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Oil of Lemon Eucalyptus as an Insect Repellent

By Alexandra Connelly Frost, PhD

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BEFORE SYNTHETIC REPELLENTS WERE DEVELOPED IN 1929, PEOPLE routinely used natural compounds to protect against insect bites. During World War II, however, the United States government began testing more than 20,000 mosquito repellents to protect troops traveling to tropical areas. As a result, a highly effective synthetic repellent (N,N-diethyl-m-toluamide or DEET) was developed in 1953 and arrived on the market in 1956.[1] Currently, DEET is the most popular commercial insect repellent, with close to 250 formulations sold worldwide.

Despite its effectiveness, many consumers are reluctant to apply synthetic chemicals to their skin and seek natural alternatives to synthetic repellents. This desire has been exacerbated by reports that DEET is dangerous for children, possibly inducing encephalitis. These cases are extremely rare (17 suspected cases worldwide reported to date)[2] and occurred in children that orally ingested DEET or were repeatedly exposed to high concentrations.[3] Nonetheless, many would rather err on the side of caution.

Commercially available insect repellents fall into one of two classes: synthetic chemicals or plant-derived essential oils.[4] Currently, there are only five active ingredients registered for topical use in the United States: two are synthetic (DEET and IR3535) and three are plant-derived (picaridin [KBR 3023], citronella, and p-menthane-3,8-diol [PMD]).[1]

One plant-derived alternative that has sparked particular attention of late is oil of lemon eucalyptus. In fact, the Centers for Disease Control and Prevention (CDC) recently reported that oil of lemon eucalyptus (PMD is the active ingredient) is one of only three products (DEET, picaridin, and PMD) recommended to protect against West Nile virus, a serious virus spread by mosquitoes that can cause neurological disease or even death.[5] The Environmental Protection Agency (EPA) lists PMD as effective against mosquitoes, biting flies, and gnats.[6]

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Botany and Pharmacology

Eucalyptus ssp. is a genus of trees and shrubs in the family Myrtaceae that originated in Australia, but now commonly grows in almost all tropical and subtropical areas. Eucalyptus trees are characterized by vertically hanging, white, leathery leaves and ragged bark.[7] There are close to 600 species of eucalyptus, one of which is *Eucalyptus citriodora* Hook. *E. citriodora* is also known as citron-scented gum, lemon eucalyptus, lemon-scented gum, *Corymbia citriodora*, and spotted gum. *E. citriodora* has been credited with anti-inflammatory, antibacterial, and antifungal activity; and, recently has gained popularity as an insect repellent.[8]

E. citriodora leaves contain many compounds with pesticide activity including: aromadendrene, citronellal, citronellic acid, citronellol, citronellyl acetate, p-cymene, limonene, linalool, alpha-pinene, PMD, tannin, terpinene, terpinolene, and ursolic acid.[8] PMD has been identified as the compound that provides the strongest insect protection in this plant. Of note, *E. citriodora* also contains citronellol, which is the active ingredient in oil of citronella products. Oil of citronella, however, is not obtained from *E. citriodora*, rather from perennial grasses indigenous to tropical Asia (*C. nardus* and *C. winterianus*).[9] Oil of citronella is reported to have considerably shorter repellent times than DEET and PMD alternatives, with complete protection times averaging only about 20 minutes at concentrations of 10%.[4]

Research Studies

In the late 1980s, a worldwide survey was conducted by the U.S. military to identify repellents not produced in the United States. Of the 65 formulations not produced in the United States, 33 contained DEET and the remainder contained natural oils or undisclosed ingredients. One of the natural formulas identified was quwenling. This formula sparked the interest of researchers because it had become China's repellent of choice.[10] Quwenling was made from the waste distillate after extraction of lemon eucalyptus oil; the main ingredient in this distillate was PMD.[11] Quwenling has been a popular insect repellent in China for more than two decades.[1]

As mentioned previously, PMD is the main ingredient in quwenling; however, products containing PMD are relatively new to the U.S. market. There is a paucity of information on the efficacy of these products in peer-reviewed literature. This will likely change over time as PMD is more widely used and evaluated in the United States. Results of studies from the current literature are discussed in the next several paragraphs.

Schreck et al studied the effectiveness of quwenling through a series of tests that involved application of quwenling (30% active ingredients, or AI) on the forearm of a volunteer, from the wrist to the elbow.[9] After 15 minutes, the volunteer's arm (a protective glove covered the hand) was exposed sequentially for three minutes in four cages, each containing 200 blood-hungry female mosquitoes of four different species (*Aedes aegypti*, *Aedes albopictus*, *Anopheles quadrimaculatus*, and *Anopheles albinmanus*). Volunteers were also taken to the Everglades National Park to test the repellent in an authentic environment. Treated arms were exposed continuously to the natural environment to calculate time until first bite. The same tests were done with a DEET standard (15% AI) and the two repellents were then compared. Collectively, the results from these series of tests suggested that quwenling was not as effective as DEET in terms of duration of protection: The mean number of hours until the first bite by *Aedes aegypti* was 1.1 hours with quwenling and 4.8 hours with DEET.

Fradin et al compared several different insect repellents on the national market by using arm-in-cage studies with variable protocols depending on the time at first bite.[4] This study reported that 11 of 12 non-DEET repellents had mean protection times from *Aedes aegypti*

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mosquitoes of less than 23 minutes, whereas DEET topical formulas provided mean protection times ranging from 88 minutes (4.75% DEET) to 301 minutes (23.8% DEET). After the study was started, a new botanical product was introduced in the United States under the trade names of Repel Lemon Eucalyptus Insect Repellent (Wilson Pharmaceutical Company) and Fite Bite Plant Based Insect Repellent (Travel Medicine). The authors evaluated this product using the same method that they used for the products originally specified in the study using six test subjects. The lemon eucalyptus repellent had a mean protection time of 120 minutes, which made it the most effective of all non-DEET repellents tested in this study and more effective than low-concentration DEET products (6.65% and lower); however, the concentration of lemon eucalyptus or PMD was not stated in the study. Another important point from this study was that wristband repellents were not effective, regardless of the formula.[4]

In 2002, Barnard et al tested IR3535, KBR 3023, PMD repellent (40% PMD), and DEET (25%) against *Ochlerotatus taeniorhynchus* in the Everglades National Park.[12] During seven, three-minute observation periods over six hours, bites were surveyed on test subjects. The PMD repellent had a mean complete protection time of 3.7 hours (compared to 5.6 hours with DEET) and an overall mean percent repellency of 89%. Authors stated that all three non-DEET repellents were effective insect repellents for human use.

In 2004, Barnard and Xue tested 12 commercially available synthetic and botanical insect repellents against *Aedes albopictis*, *Culex nigripalpus*, and *Ochlerotatus triseriatus* by exposing treated forearms to three-minute cage exposures every 30 minutes until the subject received two or more mosquito bites in the same observation period or one bite in two consecutive observation periods.[11] When estimated mean time of protection was averaged over the three species, Repel Lemon Eucalyptus Insect Repellent (26% oil of lemon eucalyptus or 65% PMD) provided more than seven hours of protection from mosquitoes of these species. Repel's protection time was comparable to the 15% DEET formula in the study.

Similarly, Govere et al reported that 0.574 g of quwenling (Mosiguard towelettes) was comparable to 15% DEET for protection against *Anopheles arabiensis* mosquitoes in their arm-in-cage study.[13] Both formulas protected against this species of mosquitoes for 5-6 hours of one-minute, hourly cage exposures.

Trigg also found spray, gel, and stick formulations of 50% PMD effective against *An. gambiae* and *An. funestus* mosquitoes in the field in Tanzania.[14] Their results, however, are misleading: They reported six hours and 42 minutes average time until first bite when the first five hours were spent unexposed to mosquitoes before the trial began at 10 pm. Once they went into the field where the experiment tool place, it took an average of one hour and 42 minutes using PMD spray compared to one hour and 55 minutes using DEET spray until the first bite was received.

Hadis et al reported comparable efficacy of DEET and PMD (greater then 90% for both) in terms of mean number of bites and average percent protection at concentrations of 40% and 75%, respectively, against *Mansonia* mosquitoes.[15] They did not compare time until first bite for the different repellents, but rather the overall effectiveness during the test period (from 7:00 to 7:30 pm) in Pugnudo, Ethiopia. Both the time to first bite and the average number of bites over a time period are important in terms of disease protection.

Recently, it has also been shown that burning *E citriodora* leaves could provide a cost-effective means of household protection in addition to mosquito nets in sub-Sahara Africa where 90% of deaths from malaria occur and much of the exposure time is before individuals go to bed (where they are protected by mosquito nets) in the evening.[16]

Mechanism of Action

Curiously, none of the above articles discussed the mechanism by which PMD repels insects. The mode of action of many repellents is unclear, but it is believed that these products do not repel insects, they simply mask or confuse the attractive signals that humans emit so that mosquitoes are unable to locate us. Mosquitoes have specific sensory receptors that provide them with the information they need to detect a source, orient to it, and travel to it to sample a blood meal. Host location is determined by many factors including lactic acid, ammonia, carbon dioxide, octenol, phenols, temperature, and humidity.[17] For example, DEET interferes with the transmission of spikes from a lactic acid-excited neuron stimulated by lactic acid from a host.[16] The precise mechanism for PMD has not been reported.

Adverse Effects

All pesticides distributed or sold in the United States must be registered by the EPA. To be registered, the manufacturer must present scientific studies showing that they can be used without posing unreasonable risks to humans or the environment. As part of the registration process, the EPA collects and reviews a complete set of studies from the pesticide producers describing the health and environmental effects of the product.

Accordingly, the EPA imposes regulations to manage any of the risks the pesticide might pose. PMD was registered with the EPA as a product that can be used against public health pests in March of 2000.[18]

In animal studies evaluated by the EPA during the registration process of PMD, the only adverse effect that PMD showed was eye irritation.[6] Eye irritation, however, has not been reported in peer-reviewed, epidemiologic literature. However, one peer-reviewed research study reported that a subject experienced significant skin irritation at the site of application.[4]

There are special warning labels on products containing PMD advising users not to get the product in their eyes and to avoid spraying directly on or near the face. Users are also advised not to use PMD on the faces or hands of small children.[6] PMD is not to be used on children younger than three years of age (the product has not been adequately tested in this population).[19]

Dosage and Formulation

There are a few oil of lemon eucalyptus repellents on the market in the United States. EPA-registered lemon eucalyptus repellents include: Repel Lemon Eucalyptus Insect Repellent Lotion and Spray Lotion, Survivor Lemon Eucalyptus Insect Repellent Lotion, and Off! Botanicals Insect Repellent. Repel Lemon Eucalyptus Insect Repellent Lotion and Spray Lotion and Survivor Lemon Eucalyptus Insect Repellent contain 30% oil of lemon eucalyptus (65% PMD). Off! Botanical Insect Repellent contains 10% PMD. Of note, most commercial products contain a synthetic PMD molecule, but the active ingredient was originally isolated from waste distillate of lemon eucalyptus oil extract.[11]

In general, it appears that PMD is roughly half as effective as DEET by level of concentration; therefore, a 30% PMD product would be about as effective as a 15% DEET product. Keep in mind, however, that the innate attractiveness of human subjects to mosquitoes ranges from 30% to 70%; therefore, different concentrations and intervals of application may be effective depending on the individual.[20]

Important Information on Using Pesticides

Patients should be particularly vigilant between dusk and dawn—the prime mosquito-biting hours—and should follow instructions on the product label carefully. General instructions specified by the EPA are as follows: only apply repellents to exposed skin and/or clothing; never use repellents over cuts, wounds, or irritated skin; do not apply to eyes and mouth; apply sparingly around ears; when using sprays do not spray directly onto face (spray on hands first and then apply to face); do not allow children to handle the products and do not apply to children's hands; do not spray in enclosed areas; avoid breathing a repellent spray; do not use repellent near food; after returning indoors, bathe or wash treated skin with soap and water; and finally, always store repellents and pesticides out of the reach of children (regardless of whether they are botanical or synthetic).[21] When using an insect repellent, the EPA recommends that users always check the container to make sure that the product has an "EPA-approved" label and registration number. Patients should always read the label of any product they are using, even if they have used the same product before, as safety and efficacy information is updated and reflected on product labels.[21]

In case of a rash or an adverse reaction from a repellent, patients should: stop using the product, wash the area with soap and water, and call the local poison control center for guidance. If a severe reaction occurs, patients should call 911 and make sure to take the insect repellent product to the hospital.[21]

Conclusion and Recommendation

In the United States, where the greatest disease threat from a mosquito bite is West Nile virus, PMD-based repellents are a safe and effective alternative to synthetic formulas; however, at concentrations tested, DEET formulas usually provided protection for a longer period of time.

When traveling to a tropical or malaria endemic area, it is still advisable to use a DEET repellent because oil of lemon eucalyptus has not been adequately tested against mosquitoes that spread malaria. DEET is the safest, best studied, and longest-lasting repellent against malaria-carrying mosquitoes, according to the CDC. Refer to the CDC Travelers' Health web site (www.cdc.gov/travel/bugs.htm) for specific recommendations concerning protection from insects when traveling outside the United States.[19] The CDC (www.cdc.gov) and EPA (www.epa.gov) are the most reliable resources for updates on safety and efficacy of all pesticides. ❖

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Use of Hawthorn for Mild Congestive Heart Failure

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CONGESTIVE HEART FAILURE (CHF) IS A CHRONIC, USUally progressive condition that has a major impact on patients' quality of life and life expectancy. Small exertions—even walking a short distance on a flat surface—can be extremely tiring. Edema of the lower extremities can be painful and require prolonged elevation and the use of compression garments. Most critically, the long-term stress of the body's strategies to compensate for reduced cardiac efficiency—hypertension and accelerated heart rate—creates a vicious cycle that typically ends in progressive clinical deterioration and death.

In Europe and the United States, the severity of CHF is classified according to the New York Heart Association's four-stage system (i.e., NYHA I-IV) *(see Table)*. The stages are defined practically, by the degree to which a patient's normal activity is limited by CHF. It is noteworthy that this system separates the impact of disease from underlying physiologic functioning. As a consequence, many studies of CHF interventions focus on practical outcome measures such as exercise tolerance or dyspnea, rather than more physiologic factors such as ejection fraction (EF).

Treatments for CHF typically seek either to reduce the burden on the heart, or to shore up the heart's functional capacity. Given the changeable nature of the disease, the frequency of comorbid diseases (diabetes, renal disease, essential hypertension) in CHF patients, and the necessity of poly-drug therapy to aggressively meet and maintain clinical targets, CHF patients typically require relatively intensive case management. This need is only

Table

NYHA classifications for congestive heart failure

Class I	Patients with no limitation of activities; they suffer no symptoms from ordinary activities.
Class II	Patients with slight, mild limitation of activity; they are comfortable with rest or with mild exertion.
Class III	Patients with marked limitation of activity; they are comfortable only at rest.
Class IV	Patients who should be at complete rest, confined to bed or chair; any physical activity brings on discomfort and symptoms occur at rest.

heightened by the potential for drug interactions and adverse reactions to agents that should be carefully titrated (i.e., digoxin, ACE inhibitors, beta blockers).

Pharmacology

Hawthorn is an herbal remedy frequently used in traditional Chinese medicine and by European naturopaths and homeopaths to treat a variety of conditions, including the milder stages of CHF.[1] Preparations are derived from the fruit, leaves, and flowers of trees and shrubs of the genus *Cratægus*. Consumption by patients may be in the form of pills, tea, extract, or whole dried fruit. Among the key constituents are flavonoids and oligomeric proanthocyanidins (OPC), each of which is present in varying amounts in different parts of the plant.[2] Hawthorn extracts are often formulated to contain standard amounts of the various constituents. A compound called WS 1442, among the most commonly used in clinical studies, is standardized to 18.8% OPC.[3]

Studies of the effect of hawthorn have focused on whole-plant extract, the flavonoid and OPC fractions, and individual components. Information on the pharmacodynamics of hawthorn compounds is speculative at best, and animal studies are the source of most of the theoretical data to date. There is some evidence that hawthorn may act through its effect on cyclic AMP, altering the sodium-calcium balance in cardiac tissue, as do the prescription inotropes.[4] Another possible mechanism is through induction of hypotension, mediated by endothelium-dependent arterial relaxation.[5] A third potential means of action involves hawthorn's antioxidant and nitric oxide (NO) synthesis-enhancing properties.[6] These would have the effect of reducing cardiac ischemia, thus improving myocardial efficiency.

(Note: A limitation in assessing the relative merits of these hypotheses, as well as the clinical studies of hawthorn preparations, is that much of the research to date has been conducted outside the United States, and has been reported in non-English-language journals [some with English abstracts] that are difficult to obtain in this country.)

Clinical Evidence

The possibility that hawthorn might be effective in reducing symptoms of mild CHF is especially appealing. Early treatment of the disease is often deferred or used to a suboptimal extent because of the side effects of many of the drugs currently in use. If another agent that combined similar clinical results with fewer side effects were available, better preservation of routine functioning might be possible for a greater number of patients and for a longer time.

The best available evidence of clinical efficacy is a meta-analysis published in 2003 by Pittler et al.[3] It included results from eight randomized trials that enrolled a total of 632 patients. With one exception *(see Tauchert below)* participants had NYHA Class I or II heart failure. Most studies were of short duration (range, 3-16 weeks), and all but one used WS 1442 in daily doses ranging from 160 mg to 1,800 mg. Common study endpoints were maximal workload in watts (W) (four studies, 310 patients) and pressure-heart rate product (defined as units of systolic blood pressure [mm Hg] multiplied by heart rate per minute, the quantity then divided by 100) (six studies, 264 patients). In most studies, participants' use of other medications was not restricted, and typically included a number of other agents that might influence CHF symptoms. The result of the meta-analysis showed a significant improvement in maximal workload among patients receiving hawthorn (weighted mean difference 7 W, 95% confidence interval [CI] 3-11 W), and in pressure-heart rate product (weighted mean difference -20, 95% CI -32 to -8). These findings remained when the analysis was limited to studies in which participants were known to have been taking other cardioactive medications. Improvements were also noted in exercise tolerance. A wide range of side effects was reported, the most common of which was vertigo (n = 8).

A later study not included by Pittler et al was published by Degenring and colleagues in 2003.[7] They randomly assigned 143 patients with NYHA Class II CHF to an extract of two species of fresh hawthorn berries or placebo. The dose was reported as milligrams of OPC, but would standardize to between 200 mg and 650 mg of whole hawthorn extract per day. Treatment continued

for approximately two months. The primary outcome was exercise tolerance, as determined by bicycle ergometry. Concomitant medications were not permitted beginning four weeks before enrollment in the study. At the end of the treatment period, there was a statistically significant difference in exercise tolerance in favor of the hawthorn group (mean -8.3, 95% CI -16.3 to -0.3). Similar proportions of hawthorn and placebo patients (13% hawthorn, 15% placebo) reported mild-to-moderate side effects, most of which were judged by study physicians as unlikely to be consequences of treatment.

Another report, for which full details were not immediately available in English, gave interim analysis results for the WISO cohort trial.[8] A total of 952 patients with NYHA Class II CHF were enrolled, of whom 588 received hawthorn treatment. Treatment assignment was not random, and there were meaningful differences in the two groups with respect to age, sex, and concomitant medications. For the interim analysis, 130 matched pairs of patients were identified. At the time of the interim analysis, treatment had been ongoing for two years on average. Comparison of the hawthorn and non-hawthorn groups showed statistically significant improvements in fatigue, stress dyspnea, and palpitations, although definitions of these symptoms were not provided. The author also noted that hawthorn patients received fewer concomitant cardiac medications, but this may have been due to factors such as patient preference, which in turn would have influenced patients' self-assignment to hawthorn or conventional therapy. A strength of these findings is that they represent "real-world" experience—not the carefully controlled conditions of most clinical trials.

A study included in the Pittler meta-analysis, but worth mentioning individually is that by Tauchert, published in 2002.[9] This study randomized 209 patients with NYHA Class III CHF to 1,800 mg of WS 1442, 900 mg of WS 1442, or placebo. Patients with more or less severe CHF, those treated with digitalis in the previous six months, and those with serious cardiac or other comorbidities were excluded. Treatment continued for 16 weeks, after which maximal workload was assessed by bicycle ergometry. Findings included an increase in maximal workload in the 1,800 mg group as compared to the other two, and improvement in a scale score of typical heart failure symptoms in both hawthorn groups as compared to placebo. Patients in the placebo group reported adverse effects twice as often as those in either hawthorn group. While it is impressive to see results in Class III CHF similar to those shown in milder stages, this study's findings should be viewed in light of the homogeneity of the study population and the funding of the study by a manufacturer of hawthorn extract.

Conclusion

Overall, the available evidence appears to suggest that there is some benefit to patients with mild CHF from the use of hawthorn extract. However, this evidence must be weighed against its limitations. Given the nature of CHF, it has proven difficult to conduct a study in patients with no major comorbidities and no significant concomitant medications. Given the lack of clarity as to hawthorn's exact mechanism of action, it is not possible to say what other medications may confound, potentiate, or attenuate its apparent effect. It seems reasonable to assume that such effects would most likely be seen with coadministration of hawthorn and other cardioactive drugs. (It should be noted that at least one small study has found that coadministration of hawthorn and digoxin, with careful attention to dosing, appears to be safe.[10]) The concentration of studies in Germany also brings into question the reproducibility of their findings in other more diverse populations.

Finally, the wide range of dosages leaves open the question of how much is needed to achieve clinical benefit. The studies reviewed by Pittler et al used doses ranging from 160 mg to 1,800 mg per day. There appears to be a trend toward higher doses in more recently published studies, but the current evidence base offers little guidance as to appropriate thresholds for efficacy and safety.

Recommendation

No study published to date has shown significant harm from the use of hawthorn. Used carefully in a patient population that is likely to have fairly regular physician supervision, it should present no major risks and may offer therapeutic benefit. There is inadequate evidence as yet as to how it works, and many hypothesized mechanisms. Because of this, hawthorn should not be assumed to stand in for all of the potential agents that might be used together to manage CHF. Even if the use of hawthorn moderates some physical symptoms, it is most often still advisable to take other medications (such as antihypertensives) concomitantly. As has been emphasized before in this publication, it is critical for the treating clinician to have a clear picture of what the patient is taking, both prescription and over-the-counter agents. Given the focus on functional status in grading CHF, this physician-patient communication will help establish response to treatment and have the added benefit of making the patient's concerns and preferences clear. ❖

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Yoga for Prevention of Cardiovascular Diseases

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CARDIOVASCULAR DISEASES (CVD) ARE THE MOST common cause of mortality in the United States. Approximately 70 million people in the United States have some form of CVD, and in 2002 CVD accounted for 38% of all deaths in the United States.[1] Despite advances in therapeutic procedures and medications, the morbidity and mortality from CVD continue to burden society. The American College of Cardiology's sponsorship of its first course on complementary and alternative medicine (CAM) in 2003 is an indication of growing interest among medical professionals in employing various CAM modalities to aid in the effective treatment of cardiovascular diseases.[2]

Table

Types of yoga described in ancient Vedic texts[3]

Name	Emphasis
Bhakti yoga	Spirituality and devotion
Jnana yoga	Wisdom
Karma yoga	Services without selfish motive
Raja yoga	Mastery of mind through focused concentration
Dhyana yoga	Meditation
Mantra yoga	Repetition of sacred words
Hatha yoga	Balancing of physical and mental energies

Yoga originated in India more than 2,000 years ago. In its original form, yoga was an integrated system of practice including spiritual, moral, and physical dimensions. The word yoga originates from a Sanskrit word meaning to unify or yoke, and implies a connection between body, mind, and spirit.[3] The table above lists the major methods of training in yoga described by the ancient Vedic texts.[3]

In addition to the major methods described in the above table, many specialized styles of yoga exist today. Transcendental meditation can be considered an example of a specialized form of yoga developed by Maharishi Mahesh Yogi as a mind-body method of self-regulation. The protective benefits of transcendental meditation for CVD have been covered in a previous article appearing in this newsletter *(see the July 2002 issue of* Alternative Medicine Alert*)*.[4]

The practice of yoga has become extremely popular in the United States. Among the many styles, Hatha yoga is the most popular.[5] The practice of Hatha yoga combines postures (*asanas*) and breathing techniques (*pranayama*), with meditation often practiced in the beginning and at the end of Hatha yoga classes. A telephone survey conducted in 1998 by Saper et al revealed that an estimated 15 million American adults have used yoga at least once in their lifetime and 7.4 million during

the previous year. Yoga was used for both wellness and specific health conditions, often with perceived benefit.[6]

Mechanism of Action

Western scientific exploration of yoga was stimulated by extraordinary feats achieved by yoga masters. The following are two examples of such feats performed by yoga masters where no scientific explanation exists. The first was documented in 1973; a single yogi remained in an underground pit for eight days, with an absence of electrical activity in the EKG during the period.[7] He was then removed and shown upon examination to be in good health. In the second case, documented in 1982, practitioners of a Tibetan form of Buddhist meditation, g-Tum-mo yoga, increased the temperature of their digits by 5-15° C.[8] Both examples suggest that yoga training could provide an advanced practitioner voluntary control of the autonomic system. In 2004, Telles et al conducted a clinical trial to investigate the ability to voluntarily reduce the heart rate after one month of yoga practice.[9] In this study, the yoga group was given instruction whereas the control group received no instruction. At the end of one month, the yoga group was able to reduce their heart rate by an average of 10.7 beats per minute compared to the control group ($P < 0.05$). The significance of this study is that the heart rate, an autonomic function, can be modulated in a novice practitioner with one month of yoga training.

A common pathway for the effect of regular yoga practice appears to be the autonomic nervous system; specifically, yoga practice decreases sympathetic activity and increases parasympathetic activity resulting in decreased catecholamine and cortisol secretion.[5] It appears that various components of yoga practice, such as meditation, postures, and breathing exercises, individually can result in the described autonomic changes. Telles et al conducted another study investigating the meditative aspect of yoga, comparing a group mentally chanting "om" to a random thinking group.[10] The om meditation group had decreased heart rates compared to the random thinking group. Madanmohan et al conducted a study investigating the postural aspects of yoga practice using the shavasana position and demonstrated both decreased sympathetic activity and increased parasympathetic activity.[11] Udapa et al conducted a study investigating the effect of yoga breathing vs. no intervention (control group) and also demonstrated decreased sympathetic activity and increased parasympathetic activity.[12] Luciano et al conducted a study comparing the effect of yoga mantra recitation vs. Ave Maria prayer.[13] The results demonstrated that both recitations of the rosary and yoga mantras slowed breathing to six breaths per minute resulting in enhanced heart rate variability. Lastly, Raghuraj et al described the ability to increase or decrease sympathetic activity by utilizing two different types of yogic breathing known as kapalabhati (breathing at high frequency) vs. nadisuddhi (alternate nostril breathing).[14] The kapalabhati was found to increase sympathetic activity while nadisuddhi was found to decrease sympathetic activity.

Clinical Evidence

An early study documenting the benefits of yoga for hypertension was conducted in 1975 by Patel.[15] The trial compared an intervention group and an age- and gender-matched control group where 12 hypertensive patients in the intervention group were treated by yoga and biofeedback for 12 months. Results showed a statistically significant reduction in blood pressure in the group using yoga and biofeedback compared to the control group.

There are a large number of non-randomized, uncontrolled studies providing foundational support for the benefits of yoga for cardiovascular risk reduction, particularly in reducing blood pressure. However, many studies lack the rigor of a randomized controlled trial. In 1984, Sundar et al conducted an intervention study demonstrating that six months of yoga practice results in statistically significant reductions in systolic and diastolic blood pressure.[16] In 1997, Schmidt et al reported results of an interventional study demonstrating that a comprehensive residential three-month yoga and meditation program where participants lived on a low-fat vegetarian diet reduced body mass index, cholesterol, and blood pressure.[17] In 2002, Damodaran et al conducted an intervention study involving three months of yoga practice, which resulted in decreased blood pressure, cholesterol, and blood sugar.[18] In addition, decreases in vanillylmandelic acid catecholamine and malondialdehyde levels were documented, suggesting decreased sympathetic activity and decreased oxidative stress. In 2004, Singh et al conducted a yoga intervention study on Type 2 diabetic patients, demonstrating reduction of pulse rate, blood pressure, and fasting glucose level.[19] In 2005, Bijlani et al conducted a comprehensive lifestyle education program based on yoga lasting 10 days.[20] At trial's end, the authors reported a reduction in fasting blood glucose and cholesterol. Overall, the results of the studies are consistent for improvement of risk profile for developing CVD in as little as 10 days of yoga training. However, the significance of the studies is reduced as they employ pre-post design rather than more rigorous randomized, controlled methodology. It is also important to note that the above trials integrated the physical practice of yoga with a more complete yogic lifestyle.

Another non-randomized study that has important implications was conducted by Bharshankar et al comparing 50 sedentary subjects with 50 yoga practitioners age 40 years and older.[21] Blood pressure was positively correlated with age in both groups, but results of the study showed that yoga practitioners had a lower pulse rate ($P < 0.001$) and lower systolic and diastolic blood pressure ($P < 0.01$). The significance of this study is that yoga appears to reduce the age-related deterioration in cardiovascular functions. However, the groups were not age-matched, which decreases the strength of the authors' conclusions.

In 2000, Murugesan et al conducted a randomized controlled trial investigating the effect of yoga practice on the management of hypertension.[22] Thirty-three subjects were randomly assigned to three groups. The first group participated in yoga practice, the second group received antihypertensive medications, and the third group received no treatment. The results demonstrated that both the yoga and antihypertensive medication groups achieved reduction in blood pressure, heart rate, and body weight compared to the control group receiving no treatment.

In 2000, Manchanda et al conducted a randomized controlled trial investigating the effects of a yoga lifestyle on coronary artery disease.[23] The study enrolled 42 men with coronary artery disease who were randomly assigned to a yoga intervention group or a control group, and followed for one year. The yoga lifestyle program included a strict control of risk factors such as smoking, diet control, moderate aerobic physical exercise, breathing and relaxation exercises, stress management, and meditation. The control group was managed by conventional methods, such as risk factor control and a diet plan outlined by the American Heart Association. At the end of one year, the yoga group showed significant improvements including a reduction in the number of anginal episodes, an improved exercise capacity, and decreased body weight. The results also showed the statistically significant regression of coronary artery lesions in the intervention group vs. the control group (20% vs. 2%) as determined by coronary angiography.

Experiencing a Class

A yoga session can vary in content and time depending on the style of yoga, and can be individualized to suit the needs and limitations of any patient. Classes can be extremely gentle as with restorative yoga. A typical session lasts 45-90 minutes, and usually includes breathing exercises characterized by long and deep diaphragmatic breathing. These can be performed either sitting or lying down. Asana practice, or the assuming of various postures in association with breathing exercises, is typically performed next. The postures further facilitate the connection of body, mind, and spirit and help promote relaxation. The end of a yoga class usually employs meditation, visualization, or guided imagery.

Safety

Yoga is a relatively safe activity; however, injuries can result from improper practice. It is important to seek an experienced teacher and to communicate any physical concerns with the teacher prior to beginning the lesson.

Conclusion

There is a small amount of evidence suggesting that yoga lowers blood pressure and protects the practitioner from cardiovascular diseases. The complete practice of yoga and a yoga-based lifestyle including vegetarian diet appears to reduce risk profiles in as short as 10 days. That stated, there is a significant need for additional research if yoga, especially as practiced in the United States, is to be recommended as a therapeutic adjunct to conventional care.

Recommendation

Yoga offers multiple benefits arising from various components including posture, breathing exercises, and meditation. Select patients may benefit from a gentle practice, as data suggest modest improvements in specific cardiovascular parameters, but much of the research focuses on a yogic lifestyle, something not often employed by the majority of yoga practitioners in the United States. As cardiovascular disease is prevalent in our society and commonly employed interventional approaches have associated morbidity and mortality, utilizing yoga practice and yogic lifestyle as a complement to the conventional medical approach is likely to contribute to a positive outcome in select patients with cardiovascular diseases. Identifying a well-trained yoga instructor/therapist with whom the patient can pursue one-on-one instruction can promote individualized programs and allay misperceptions about the practice. ❖

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CME Questions

CME Instructions: Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a certificate of completion. When an evaluation form is received, a certificate will be mailed to the participant.

29. It appears that PMD is roughly twice as effective as DEET by level of concentration; therefore, a 15% PMD product would be about as effective as a 30% DEET product.
a. True
b. False

30. The results of the Pittler meta-analysis on hawthorn showed improvements in:
a. maximal workload.
b. pressure-heart rate product.
c. exercise tolerance.
d. All of the above

31. Research suggests that various components of yoga practice can result in autonomic changes. These components include:
a. meditation.
b. postures.
c. breathing exercises.
d. All of the above

Answers: 29. b, 30. d, 31. d.

With Comments from Russell H. Greenfield, MD

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On Pains and Needles (Acupuncture for Fibromyalgia)

Source: Asseffi NP, et al. A randomized clinical trial of acupuncture compared with sham acupuncture in fibromyalgia. *Ann Intern Med* 2005;143:10-19.

Goal: To assess the effectiveness of directed acupuncture for relieving symptoms associated with fibromyalgia.

Study design: Twelve-week randomized, controlled trial including three different sham acupuncture treatments.

Subjects: Ninety-six people > age 18 years (mainly Caucasian women) diagnosed with fibromyalgia and with a pain score > 4 on a visual analog scale who had never previously experienced acupuncture.

Methods: Subjects were randomly assigned to one of four treatment groups: 1) directed acupuncture according to a practice of traditional Chinese medicine (TCM); 2) stimulation of points used for a condition unrelated to fibromyalgia (control for acupoint specificity); 3) sham needling using false acupoints (another control for acupoint specificity); and 4) non-insertive simulated acupuncture using a toothpick in a needle guide-tube. Treatment was offered twice weekly for 12 weeks with needles remaining in place for 30 minutes at a time (in group four, simulated needle withdrawal occurred at 30 minutes). One investigator instructed eight other U.S.-trained acupuncturists in the provision of all four treatments and also monitored protocol compliance. Subjects were assigned to a particular acupuncturist according to schedule and geography. Outcome measures included subjective pain, fatigue, sleep quality, and overall well-being, and data were collected at baseline and at weeks 1, 4, 8, 12, 24, and 36.

Results: There were no significant differences in study outcomes noted between the directed acupuncture and sham acupuncture groups. Some benefit was noted within all four treatment groups immediately after beginning the intervention, but the beneficial effects waned over the course of the treatment and subsequent follow-up.

Conclusion: True acupuncture is no better than sham acupuncture for the treatment of fibromyalgia.

Study strengths: Use of three separate sham acupuncture treatments; degree of blinding; follow-up; use of standard outcome measures.

Study weaknesses: Acupuncture therapy was provided in prescriptive form (fixed points stimulated), rather than in an individualized nature as is usually the case in TCM; small subject pool; some of the eight acupuncturists treated many more patients than did others (range, 4-33 subjects); missing data; no usual care comparison group.

Of note: Prior to randomization subjects were evaluated for tender points to confirm the diagnosis of fibromyalgia per the 1990 American College of Rheumatology criteria; subjects were permitted to use other therapies to help relieve discomfort during the trial provided use remained consistent; not all of the acupuncture treatments were offered to subjects by their same practitioner; acupoints and sham points were chosen by a single experienced practitioner and approved by three senior acupuncturists; subjects in the directed acupuncture group had slightly higher levels of pain and fatigue, slightly lower levels of sleep quality and overall well-being, than those in the control groups; all three sham acupuncture groups were combined for the purpose of analysis; the main side effects noted were discomfort at the site of needle insertion and bruising.

We knew that: Fibromyalgia affects 2-4% of the U.S. population, making it (after osteoarthritis) the second most common rheumatologic disorder; use of complementary and alternative medicine (CAM) is common among people with fibromyalgia, as most conventional medical interventions have not shown sustained benefit; a 1992 controlled trial of electroacupuncture for fibromyalgia suggested significant benefits during three weeks of treatment; the toothpick sham technique was shown to be indistinguishable from true acupuncture in one study of acupuncture-naïve patients with back pain; challenges to the performance of acupuncture research include blinding of both practitioners and participants.

Comments: A significant number of trials of acupuncture for painful conditions has been published, many with positive outcomes. Clinical experience would also strongly suggest that acupuncture can benefit patients with fibromyalgia, yet this intriguing study (funded by the National Center for Complementary and Alternative Medicine) detailed no significant benefit from a course of fixed-point acupuncture. As the authors readily point out, however, there is no "gold standard" for the selection of acupoints for treating people with fibromyalgia. Many practitioners espouse the belief that individualized acupuncture for any ailment is significantly more effective than fixed-point treatments. This perspective has never been adequately tested in a clinical trial, and that is exactly what is needed—a methodologically sound comparison of fixed-point acupuncture and individualized TCM treatment in the setting of fibromyalgia. Good trials of CAM therapies for fibromyalgia are still relatively hard to find, so this paper is one to hold on to, both to further the discussion of appropriate treatment and for the creative manner in which control and blinding were accomplished.

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Supplement to *Alternative Medicine Alert*
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ALTERNATIVE MEDICINE ALERT™

A Clinician's Evidence-Based Guide to Alternative Therapies

Fight The Bite! Avoid Mosquito Bites to Avoid Infection

WHEN DEALING WITH WEST NILE VIRUS, PREVENTION IS YOUR BEST BET. FIGHTING MOSQUIto bites reduces your risk of getting this disease, along with others that mosquitoes can carry. Take the common sense steps below to reduce your risk.

Clothing and repellent can help reduce mosquito bites

Insect repellents and protective clothing can help reduce exposure to mosquito bites that may carry viruses such as West Nile virus. When possible, wear long-sleeves, long pants, and socks when outdoors. Mosquitoes may bite through thin clothing, so spraying clothes with an insect repellent will give extra protection.

Research reviewed by the Centers for Disease Control and Prevention (CDC) suggests that repellents containing DEET (N,N-diethyl-m-toluamide) or picaridin (KBR 3023) typically provide longer-lasting protection than the other products, and oil of lemon eucalyptus (p-menthane-3,8-diol) provides longer lasting protection than other plant-based repellents. In general, the more active ingredient (higher concentration) a repellent contains, the longer time it protects against mosquito bites.

Use of repellents products may cause skin reactions in rare cases. Most products also note that eye irritation can occur if product gets in the eye. If you suspect a reaction to a product, discontinue use, wash the treated skin, and call a poison control center. If product gets in the eyes, flush with water and consult your health care provider or poison control center. If you go to a doctor, take the product with you. Follow these guidelines when using a repellent:

- Always follow the recommendations appearing on the product label.
- Use enough repellent to cover exposed skin or clothing. Don't apply repellent to skin that is under clothing. Heavy application is not necessary to achieve protection.
- In general you should re-apply repellent if you are being bitten by mosquitoes. Sweating, perspiration, or getting wet may mean that you need to re-apply repellent more frequently.
- Do not apply repellent to cuts, wounds, or irritated skin.
- After returning indoors, wash treated skin with soap and water.
- Do not spray aerosol or pump products in enclosed areas.
- Do not spray aerosol or pump products directly to your face. Spray your hands and then rub them carefully over the face, avoiding eyes and mouth.
- Do not apply repellents containing permethrin directly to skin.

Be aware of peak mosquito hours

The hours from dusk to dawn are peak mosquito biting times for many species of mosquitoes. Take extra care to use repellent and protective clothing during evening and early morning—or consider avoiding outdoor activities during these times.

Mosquito-proof your home

Drain standing water. Mosquitoes lay their eggs in standing water. Limit the number of places around your home for mosquitoes to breed by getting rid of items that hold water. In

this way, you reduce the number of places mosquitoes can lay their eggs and breed. For example:

- At least once or twice a week, empty water from flower pots, pet food and water dishes, birdbaths, swimming pool covers, buckets, barrels, and cans.
- Check for clogged rain gutters and clean them out.
- Remove discarded tires, and other items that could collect water.
- Be sure to check for containers or trash in places that may be hard to see, such as under bushes or under your home.

Install and repair screens. Some mosquitoes like to come indoors. Keep them outside by having well-fitting screens on both windows and doors. Offer to help neighbors whose screens might be in bad shape.

Help Your Community

Report dead birds to local authorities. Dead birds may be a sign that West Nile virus is circulating between birds and the mosquitoes in an area.

Clean up. Mosquito breeding sites can be anywhere. Neighborhood clean up days can be organized by civic or youth organizations to pick up containers from vacant lots and parks, and to encourage people to keep their yards free of standing water. Mosquitoes don't care about fences, so it's important to control breeding sites throughout the neighborhood.

Find out more about local prevention efforts. Find state and local West Nile virus information and contacts on the Links to State and Local Government Sites (www.cdc.gov/ncidod/dvbid/westnile/city_states.htm) page on the CDC web site.

Source: Centers for Disease Control and Prevention. Available at: www.cdc.gov/ncidod/dvbid/westnile/prevention_info.htm. Accessed July 18, 2005.

West Nile Virus: What You Need To Know

West Nile virus (WNV) is a potentially serious illness. Experts believe WNV is established as a seasonal epidemic in North America that flares up in the summer and continues into the fall.

Approximately 80% of people who are infected with WNV will not show any symptoms at all. Up to 20% of the people who become infected will display mild symptoms, including fever, headache, and body aches, nausea, vomiting, and sometimes swollen lymph glands or a skin rash on the chest, stomach, and back. Symptoms typically last a few days. About one in 150 people infected with WNV will develop severe illness. The severe symptoms can include high fever, headache, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness, vision loss, numbness, and paralysis. These symptoms may last several weeks, and neurological effects may be permanent.

Generally, WNV is spread by the bite of an infected mosquito. Mosquitoes are WNV carriers that become infected when they feed on infected birds. Infected mosquitoes can then spread WNV to humans and other animals when they bite.

In a very small number of cases, WNV also has spread through blood transfusions, organ transplants, breastfeeding, and even during pregnancy from mother to baby. WNV is not spread through casual contact such as touching or kissing a person with the virus.

People typically develop symptoms 3-14 days after they are bitten by the infected mosquito. There is no specific treatment for WNV infection. In mild cases, people experience symptoms such as fever and aches that pass on their own. In more severe cases, people usually need to go to the hospital where they can receive supportive treatment including intravenous fluids, help with breathing, and nursing care. Pregnant women and nursing mothers are encouraged to talk to their doctor if they develop symptoms that could be WNV.

For most, risk of getting WNV is low. Less than 1% of people who are bitten by mosquitoes develop any symptoms of the disease and relatively few mosquitoes actually carry WNV.

People who spend a lot of time outdoors are more likely to be bitten by an infected mosquito. They should take special care to avoid mosquito bites.

People older than age 50 are more likely to develop serious symptoms of WNV if they do get sick and should take special care to avoid mosquito bites.

The risk of getting WNV through blood transfusions and organ transplants is very small, and should not prevent people who need surgery from having it. If you have concerns, talk to your doctor before surgery.

Pregnancy and nursing do not increase risk of becoming infected with WNV.