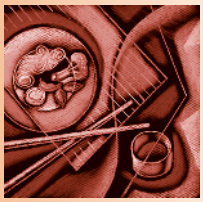

Oregano

Overview of the Literature on Health Benefits

Keith Singletary, PhD

Oregano is an herb that has been cultivated for centuries in the Mediterranean area, although it now can be found on most continents. Actually, there is not simply one "oregano," but rather several species that may contribute to the oregano used for culinary purposes. *Origanum vulgare* (also referred to as Spanish thyme and wild marjoram), a member of the plant family Lamiaceae, is generally the spice variety sold as oregano in Europe and the United States. Medicinal uses for oregano date back to the ancient Greek and Roman empires where applications of the leaves were used to treat such maladies as skin sores and relieve aching muscles and as an antiseptic. Oregano also has been used in traditional medicines for such ailments as asthma, cramping, diarrhea, and indigestion. In Greece, an oregano infusion is still used as a folk remedy against colds and upset stomach and to maintain general health. Based on the current scientific literature, oregano extracts and individual constituents consistently have demonstrated antimicrobial actions in vitro toward food-borne pathogens, although the capacity to counter human infections is not well studied. Oregano contains several potent antioxidants that may contribute to the findings in preliminary studies that oregano exhibits benefits toward the cardiovascular and nervous systems, relieves symptoms of inflammation, and modulates blood sugar and lipids. Well-controlled human studies substantiating these health effects are lacking. Nutr Today. 2010;45(3):129–138

Oregano is an herb that has been cultivated for centuries in the Mediterranean region, although now it can be found in most continents. The name *oregano* translates roughly into "mountain joy," which explains in part its association for ancient Greeks and Romans with joy and happiness. Actually there is not simply one "oregano," but rather several species that may contribute to the oregano used for culinary purposes. *Origanum vulgare* (also referred to as Spanish thyme and wild marjoram), a member of the plant family Lamiaceae (Labiatae), is generally the spice variety sold as oregano in Europe and the United States. Its light green leaves are used either "dry" or "fresh" as a culinary seasoning, and its use has elicited such sensory responses as "pungent," "pleasantly bitter," "herbaceous," and "aromatic," to name a few. Two constituents of oregano, carvacrol and thymol, contribute to the sensation of warmth in the mouth due to their actions on temperature-sensitive structures called ion channels.[1,2]

Oregano is most well known for imparting an "Italian taste" to Mediterranean cuisine and may be used to enhance the flavors of a variety of foods including baked goods, vegetables, legumes, fish, pizza, pasta sauce, and chilis. It has been included in aromatic teas and is a frequent addition to Mexican dishes. Mexican oregano is prepared from *Lippia* spp (Verbenaceae).[3] In the Philippines, a related herb suganda (*Coleus amboinicus*) also is used as oregano in cooking.[4]

Medicinal uses for oregano date back to the ancient Greek and Roman empires where applications of the leaves were used to treat skin sores, to relieve aching muscles, and as an antiseptic. Oregano also has been used in traditional medicines for such ailments as asthma, cramping, diarrhea, and indigestion.[5] In Greece, an oregano infusion is still used as a folk remedy against colds and an upset stomach and to maintain general health.[6]

Because there are so many species of *Origanum* used around the world as an "oregano" condiment and for medicinal purposes, it is not surprising that there are variations in their profiles of bioactive constituents and in the purported beneficial effects.[7–12] For example, the carvacrol content of essential oils from *Origanum* plants may vary over 20-fold, and similarly thymol content may vary 3-fold to almost 30-fold among plant oils.[7,9] The amounts of the terpene alcohol linalool could range from nondetectable in one plant oil to approximately 30% of the essential oil composition of another.[9]

Figure. Oregano leaves. Obtained from McCormick Inc.

The volatile compounds carvacrol (isopropyl-*o*-cresol or 5-isopropyl-2-methylphenol) and thymol (isopropyl-*m*-cresol) are considered major terpene components of oregano essential oils,[7,9,13] along with *p*-cymene (4-isopropyl toluene) and γ-terpinene, which are precursors in the biosynthesis of thymol and carvacrol. Thymol is used in perfumes and mouthwashes. Other bioactive compounds identified in oregano leaf include phenolic acids (caffeic acid, *p*-coumaric acid), rosmarinic acid and caffeoyl derivatives, ursolic acid, and carnosic acid, as well as a mixture of flavonoids.[5] In fact, rosmarinic acid is one of the most abundant phenolic compounds present in aqueous extracts of oregano leaf and is known to be the dominant phenolic compound in Labiatae spices (such as oregano, rosemary, sage, etc).[5]

It should be mentioned at the onset of this overview of oregano and health that the benefit of oregano to humans ultimately will depend on the bioavailability of its biologically active constituents following ingestion, that is, how well those components are absorbed, distributed, metabolized, and eliminated from the body. This will be of critical importance in establishing any link between health effects detected in vitro and those that might be expected to occur in vivo. Investigations evaluating the bioavailability of oregano in humans are limited. Two reports in humans have indicated that the intake of oregano extracts containing doses of 300 to 600 mg/d total oregano-derived phenolics resulted in the absorption and quick elimination of the phenolic acids.[14,15] Yet, even given a dose of 600 mg/d for 4 weeks, no significant changes in biomarkers of lipid peroxidation were detected in these subjects.[14] A number of issues were identified by the authors of this study that may explain variations in natural product bioavailability and bioactivity. For example, the bioactivity of metabolites of a parent antioxidant phytochemical can be markedly different than that of the parent compound. Also, phytochemicals in a complex mixture may differ individually in their extent of absorption, their manner of metabolism, and thus their distribution in various body tissues. The bioavailability of single compounds identified in oregano, such as rosmarinic acid and thymol, also has been reported. In a clinical trial involving 12 healthy volunteers, the systemic availability and pharmacokinetics of thymol following a single 1.08-mg dose were examined. The metabolite thymol sulfate was detected in plasma, with a half-life of 10.2 hours[16] and a maximum plasma concentration of approximately 93 ng/mL. In another small clinical trial, 6 healthy men were given a single oral dose of 200 mg rosmarinic acid in an extract of *Perilla frutescens*.[17] They observed that rosmarinic acid was absorbed and detected in sulfate- and glucuronide-conjugated forms, with 75% of the rosmarinic acid metabolites being rapidly excreted within 6 hours after intake. Similar results were obtained in a study in rats orally administered rosmarinic acid at 50 mg/kg body weight.[18] The absorption efficiency of rosmarinic acid in rats was determined to be much less than that of other phenolic acids such as caffeic acid and *p*-coumaric acid following a 100-μmol dose per kilogram of body weightt.[19] This important area of study in humans warrants additional attention.

Summary

A variety of health benefits of oregano or its individual constituents have been the subject of scientific study. Oregano extracts and individual constituents consistently have demonstrated antimicrobial actions in vitro toward food-borne pathogens, although the capacity to counter human infections is not well studied. Oregano contains several potent antioxidants that may partly contribute to findings in preliminary studies in which oregano exhibits benefits toward the cardiovascular and nervous systems, relieves symptoms of inflammation, and modulates blood glucose and lipid levels. Well-controlled human studies substantiating these health effects are lacking.

Examples of several uses for oregano are presented in the following, and an effort was made to give an overview of the variety of scientific research on this topic. Points of view for rating of evidence in each category are based on consideration of cell culture and animal and human clinical data from the peer-reviewed scientific literature. A higher rating was given when there were both preclinical and clinical data and when there was consistency of findings among well-controlled human studies.

Summary of Scientific Research

Scientific Evidence for Select Uses	Rating
Antimicrobial actions	Preliminary, inconclusive
Oregano and some of its constituents are reported in in vitro models to suppress microbes that cause food spoilage and those that contribute to human and animal disease. Both the essential oil and other extracts of oregano can suppress the growth of gram-positive and gram-negative bacteria, yeast, and some fungi.[20–29] Depending on the test system and microorganism evaluated in these assays, the effective concentrations of oregano ranged from 0.4 to 4000 μg/mL. Oregano oil added at 4% wt/wt has been used to fortify flexible polypropylene film as an antimicrobial strategy.[30] Oregano oil tested in a range of concentrations from 0.1 to 2.0% wt/wt was effective in suppressing microbial growth in beef and sausage products.[31,32] However, in another study, oregano did not suppress growth of *Yersinia enterocolitica* or *Listeria monocytogenes* in barbequed chicken.[33] Oregano was reported to inhibit *Helicobacter pylori*, the bacterium associated with gastritis in humans, to kill human intestinal parasites in vitro (at ~175 μg/mL concentration), and at a dose of 10 mg oregano oil/kg body weight to effectively treat colibacillosis of newborn calves.[34–37] In a short-term study in humans infested with enteric parasites, daily intake of 600mg of emulsified oregano oil resulted in noticeable decreases in occurrence of some of the parasites.[38] Individual components of oregano, such as carvacrol and thymol, also have antimicrobial actions.[39–43] The effective doses of thymol or carvacrol may range from 20 to 50 μg/mL.[20] Of interest is the observation that oregano phytochemicals can suppress microorganisms associated with oral disease and ear infections.[44–47] Although the antiviral efficacy of spice phytochemicals can vary,[24] rosmarinic acid was reported to reduce the mortality of mice infected with an encephalitis virus[48] and has been identified as an inhibitor of HIVE type 1 reverse transcriptase.[49]	
Effects on inflammation and immunity	Preliminary, inconclusive
Several investigators have provided evidence that oregano extracts or constituents thereof can suppress inflammation in vitro and in vivo. Thymol (at doses of 2.5–20 μg/mL) inhibited the release of elastase, a marker of inflammatory disease, from human neutrophils induced by a chemotactic peptide,[50] an action in part mediated through inactivation of calcium-channel machinery. Likewise, rosmarinic acid inhibited neutrophil elastase release and weakly suppressed thrombin activity.[51] On the other hand, neither an essential oil of oregano nor the phytochemicals thymol, carvacrol, *p*-cymene, or γ-terpinene possessed anti-inflammatory actions in a chorioallantoic membrane assay, and in fact, thymol, at the dose used (10 μg), was shown to be an irritant.[52] Rosmarinic acid induced apoptosis of lymphocytes and was able to kill T and natural killer cells, which are means by which harmful immune responses can be mitigated.[53,54]	
Oregano essential oil, administered intrarectally (0.1–1.0 mg/kg body weight) or in the diet (0.05%–2.0%) had a significant protective effect in rodents against chemically induced colonic damage, inflammatory cell infiltration, and vascular dilation along with suppressing production of proinflammatory cytokines IL-1β and IL-6.[55,56] In several mouse studies of inflammation rosmarinic acid (50 mg/kg body weight intraperitoneally or 1.5 mg/d orally) dramatically decreased inflammatory autoimmunoarthritis and allergic asthma and markedly reduced inflammatory markers and cyclooxygenase 2 expression.[57–59] In human patients with seasonal allergic rhinoconjunctivitis who were treated with 50 or 200 mg/d of rosmarinic acid, there was a significant decrease in seasonal allergic rhinoconjunctivitis symptoms compared with controls.[60] In activated T cells obtained from patients with rheumatoid arthritis, rosmarinic acid induced apoptosis, which was suggested by the authors as a potential strategy to inhibit pathogenic T cell–mediated progression of rheumatoid arthritis.[61–63]	

(continues)

Summary of Scientific Research, continued

Scientific Evidence for Select Uses	Rating
Antioxidant properties	Preliminary, inconclusive
The antioxidant properties of the volatile oils are not as robust as that of water-soluble constituents. However, because of variability in composition and origin of different *Origanum* spp, the antioxidant capacity reported can vary substantially. In one study,[5] oregano had the highest total antioxidant capacity and phenolic content compared with 5 other Labiatae herbs, thyme, sage, rosemary, mint, and sweet basil. Oregano extracts have demonstrated radical scavenging action, suppression of lipid peroxidation, inhibition of nitric oxide activity, and protection of DNA against H_2O_2-induced oxidant damage.[64–67] The constituents reported to be responsible for the antioxidant strength of oregano have been variously attributed to carvacrol, γ-terpinene, rosmarinic acid, ursolic acid, protocatechuate-glycosides, and thymol.[67–77] Oregano also contains homologs of the nutrient antioxidant tocopherol.[78] In rats, oregano or constituents (42.5 mg/kg body weight) increased aging brain antioxidant activity and total antioxidant status.[79] Dietary oregano leaf (1% wt/wt) alleviated carbon tetrachloride–induced oxidative stress in rats.[80] Rosmarinic acid, given to rats orally at 100 mg/kg body weight, suppressed mesangioproliferative glomerulonephritis apparently due to its fibrinolytic and antioxidative properties.[81] However, in healthy nonsmoking males, oregano extract administered at a dose up to 600 mg/d total phenolics in a fruit drink had no effect on markers of lipid peroxidation.[14]	
Nervous system benefits	Preliminary, inconclusive
Oregano and some constituents (such as carvacrol, thymol, and γ-terpinene) have been reported in preliminary studies to influence nervous system chemistry and diverse functions, including responses to olfactory stimulation.[82–85] Intriguing evidence from animal studies suggests that rosmarinic acid (2 mg/kg body weight intraperitoneally) produces antidepressive activity and may inhibit an emotional abnormality produced by stress.[86–88]	
Blood glucose and lipid regulation	Preliminary, inconclusive
There is limited evidence that oregano extracts or constituents have the potential to benefit the management of diabetes and cardiovascular disease. For example, water extracts of oregano and rosmarinic acid exhibited considerable α-glucosidase inhibitory activity in vitro.[89] Rosmarinic acid–containing oregano extracts also inhibited porcine pancreatic amylase activity.[90] In 2 animal studies using diabetic rats, a water extract of *Origanum vulgare* administered orally at 20 mg/kg body weight demonstrated antihyperglycemic activity.[91,92] In rats, the tissue injury resulting from treatment with the diabetes-inducing drug streptozotocin was substantially lessened by long-term administration of the essential oil of *O onites* L.[93] In several assay systems, extracts of *Origanum* spp and individual constituents such as γ-terpinene and carvacrol have been shown to inhibit blood platelet aggregation and adhesion, decrease cholesterol biosynthesis, and reduce serum total cholesterol and triglyceride levels.[89,94–97] In normotensive rats, administration of carvacrol (100 μg/kg intraperitoneally) decreased systolic and diastolic blood pressures.[94] In cockerels, dietary supplementation with thymol and carvacrol (1 mmol/kg diet) suppressed serum cholesterol levels, which in part could be due to increased activity of geranyl pyrophosphate pyrophosphatase.[95]	
Anticancer actions	Preliminary, inconclusive
Oregano constituents have antimutagenic, antigenotoxic, and antiproliferative properties. For example, in cell culture studies, oregano extracts protected cells from oxidative stress–, mitogen- and radiation-induced DNA damage.[98,99] Likewise, carvacrol and rosmarinic acid have each been reported to protect DNA from a variety of damaging agents and to suppress proliferation of cancer cells or cells with active oncogenes.[100–107] Carvacrol and thymol, for example, suppressed the in vitro growth of melanoma cells,	

Summary of Scientific Research, continued

Scientific Evidence for Select Uses	Rating
demonstrating IC_{50} values of 120–150 μmol/L.[104] Furthermore, an extract of oregano was capable of upregulating the activity of the DNA repair enzyme MGMT (O_6-methylguanine-DNA methyltransferase) as well as the phase II detoxification enzyme glutathione-*S*-transferase.[108] It also induced levels of MGMT protein and activity and thus may have beneficial chemoprevention activity in inhibiting alkylating agent–induced DNA lesions. Mice treated orally with thymol and carvacrol (200 mg/kg body weight) evidenced significant increases in liver activities of glutathione-*S*-transferase, NAD(P)H-quinone reductase, and 7-ethoxycoumarin-*O*-deethylase.[101] Rosmarinic acid blocked processes associated with cancer invasion and metastasis.[109,110] Also, rosmarinic acid administered topically (1.3 mg per mouse) inhibited epidermal inflammatory responses in a murine 2-stage model of skin cancer.[111]	
Miscellaneous	Preliminary, inconclusive
Oregano oil, rosmarinic acid, or carvacrol (73 mg/kg body weight) has been shown to protect liver cells in rodents from lead toxicity and to stimulate liver regeneration following partial hepatectomy.[112,113] Carvacrol (73mg/kg body weight) also protected rat liver from defects caused by ischemia and reperfusion and was not hepatotoxic.[114] Rosmarinic acid (100–200 μM) can protect cardiomyocytes in culture from doxorubicin and adriamycin-induced toxicity and thus was suggested as a potential chemotherapeutic agent to inhibit cardiotoxicity in patients undergoing drug treatments.[115,116]	

The safety of oregano extracts and individual constituents for medicinal use in humans has not been thoroughly studied. The German Commission E and the American Herbal Products Association have reported no known safety risks associated with typical uses of oregano leaf. A similar report for the essential oil has not been issued.[117,118] Furthermore, the Commission E does not recommend therapeutic use of this herb, because efficacy has not been well documented. An aqueous distillate of *Origanum onites* L containing carvacrol as the major constituent was shown to be nontoxic in acute and chronic preclinical toxicity models,[119] and carvacrol is not hepatotoxic in the rat.[114] Some oregano constituents such as the monoterpenoids carvacrol and thymol are known to be activators of the transient receptor potential channel (TRPV3), although they do not consistently induce skin sensitization[120,121] and are not skin irritants.[1] There are a few cases of systemic allergic reactions following ingestion of oregano.[122] In light of the concern that the volatile components of oregano oil can be irritating to mucous membranes, it has been recommended that the oils not be applied topically to mucous membranes at greater than a 1% concentration.[123] Oregano essential oil administered in the diet at 0.1% to female mice for 2 weeks resulted in a significant increase in cell death of mouse preimplantation embryos.[124] Dose-response effects of oregano essential oil following internal use in humans have not been well characterized, especially considering the potential variability in bioactive component profiles. Oregano was reported to have biological activity as a progestin in in vitro assays.[125] However, because the bioavailability of oregano and any subsequent effects on hormones have not been well studied in vivo, the biological significance of these in vitro findings, if any, remains to be determined.

Conclusions

Oregano has several properties that deserve further characterization and confirmation. It is clear that oregano's chemical constituents can suppress the growth of a broad range of microorganisms in vitro. The conditions under which it can act effectively to counteract microbial contamination in food products need to be better examined. Particularly valuable will be characterization of the conditions under which its constituents may combat human infection.[20] There is limited but suggestive evidence that oregano bioactive components may suppress inflammation and improve blood glucose and lipid regulation. Such properties warrant additional preclinical evaluation to determine the active agents, potential mechanisms, and consistency among experimental models. In particular, confirmation of the potential capacity of oregano to decrease hyperglycemia and enhance insulin sensitivity and the doses necessary to do so warrant further investigation. Lastly, despite numerous reports that oregano's phytochemicals have antioxidant actions in vitro, the in vivo evidence in animals is limited and in humans is unsubstantiated.[14] This lack of effect clinically in part may be due to poor oral bioavailability that has been

observed. Thus, it will be of value to determine the specific oregano extracts, active constituents, effective doses, and conditions for which oregano may have measurable impact on markers of antioxidant status in humans after supplementation.[14]

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Vitamin D Deficiency Likely Among Some Kidney Disease Patients Starting Dialysis

Vitamin D deficiency is very common among patients with kidney disease who have low blood protein levels and who start dialysis during the winter according the results of a new study. The research identifies a group of patients who are at extremely high risk of being deficient in vitamin D and provides some clues as to why the deficiency occurs in them. Vitamin D deficiency is common in patients with end-stage renal disease on dialysis, but it is not clear which patients are at increased risk. The study sought to determine whether routinely measured clinical and demographic characteristics could identify dialysis patients who have a high risk of vitamin D deficiency. Researchers analyzed data from 908 patients in the ArMORR (Accelerated Mortality on Renal Replacement) cohort, a nationally representative group of US dialysis patients. Data from 60% of the patients were used to find potential predictors of vitamin D deficiency, whereas data from the other 40% of patients were used to validate the predictors. Fully 79% of the study population was vitamin D deficient. Black race, female sex, winter season, and low blood levels of the protein albumin (≤3.1 g/dL) were the strongest predictors of vitamin D deficiency. In the validation set, the presence of low blood albumin levels and winter season increased the likelihood of vitamin D deficiency in black females (from 90% to 100%), black males (from 85% to 100%), white females (from 82% to 94%), and white males (from 66% to 92%).One interpretation of the finding that low blood albumin levels were associated with deficiency is that at-risk patients leak large amounts of protein in their urine. The investigators suspect that vitamin D–binding protein, which transports the vitamin through the blood, may also be lost through the urine. Its loss could lead to the loss of vitamin D as well. In addition, whereas previous studies have demonstrated that patients on dialysis have an impaired ability to generate vitamin D from sun exposure, these findings emphasize that skin-based production of the vitamin is likely to be important in patients with end-stage renal disease.
Source: *Clin J Am Soc Nephrol*. 2010;5:460–467.

Dairy Avoiders: Are You Getting Enough?

Lactose intolerance is a real and important clinical syndrome, but quantifying its public health burden is challenging. A National Institutes of Health Consensus Development panel recently assessed the available evidence on lactose intolerance and health across the age spectrum and across racial and ethnic groups. Many individuals with diagnosed or perceived lactose intolerance avoid dairy products, which constitute a readily accessible source of calcium, other nutrients, and vitamin D (when fortified). Inadequate consumption of these nutrients may increase the risk for chronic health problems, including osteoporosis and decreased bone health. The panel defined lactose intolerance as the onset of gastrointestinal symptoms—diarrhea, abdominal pain, flatulence, and/or bloating—after ingesting lactose-containing foods and beverages; this is due to deficient levels of lactase, an enzyme necessary to break down lactose. Lactose malabsorption occurs when lactose is incompletely broken down in the intestine, which may or may not result in gastrointestinal symptoms after eating dairy products. Reduction of lactase enzyme in humans occurs in childhood and persists through the life span in most individuals (lactase nonpersisters). These individuals may or may not have the gastrointestinal symptoms of lactose intolerance. Understanding the distinction and interplay between these conditions is important when considering ways to meet nutritional needs.

For diagnosed lactose-intolerant individuals, multiple management strategies have been proposed. These include distributing lactose intake throughout the day and/or combining it with other foods, choosing nondairy foods rich in the nutrients found in dairy products, taking dietary supplements, ingesting incremental amounts of dairy products over time to increase tolerance, consuming reduced-lactose dairy products, and using probiotics (in supplements and foods). The panel emphasized the need for additional research to better understand the effectiveness of these approaches for decreasing symptoms, optimizing nutritional intakes, and improving health outcomes, with special emphasis on diverse populations. Depending on a variety of factors, some affected individuals could be counseled on ways to increase dairy intake, whereas others could be urged to meet nutrient requirements from other sources. For example, studies show that when consumed with other foods, even individuals diagnosed with lactose malabsorption can consume at least 1 cup of milk with few or no symptoms.
Source: *http://consensus.nih.gov/2010/lactosestatement.htm*