled the interest of scientists and clinicians alike because of its potent medicinal value. The olive is a hardy tree that manufactures its own potent antibiotic substances to fend off disease causing bacteria, fungi, parasites and insects. In 1908, Bourquelot and Vintilesco isolated a bitter glucoside (structurally classified as an iridoid) from olive leaves and named it oleuropein. In 1960, scientists from Holland further isolated elenolic acid (a monoterpene), which was eventually determined to be the chemical constituent with the greatest activity against infectious microbes. Later in that same decade, viral researchers at a U.S. pharmaceutical company (Upjohn Co., Kalamazoo, MI) demonstrated that elenolic acid evidenced remarkable inhibition of viruses and bacteria without

damaging the host cells in vitro.

Although it is not known exactly how oleuropein acts as an antiviral agent, there are several proposed mechanisms:

- interference with specific amino acid production processes vital to the life cycle of the virus;
- interference with viral infection and/or spread by inactivating the virus or by prohibiting shedding, budding or assembly at the cell membrane;
- immune activation of host defense through direct stimulation of phagocytosis;
- neutralization of the production of reverse transcriptase and protease (relates to retroviral ability to alter the host cell RNA);
- penetration of infected host cells while achieving an irreversible inhibition of viral replication.

The antiviral activity of elenolic acid was shown to be greatest in an alkaline environment (pH 7.5), which is very close to the normal human pH range of 7.35-7.45. Virucidal activity was diminished by incubation with amino acids lysine, glycine, cysteine and histidine, and to a lesser extent with phenylalanine, tryptophan, serine and threonine. Because the elenolic acid could be inactivated by free amino acids circulating in the bloodstream, research was apparently discontinued. Then in 1994, an independent research team achieved a breakthrough that apparently overcame this hurdle, allowing sufficient levels of elenolic acid to be delivered to the body. Today, preparations of olive leaf extract are standardized to contain approximately 5% elenolic acid content, and researchers are presently working to increase that percentage to 15%.

Viruses that have shown susceptibility to elenolic acid in vitro include:

- herpes (MRS); vaccinia; pseudorabies; influenza A & B; Newcastle disease; parainfluenza 1, 2, & 3; coxsackie A21; encephalomyocarditis; polio 1, 2, & 3; vesicular stomatitis; sindbis; reovirus; Moloney murine leukemia; Rauscher murine leukemia; Moloney sarcoma. In vivo activity has been demonstrated in hamsters with reduced viral yields from animals infected with parainfluenza 3 virus.

Reportedly, some clinicians have been testing oleuropein with HIV patients. Interestingly, protease inhibitors have gained a great deal of press for their potential in the fight against AIDs. These are believed to actively block the site of HIV protease. When combined with other classes of drugs researchers have reported remission in infected patients. We anxiously await their reports on effectiveness.

Oleuropein has also been shown effective against many bacteria. The proposed mechanisms of antibacterial activity are as follows:

- slows the growth rate and inhibits a number of enzymes;
- induces damage to the cell membrane thus affecting its permeability and resulting in a leakage of cytoplasmic constituents;
- inhibition of micrococcal nuclease and lysozyme;
- inhibits enzymes by reacting with the ε-amino group of exposed lysine residues and the exposed n-terminal amino group of polypeptide chains;
- irreversible inhibition of DNA polymerase II and inhibition of DNA polymerase III holoenzymes;
- immune activation of host defense through direct stimulation of phagocytic activity.

Bacteria that have shown susceptibility include:

- *Lactobacillus plantarum*; *L. brevis*; *Pediococcus cerevisiae*; *Leuconostoc mesenteroides*; *Bacillus cereus*; *Staphylococcus aureus*; *Bacillus subtilis*; *Enterobacter aerogenes*; *E. cloacae*; *Escherichia coli*; *Salmonella typhimurium*; *Pseudomonas fluorescens*; *P. solanacearum*; *P. lachrymans*; *Erwinia carotovora*; *E. tracheiphila*; *Xanthomonas vesicatoria*; and *Corynebacterium michiganense*.

Oleuropein has also been found effective against strains of malaria, including *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale* and *Plasmodium malariae*. Malaria is a protozoan infection characterized by fever, chills and profuse sweating, and occurs primarily in tropical regions. Malarial infection can occur by transmission of the protozoa parasite following the bite of an infected *Anopheles* mosquito. First the sporozoites multiply in cells of the liver, then after a period usually lasting 2-4 weeks, the parasite may invade the red blood cells. Next, the merozoites may multiply before being released into the bloodstream. Antimalarial activity was reported by clinicians in the 1850s who administered decoctions of olive leaf to infected patients. In 1906, scientists claimed that olive leaf extracts were superior to quinine, the primary treatment of malaria at the time. Since malaria has developed resistance to many of our present day drugs, clinicians may want to consider olive leaf extract as an addition to the treatment of malaria once again.

Fungal and yeast infections have been the focus of a great deal of attention from many health care providers. A major contributing factor to this increase is theorized to result from the overuse and overprescription of

bacterial antibiotics. These substances, once believed to be a panacea or cure-all, are now realized to have resulted in superstrains of antibiotic resistant bacteria that are increasingly more difficult to treat.

Furthermore, the natural bacteria living on our skin and mucous membranes (such as the lungs and intestinal tract) provide a blanket of protection from other harmful organisms. These microbes secrete substances that may be toxic to other invading organisms and either benefit or have a neutral effect on our bodies and cells.

Because antibiotics kill both the friendly and unfriendly organisms, they can upset the delicate balance of our body's natural defenses. The result has been a paradise for yeast and fungi not harmed by the antibiotics, which may flourish without competition from our natural bacterial allies. Since yeast prefer a diet high in sugars, our overindulgence in sweets has further benefited yeast populations and contributed to illness and disease. Fungi and yeast species that have shown sensitivity to oleuropein include *geotrichum candidum*, *rhizopus* sp. and *rhizoctonia solani*.

Oleuropein and other structurally related iridoids have also demonstrated anti-inflammatory properties when administered either orally or topically. Although oleuropein's activity as an anti-inflammatory may be moderate in comparison to other naturally occurring iridoids, it could still be considered noteworthy. And since virtually all disease results in an inflammatory response, oleuropein might offer some benefits in any health condition.

In the United States, as in most Western countries, atherosclerotic heart disease and stroke remain the number one killer despite all the advancements in medicine. A major risk factor for atherosclerosis is the elevation of serum lipids (specifically low density lipoproteins or LDLs). Oxidized low density lipoproteins can be taken up by endothelial cells and monocytes by way of their scavenger receptor. This can lead to the formation of cholesterol ester-loaded foam cells and atherosclerotic plaques. In the advanced stages, this can lead to the death of the endothelial cell (which is the cell at the innermost layer of the blood vessel).

Oleuropein is a polyphenolic compound; these naturally-occurring phytochemicals are considered to be very potent antioxidants. Oleuropein has been shown to inhibit the oxidation of LDLs.

This may be the reason oleuropein has shown antiatherogenic activity. Oleuropein content in the diet of the Mediterranean population has been proposed among other postulates for the decreased incidence of coronary heart disease when compared to its Western counterpart.

Hypertension is a common disorder encountered and diagnosed by many physicians. Because there is usually no pain associated with its occurrence, many patients are unaware of problems until they visit their doctors or until it is too late, as in the case of a stroke. An important component of olive leaf extract is oleuropein. This compound has been shown to act as a hypotensive by activating the vasodilation of blood vessels. Decreased arterial blood pressure, decreased atrial rate, decreased cardiac contractility and anti-arrhythmic effects have all been attributed to oleuropein. It appears that other olive leaf ingredients act synergistically to potentiate the relaxant effect of oleuropein; thus, the whole is greater than the individual parts.

Diabetes mellitus is a syndrome characterized by increased blood sugar resulting from impaired insulin secretion and/or effectiveness. Numerous complications include retinopathy, atherosclerotic disease, nephropathy and neuropathies. Olive leaves have long been touted as an antidiabetic agent in herbal folklore. Scientists have demonstrated that the oleuropein content of the plant is responsible for its hypoglycemic activity. The potentiation of glucose-induced release of insulin and an increased peripheral uptake of glucose are two proposed methods of antihyperglycemic activity.

The oleuropein content is highest in the winter months and samples collected in these months evidenced the greatest hypoglycemic and antihyperglycemic activity. Olive leaves collected in the summer months may contain little or no oleuropein. Individuals with insulin dependent diabetes should be cautioned against using oleuropein or other plant extracts to control diabetes as this could be extremely dangerous. However, individuals with non-insulin dependent and insulin dependent diabetics may want to closely monitor their glucose levels when taking oleuropein rich oleuropein.

Hyperuricemia is a finding that is commonly associated with gout. Because of the high uric acid content in the bloodstream, crystals may deposit in the joints. Swelling, warmth, redness and exquisite tenderness most often affects the metatarsophalangeal joint of the great toe, but the instep, ankle, knee, wrist and elbow are also common sites. Uric acid may also precipitate in organs, such as the kidney, where aggregates of gravel or stones may lead to obstructive uropathy. A report in the *Belgian Pharmacology Journal* (March-April 1994) recorded hypouricemic activity in aqueous olive leaf extracts. This may lead to a promising method of managing hyperuricemia and its complications.

Although the following accounts are anecdotal, I have seen numerous benefits in practice using oleuropein. Perhaps the most common is patients reporting tremendous increases in energy, even patients with chronic

fatigue. Patients have also reported toenail fungus that disappeared in cases that had been unresponsive to medical care, decreased severity and length of herpes outbreaks, and hasty recovery from colds and flus.

Oleuropein is best taken with water, one hour or more away from food, as the activity of elenolic acid in the oleuropein may be decreased by certain amino acids found in protein- containing foods and supplements. Therefore, if one wishes to take amino acids such as lysine they may wish to take the oleuropein at a different time of the day. Some individuals may experience symptoms of detoxification resulting from toxins released into the bloodstream following the death of a virus, bacteria, fungus or parasite. Symptoms of detoxification are natural and may include headaches, muscle and joint aches, skin rash or sensitivity, irritability, nervousness, fatigue and mental dullness. Individuals with hypoglycemic tendencies may likewise experience similar symptoms. In either case, proceed slowly by taking only one or two pills and gradually increase the dosage when symptoms subside. A reasonable therapeutic dose would be 6-9 pills in divided doses per day (some practitioners have reportedly used doses double this amount).

The olive has long been a symbol of hope, victory and friendship since biblical days. Perhaps the time has come for us to reconsider the powerful role this tree can play in contemporary health care.

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