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## HERBAL MEDICINE

### BOTANICAL ANTIBIOTICS

# Oregano Oil Offers Alternative for Fungal, Bacterial Infections

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Herbal medicine truly represents a cross-road between the culinary and medical arts. Nowhere is this more apparent than in the emerging body of data showing that a number of commonly used cooking herbs contain powerful antimicrobial and antioxidant compounds.

The disease-averting properties of plants like oregano, rosemary, marjoram, cloves, garlic and various peppers were certainly recognized by healers and common folk in the ancient world. In fact, the primary motive for using many of these herbs in cooking may have been hygienic—to retard food spoilage and prevent food borne illnesses. The fact that they have pleasing flavors is an added bonus.

In recent years, the essential oil of oregano has received considerable attention as an alternative to pharmaceutical antibiotics or antifungals. While much of the data is still preliminary, there is enough convincing lab work to make a solid case that compounds within this plant—especially wild types of oregano—are capable of outright killing or inhibiting a number of common pathogens, most notably *Staphylococcus aureus* and *Candida albicans*.

Oregano is a member of the Lamiaceae (AKA Labiatae) family of plants, which also includes all species of thyme, rosemary, lavender, basil, and mint. Indigenous to the Mediterranean, they have figured into both cooking and medicine in that region for centuries. The bac-

teriostatic and fungistatic effects of these herbs are linked to their high content of phenolic compounds, particularly one known as carvacrol.

Harry G. Preuss, MD, and his team at the Department of Physiology and Biophysics, Georgetown University Medical Center, are currently engaged in an ongoing assessment of the physiologic effects of various culinary and medicinal herbs. They recently published their data on the anti-candidal effects of origanum P73, the essential oil of wild oregano.

Using broth cultures of *C. albicans*, they compared the anti-candidal effect of origanum P73 essential oil infused into extra virgin olive oil at various concentrations against olive oil alone. They also

anum—olive oil infusion was provided by North American Herb and Spice Co., which markets the product as P73 Oreganol.

At a concentration of 0.25 mg/ml, the P73 essential oil completely inhibited candidal growth; at 0.125 mg/ml, it inhibited growth by 75%; and at 0.0625 mg/ml, it still blocked greater than 50% of the fungal growth. Both germ-tubule formation and mycelial elongation were disrupted. The effects were equivalent to what was observed with nystatin at 0.005 mg/ml, and amphotericin B at 0.0015 mg/ml.

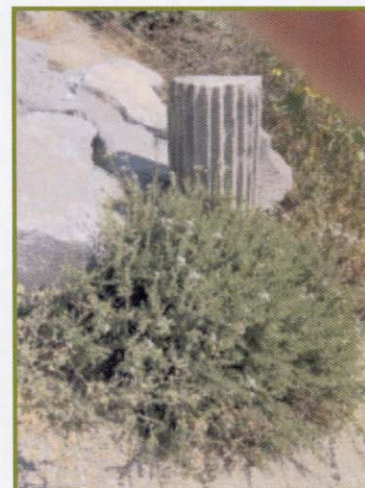
Olive oil alone had no fungistatic or fungicidal effect. Carvacrol isolated from the oregano oil was able to stop fungal growth, though it required twice the concentration to achieve the same effects.

The same team then tested this essential oil at various concentrations against plain olive oil or an olive oil suspension of amphotericin B, 1 mg/kg body weight, in mice infected systemically with *C. albicans*. Infusions of  $2.5 \times 10^6$  live *C. albicans* cells are typically fatal to mice, resulting in disseminated organ system infections within 10 days. Mice in this experiment were injected with five times as much.

The various treatments were fed orally to the mice for a total of 8 days. At a dose of 325 mg/kg body weight, the oregano essential oil ensured 100% survival at 30 days. Amphotericin B exerted the same effect, with all treated animals surviving the full 30-day period. In contrast, all those receiving plain olive oil were dead within 10 days. The investigators point out that the essential oil need



compared P73 to carvacrol alone, as well as the pharmaceutical antifungals nystatin and amphotericin B. The P73 orig-



Photos courtesy of North American Herb & Spice

not be as high as 325 mg/kg; a dose as low as 8.66 mg/kg/day gave 80% survival rates (Manohar V, et al. *Mol Cell Biochem* 2001; 228(1-2): 111-17).

Carvacrol alone gave similar survival rates as the whole P73 oil, but qualitatively, the mice treated with the complete oil had more lustrous coats and less of the "scruffiness" associated with murine candidal infections.

Last fall, the same research team presented data at the annual meeting of the American College of Nutrition, indicating that origanum P73 essential oil at a concentration of 0.25 mg/ml was able to completely inhibit the growth of *S. aureus* in culture. The *in vitro* effect was similar to that of penicillin and vancomycin.

In mice infected with five times the lethal murine dose of *S. aureus*, the P73 oregano oil reduced mortality in a dose-dependent manner. Fifty percent of the mice treated with 4  $\mu$ l of origanum P73, and 50% of those treated with 400  $\mu$ g vancomycin were alive at 30 days. In contrast, all the animals treated with olive oil alone were dead within 3 days.

While carvacrol alone enhanced survival in a dose-dependent fashion, none of the carvacrol treated mice lived for

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## Oregano Oil

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more than 21 days, suggesting that the whole P73 oil has antibacterial efficacy not obtainable with the isolated "active" phenol. This is important to consider, given the modern trend in herbal medicine to identify and isolate so-called "active" compounds from a complex phytochemical matrix. While this may facilitate standardization, it does not necessarily optimize therapy.

Not surprisingly, researchers in the Mediterranean have taken to studying oregano and other Lamiaceae herbs, which have been a part of both their cuisine and their medicinal traditions for thousands of years. Investigators at the University of Athens school of pharmacy recently assessed the antibiotic capacities of two oregano species (*O. scabrum* and *O. microphyllum*), both of which are endemic to the Hellenic world. Both were able to kill or inhibit 6 Gram-negative and 6 Gram-positive bacteria, as well as three pathogenic fungi (Aligiannis N, et al. *J Agric Food Chem* 2001; 49(9): 4168-70).

Another team at the Agricultural University of Athens studied aqueous extracts of various Lamiaceae species including *O. dictamnus*, *O. majorana*, and *Rosmarinus officinalis*. They found that all of them inhibit the growth of *Yarrowia lipolytica*, a form of yeast commonly found in some cheeses of the Mediterranean region. The effect was strongest for *O. dictamnus* and *R. officinalis*

(Karanika MS, et al. *Int J Food Microbiol* 2001; 64(1-2): 175-81).

Of all the plants in the Lamiaceae family, those classed as oregano have the highest phenolic content, typically well above 60% in the essential oil. Daferera et al. at the Agricultural University of Athens found that essential oils derived from various oregano species, as well as from thyme and marjoram, can inhibit the radial growth and conidial germination of *Penicillium digitatum*, even at relatively low concentrations. They concluded that various monoterpenes in the oils act synergistically against fungal growth (Daferera DJ, et al. *J Agric Food Chem* 2000; 48(6): 2576-81).

Oregano oil also appears to have strong antioxidant properties, again due to its high phenolic content. Researchers at the Beltsville Agricultural Research Center, USDA, recently assessed the oxygen radical absorbance capacity (ORAC) of 27 culinary and 12 medicinal herbs. They found that *Origanum ×majoricum*, *Origanum vulgare*, and *Poliomintha longiflora* have the highest ORAC values of any of the common cooking herbs. Further, for all herbs studied, the ORAC values showed a direct linear correlation with total phenolic content (Zheng W, Wang SY. *J Agric Food Chem* 2001; 49(11): 5165-70).

The study suggested that oregano had between 3 and 20 times greater antioxidant activity than any of the other herbs tested. It also had a 42-fold greater antioxidant potential than apples, 12-fold greater activity than oranges, and

4-fold greater activity than blueberries. Drs. Zheng and Wang concluded that essential oils of herbs like oregano are an excellent way to obtain antioxidants without the calories associated with fruits or other high-antioxidant foods.

Scottish researchers tested oil of oregano, along with oils from black pepper, clove, and a number of other culinary herbs, against 25 genera of bacteria including a number of animal pathogens. They found that all of these oils, to varying degrees, inhibited or killed outright bacteria that are involved in disease, food spoilage, or food poisoning, lending credibility to the view that humans originally used these plants not so much for flavoring as for health benefits (Dorman HJ, Deans SG. *J Appl Microbiol* 2000; 88(2): 308-16).

Compounds derived from oregano may have an added benefit on neurologic health. A team at Korea University, Seoul, assayed 139 commonly used herbs in search of compounds that can inhibit acetylcholinesterase (AChE). Inhibition of this enzyme and the consequent reduced degradation of acetylcholine in the brain, is a primary mechanism for drugs used in treatment of Alzheimer's disease.

Of all the plants and spices they studied, an ethanol extract of *Origanum majorana* showed the highest AChE inhibitory effect. They identified ursolic acid as the key enzyme inhibitor, and noted that this compound blocks AChE activity in a dose dependent fashion. Ursolic acid has a strong affinity for the enzyme. The con-

centration required for 50% enzyme inhibition was 7.5 nM, as compared to 1 nM for tacrine, a long-established pharmacologic treatment for Alzheimer's disease (Chung YK, et al. *Mol Cells* 2001; 11(2): 137-43).

All of these findings are provocative in that they suggest oregano oil may be a natural alternative to synthetically produced antibiotics or antifungals for both topical and systemic treatment of *Candida* or common bacterial pathogens. Certainly, herbal medicine traditions going back to ancient Greece would suggest this is the case. But human clinical studies have yet to be undertaken.

Thousands of years of common culinary use leads to the conclusion that the compounds contained in oregano are generally safe. However, clinicians should be aware that there is at least one report in the literature of systemic allergic reactions to compounds produced by the Lamiaceae plants.

Benito et al., from the Hospital Clinic Universitari, Valencia, Spain, reported one case of a patient who exhibited strong systemic reactions to both oregano and thyme. Inhalation and skin prick testing showed significant cross-reactivity. With the exception of lavender and basil, all other herbs tested (oregano, thyme, hyssop, marjoram, mint, and sage) were able to produce both clinical signs and IgE elevations (Benito M, et al. *Ann Allergy Asthma Immunol* 1996; 76(5): 426-8). The investigators noted that this patient was also allergic to grass allergens. ☺