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Garlic and Cardiovascular Disease

By Dónal P. O'Mathúna, PhD

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CARDIOVASCULAR DISEASE (CVD) IS A COMPLEX GROUP OF HEART-related conditions that is by far the leading cause of death in women.[1] More women die from CVD than die from all forms of cancer, including breast cancer. In the United States, about 42 million women have CVD, with 460,000 dying from it each year. Both numbers are higher for women than men. A woman dies from CVD almost every minute. One in five U.S. women has some form of CVD, and almost two-thirds of those who die suddenly from it had no previous symptoms. The risk of heart disease is two to three times higher after menopause than among women of the same age before menopause, and the risks among African American and Mexican American women are higher than among white women. Finding safe and effective strategies to prevent and treat CVD is a major initiative in women's health.

Many factors contribute to the development of CVD. Epidemiological studies have noted the role of elevated serum lipids, including cholesterol and triglycerides, elevated blood pressure, increased platelet aggregation, increased plasma fibrinogen and coagulation factors, alterations in glucose metabolism, and smoking.[2] Improvements have been associated with increased serum levels of high-density lipoprotein (HDL)-cholesterol, normalization of abnormal lipid levels, inhibition of platelet aggregation, and increased antioxidant status.

The latter is tied to the role of diet in CVD, including proposals that garlic may have a role in the prevention and treatment of cardiovascular disease. Garlic was the most popular herbal remedy sold in single-herb formulations in the United States in 2004.[3] It is also by far the most popular herb used by patients with CVD.[4]

History

Over the centuries, many cultures have viewed garlic as an important dietary supplement with beneficial health effects.

Ayurvedic medicine in ancient India refers to the beneficial effects of garlic for blood flow and strengthening the heart.[5] The Egyptian Codex Ebers (1500 BC) recommended garlic for treating heart disease and also for tumors, worms, bites, and many other conditions. The ancient Greek physician Hippocrates (400 BC) and the Roman authority Pliny the Elder (77 AD) similarly recommended garlic for the cardiovascular system. During the ancient Olympics, athletes were encouraged to consume copious quantities of garlic to increase their stamina.[6]

Clinical work as early as 1926 found garlic to have beneficial effects on cardiovascular disease. These effects were rediscovered in the 1960s and 1970s when a number of studies noted reductions in serum cholesterol and triglycerides levels.[5] However, these early studies were conducted with raw garlic administered at very high doses: between seven and 28 cloves per day. This amount of raw garlic has serious social ramifications, regardless of any health benefits.

Mechanism of Action

A number of mechanisms are believed to be involved in garlic's cardiovascular effects reflecting the presence of several compounds with biological activity. Some of these inhibit liver enzymes involved in making cholesterol, including HMG-CoA reductase (the enzyme inhibited by the statin drugs). Others lower plasma cholesterol and triglyceride levels via mechanisms that are as yet unclear.[7] Garlic also contains antioxidants that reduce the oxidation of low-density lipoprotein (LDL)-cholesterol, thus giving rise to beneficial effects that can counteract the development of atherosclerosis. Other constituents in garlic cause smooth muscle relaxation that can lead to reduced hypertension. Some garlic preparations have antiplatelet properties and other effects that counteract blood-clotting mechanisms.

Formulations

Because of the odor problem, much work has been conducted to find more palatable and less odorous formulations of garlic. However, this generates further problems in attempting to review the effectiveness of garlic. Garlic's cardiovascular effects are believed to be caused by sulfur-containing compounds.[3] An intact clove of garlic contains almost all its sulfur in one storage compound called alliin (a name coming from garlic's botanical name, *Allium sativum*). Raw garlic also contains an enzyme called alliinase, which rapidly converts alliin to allicin. The distinctive aroma and taste of garlic is due to allicin, but this is very volatile and unstable, breaking down either in a few hours at room temperature or after 20 minutes of cooking. Raw garlic can be consumed as whole cloves, but usually it is crushed or cut into slivers, and more commonly, it is cooked. However, depending on whether it is cooked in water, oil, or alcohol, different sets of compounds are formed.

As allicin decomposes, dozens of other more stable sulfur compounds are formed. Many of these are biologically active. To complicate matters even further, garlic supplements are prepared in different ways, resulting in different ingredients. The two most common powered formulations are dried garlic powder and aged garlic extract (AGE). During the aging process, the volatile components are lost, thus leading to AGE being called odorless garlic. Garlic oil also is available, made using three different methods, with each leading to different mixtures of the sulfur compounds. The most commonly used dosage form in clinical trials is a standardized garlic powder extract called Kwai® (200-400 mg three times daily).

This raises an important issue for clinical studies: Different preparations contain different compounds in different ratios, which may impact the effects the garlic preparations have on people.

Clinical Studies

Many laboratory and animal tests have demonstrated that garlic and its constituents have biological activities related to CVD. However, controversy continues over

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Questions & Comments

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the clinical significance of these results. An editorial in the February 2007 issue of *Archives of Internal Medicine* asked whether garlic prevents CVD and concluded, "The jury is still out."[8] Results of trials have been contradictory. Another problem has been that while earlier studies often found beneficial effects, more recent trials have not. Often, the more recent trials were larger, longer, and of higher methodological quality.

Cholesterol and lipid levels. Two meta-analyses published in 1993 and 1996 generated much interest in garlic because they reported 9% and 12% reductions in total cholesterol levels, respectively.[9] Since 1993, 25 randomized controlled trials of garlic have been published, 14 showing no effect on cholesterol but 11 showing some reduction. All the trials showing effectiveness had participants with elevated cholesterol levels, while those that were not effective used participants with normal or mildly elevated cholesterol levels.[2] However, a 2002 review noted that in spite of earlier beneficial results, "in the last five years, no randomized, double-blind, placebo-controlled study could be found in which the results indicated a clear beneficial effect of a garlic preparation alone on blood lipids."[9] The most recent controlled trial randomly allocated 192 adults with moderately elevated cholesterol levels to receive either raw garlic, one of two garlic supplements, or placebo for six months.[10] No significant differences were found between the cholesterol or other lipid levels measured.

Antioxidant effects. Although many of garlic's components have demonstrated an antioxidant effect, very few studies have been conducted on the clinical significance of this effect. The results of studies measuring serum antioxidant capacity for those taking garlic have been variable. The particular garlic preparation used here is significant. AGE products are made by soaking garlic slivers in alcohol for 20 months, which removes almost all allicin, but leaves other compounds with greater antioxidant capacity.[6]

Blood-clotting effects. In contrast to the above results, almost all trials examining garlic's impact on fibrinolysis have had positive effects. Fibrinolysis leads to the breakdown of blood clots and its impairment increases the risk of cardiovascular disease. Fibrinolytic activity, acute and chronic, has been increased with all types of garlic preparations in most of the studies examining this factor.[6] Another aspect of blood clotting, platelet aggregation, also is affected by garlic. Seven clinical trials have examined this area since 1993, and all found beneficial effects.[2] However, a review published in 2000 by the Agency for Healthcare Research and Quality concluded that these results must be taken as preliminary.[11] While positive, all the studies found for this review were very small and of limited duration, and some had serious methodological flaws.

Antihypertensive effects. Several studies have examined the role of garlic preparations in lowering blood pressure. A 2001 meta-analysis concluded that the overall effect on blood pressure was insignificant.[12] A 2002 review included almost 30 small, short studies, with most finding that various garlic preparations were of no greater benefit than placebo.[9]

Adverse Effects

Garlic is well-known for its adverse breath and body odor after oral ingestion. Eating raw garlic and high doses of some supplements also can cause mouth and gastrointestinal irritation and burning, heartburn, nausea, vomiting, and diarrhea.[10] Some people also are susceptible to allergic reactions to garlic. The effects of garlic on platelet aggregation and fibrinolysis may increase the risk of bleeding, especially when combined with warfarin or other anticoagulants. Some case reports of postoperative bleeding have been reported. However, a randomized controlled trial found no change in adverse bleeding events among people taking warfarin when given either garlic (AGE formulation) or placebo.[13]

There is some evidence that allicin may stimulate the activity of a cytochrome P450 enzyme involved in the metabolism of many drugs, including oral contraceptives, calcium channel blockers, HIV protease inhibitors, and cyclosporine.[14] Formulations containing alliin or alliinase are not believed to cause this type of drug interaction.

Conclusion

Overall, garlic preparations have some value as a complementary agent in reducing some risk factors associated with cardiovascular disease. The evidence at this stage points to limited beneficial effects for garlic as an anticoagulant and in lowering elevated cholesterol levels slightly for short periods of time. For example, when taken for up to six months, garlic lowers cholesterol levels 4-12%, which must be contrasted with statin drugs that typically reduce cholesterol levels by 17-55%.[14]

Garlic has been recommended as having other cardiovascular benefits. However, trials have been relatively small and subject to methodological problems. Results are also complicated by the diversity of formulations available. More rigorous studies of standardized preparations must be conducted before garlic can be used instead of conventional therapy.

Given the many associations between garlic and cardiovascular health, and the preliminary research results

now available, garlic can be encouraged as part of an overall heart-healthy diet. Whether garlic supplements will provide significant cardiovascular benefits remains to be seen. ❖

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Red and Potentially Red/Purple? Cranberry Juice and Warfarin

By Russell H. Greenfield, MD

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Source: Pham DQ, et al. Interaction potential between cranberry juice and warfarin. *Am J Health-Syst Pharm* 2007;64:490-494.

Abstract: Readers of *Alternative Therapies in Women's Health* will recall that grapefruit and Seville orange juice both inhibit cytochrome P-450 isoenzyme 3A (CYP3A), potentially raising serum levels of medications that are metabolized through CYP3A. More recently, reports of interaction between cranberry juice and warfarin have come to light. Warfarin is metabolized in part through CYP2C9, and concerns have been raised that cranberry juice may inhibit this enzyme. The authors of this study conducted a literature review of the topic to assess requisite level of concern regarding the use of cranberry juice.

Articles published in English were retrieved after a search of Medline, Embase, International Pharmaceutical Abstracts, and IDIS. A sum total of but three case reports (each involving an elderly patient, two of whom ingested very large quantities of cranberry juice daily) and two randomized, placebo-controlled trials were identified. In only one of the case reports was strong evidence of a causal effect of cranberry juice on a rising INR present. A randomized crossover trial assessed the effect of a number of beverages, including cranberry juice, on CYP2C9 activity (via effects on flurbiprofen) and showed no significant impact. The other trial, an open-label, randomized crossover study addressed the effect of cranberry juice on CYP3A, not CYP2C9, but likewise found no significant interaction.

As an addendum, the authors note that a recent small randomized, placebo-controlled trial of men with atrial fibrillation receiving warfarin showed that 250 mL of cranberry juice enjoyed daily for seven days had no significant effect on INR. The authors conclude that there are few data to suggest a meaningful interaction between cranberry juice and warfarin, but that patients should be apprised of a potential reason for caution.

Comments

Cranberry juice is tasty and gained popularity when data accumulated that drinking it may help protect against urinary tract infections (by preventing bacterial

adherence to the mucosal lining of the genitourinary tract). On the other hand, warfarin is the most commonly used oral anticoagulant agent. Reports of complications associated with the combination of cranberry juice and warfarin reached the attention of The United Kingdom's Committee on Safety of Medicines, and a warning to health care practitioners ensued. The warning was prudent, but also appears to be premature. A significant number of factors can impact warfarin activity, including dietary changes (low intake of vitamin K), infection (cytokine release), and drug interactions (fluconazole, isoniazid, and lovastatin all inhibit CYP2C9). The case for adverse interaction between cranberry juice and warfarin appears to be weak. For patients on warfarin whose INR results are increasing, a query into their use of cranberry juice may be a good idea. Advice against drinking cranberry juice while taking warfarin, however, appears to be unwarranted. ❖

Smarting from Fish? Seafood Consumption and Pregnancy

By Russell H. Greenfield, MD

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Source: Hibbeln JR, et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): An observational cohort study. *Lancet* 2007;369:578-585.

Abstract: An observational cohort study (part of the Avon Longitudinal Study of Parents and Children, or ALSPAC, originally designed to evaluate the impact of environmental factors both during and after pregnancy on childhood well-being) was performed to assess the possible risks and benefits to childhood development associated with different levels of maternal seafood intake during pregnancy. Expectant mothers in and around Bristol, United Kingdom, were sent questionnaires four times during pregnancy and then at specified times after childbirth to obtain data about diet, social circumstances, education, and behavioral and developmental outcomes (the latter specifically at ages 6, 18, 39, 42, and 81 months). Data regarding food consumption were obtained at 32 weeks gestation via self-completed food-frequency questionnaire (three questions focused on seafood intake, and intake levels of omega-3 fatty acids were derived from results). Children's abilities were estimated using the Denver Developmental Screening Test, with scales completed by mothers at home at 6, 18, 30, and 42 months. A questionnaire eliciting information on children's strengths and difficulties was completed at age 81 months by participating mothers.

In sum, 12% of women ate no fish during pregnancy, while 65% ate 1-340 g/week and 23% ate more than 340 g/week. Unadjusted data showed that children of mothers who ate no fish had a greater risk of adverse or suboptimal outcomes. Higher maternal fish intake was non-linearly associated with a lowered risk of suboptimal verbal IQ. Analysis of adjusted data showed that consumption of seafood during pregnancy was significantly associated with a lowered risk of suboptimal score on nine of 23 outcomes. There was no evidence of harm to the offspring (relative to child behavior or development) of mothers who ate more than three servings of fish per week during pregnancy. Instead, intake of more than 340 g of seafood per week was apparently beneficial for a child's neurodevelopment. The authors concluded that advice to limit seafood consumption during pregnancy to minimize fetal mercury exposure might significantly reduce intake of nutrients essential for optimal neurodevelopment.

Comments

U.S. governmental agencies have recommended since 2004 that expectant mothers should limit intake of seafood to 340 g/week to minimize fetal exposure to neurotoxins like mercury. The recommendation to limit seafood intake during pregnancy creates a conundrum, however, as the major dietary source of omega-3 fatty acids, including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), is fish, and prior reports have strongly suggested that low maternal omega-3 fatty acid intake during pregnancy is associated with low childhood verbal IQ. Fetal mercury exposure clearly results in harm, and that risk has been deemed greater than the potential benefit obtained from regular ingestion of fish and associated nutrients. The results of this trial throw that perspective into question.

The trial was very well done and considered many potential confounding factors including smoking and alcohol use, but conclusions are limited to a degree by the observational nature of the trial. Type of fish ingested, geographic source of the fish, and portion sizes could only be estimated, and the potential for reporting bias is very real considering that mothers filled out questionnaires about their own children. Regardless, the results are compelling, and the recommendation of the authors not to follow the 2004 U.S. guidelines on fish intake during pregnancy throws down the gauntlet. What should we practitioners recommend to our patients?

At present, the best course of action would appear to

Monterey Bay Aquarium: Seafood Watch Program

THE SEAFOOD WATCH PROGRAM AT MONTEREY BAY AQUARIum researches the environmental impacts of fisheries and aquaculture operations so that consumers can make the best possible seafood choices that are good for the oceans. To assist consumers, the Seafood Watch program compiles a national guide *(see below)* and updates it on a regular basis. The Seafood Watch program also provides regional guides that contain the latest information on seafood in your area. You can view the national and regional cards on-line or download a pocket-size version at: www.montereybayaquarium.com/cr/cr_seafoodwatch/sfw_regional.aspx. The recommendations in the guides are based on how fish are raised and caught, and where they are from.

Using the Seafood Guides

The seafood items in the Seafood Watch program guides may occur in more than one column based on how they are caught or farmed or where they are from. Be sure to read all columns, check product labels, and ask questions when shopping or eating out:

- Where is the seafood from?
- Is it farmed or wild-caught?
- How was it caught?

Make Choices for Healthy Oceans

Consumer choices make a difference. Buy seafood from the Best Choices or Good Alternatives columns to support those fisheries and fish farms that are healthier for ocean wildlife and the environment.

Best Choices: These are the best seafood choices. These fish are abundant, well managed, and caught or farmed in environmentally friendly ways.

Good Alternatives: These are good alternatives to the Best Choices column. However, there are some concerns with how they're fished or farmed—or with the health of their habitats due to other human impacts. Visit www.seafoodwatch.org to learn more.

Avoid: Avoid these products, at least for now. These fish come from sources that are either overfished and/or caught or farmed in ways that harm other marine life or the environment. ❖

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National Seafood Guide 2007

Best Choices	Good Alternatives	Avoid
Arctic Char (farmed)	Basa/Tra (farmed)	Chilean Seabass/Toothfish*
Barramundi (U.S. farmed)	Clams (wild)	Cod: Atlantic
Catfish (U.S. farmed)	Cod: Pacific (trawled)	Crab: King (imported)
Clams (farmed)	Crab: Blue*, King (Alaska), Snow (U.S.)	Flounders, Soles (Atlantic)
Cod: Pacific (Alaska longline)†	Crab: Imitation/Surimi	Groupers*
Crabs: Dungeness, Snow (Canada), Stone	Flounders, Soles (Pacific)	Halibut: Atlantic
Halibut: Pacific	Lobster: American/Maine	Lobster: Spiny (Caribbean imported)
Herring: Atlantic/Sardines	Mahi mahi/Dolphinfish (U.S.)	Mahi mahi/Dolphinfish (imported)
Lobster: Spiny (U.S.)	Oysters (wild)*	Monkfish
Mussels (farmed)	Scallops: Sea (Northeast and Canada)	Orange Roughy*
Oysters (farmed)	Shrimp (U.S. farmed or wild)	Rockfish (Pacific)*
Pollock (Alaska wild)†	Squid	Salmon (farmed, including Atlantic)*
Salmon (Alaska wild)†	Swordfish (U.S. longline)*	Scallops: Sea (Mid-Atlantic)*
Scallops: Bay (farmed)	Tuna: Bigeye, Yellowfin (troll/pole)	Sharks*
Striped Bass (farmed or wild*)	Tuna: canned light, canned white/Albacore*	Shrimp (imported farmed or wild)
Sturgeon, Caviar (farmed)		Snapper: Red*
Tilapia (U.S. farmed)		Sturgeon*, Caviar (imported wild)
Trout: Rainbow (farmed)		Swordfish (imported)*
Tuna: Albacore (British Columbia, U.S. troll/pole)		Tuna: Albacore, Bigeye, Yellowfin (longline)*
Tuna: Skipjack (troll/pole)		Tuna: Bluefin

Key: † = Certified as sustainable to the Marine Stewardship Council standard (visit www.msc.org); * = Limit consumption due to concerns about mercury or other contaminants (visit www.oceansalive.org/eat.dfm); Northeast = Connecticut to Maine; Mid-Atlantic = North Carolina to New York.

be to recommend regular fish intake during pregnancy, but to focus on those species with low risk of mercury contamination. Fish to enjoy include Alaskan salmon, herring, sardines, rainbow trout, and sablefish (black cod); fish to avoid, on the other hand, include large predatory species like shark, swordfish, king mackerel, and tilefish, also called golden snapper or golden bass *(see Sidebar on page 38 for a detailed listing of ocean-friendly and safe fish choices)*.

Additionally, a recommendation to eat more fish during pregnancy brings up a question of social justice, as the authors point out that mothers with the lowest levels of education (a surrogate for socioeconomic status) also had the lowest levels of fish intake and the highest rate of study attrition. For reasons both ethical and moral, such a disparity must somehow be corrected. ❖

News Briefs

More Than Half of Infertile Couples at Clinic Used CAM, Study Says

A survey of patients who attended an infertility clinic in South Australia found that 66% had used complementary medicine, according to a study published in the April issue of the *Australian and New Zealand Journal of Obstetrics and Gynecology*.

The researchers conducted a prospective survey of 100 consecutive new patients presenting to an infertility clinic. Subjects were requested to complete a self-administered questionnaire at their first visit and six months later. The researchers also did a retrospective audit of 200 patient records.

They found that the CAM most commonly used by the patients included multivitamins, herbs, and mineral supplements, and providers consulted most frequently were naturopaths, chiropractors, and acupuncturists.

Six months following the initial consultation, the use of CAM therapies had declined. The researchers also found that the use of CAM therapies was poorly documented by clinical staff.

Non-Caucasian Patients with CAD Higher Users of CAM

Non-Caucasian patients with established coronary artery disease (CAD) report a higher use of complementary and alternative medicine (CAM), says research published in the April 1 issue of the *American Journal of Cardiology*.

Researchers examined self-reported use of CAM and evidence-based therapies in a prospective registry of hospitalized patients with acute coronary syndrome from March 1, 2001, to Oct. 31, 2002. They then used Poisson regression models to assess whether CAM use was independently associated with lower rates of aspirin, beta-blocker, and statin use in 596 patients with CAD.

Overall, CAM use was 19% in patients with CAD, the researchers say. Higher proportions of patients who used CAM were non-Caucasian (31% vs. 12%), uninsured (12% vs. 7%), economically burdened (58% vs. 29%), and with depression (13% vs. 6%). Patients who used CAM were more likely to use beta blockers (64% vs. 46%) and as likely to use aspirin (73% vs. 74%) and statins (71% vs. 68%) as non-CAM users. Adjusting for demographic and clinical factors did not change results.

"In conclusion," the researchers say, "although CAM users with established CAD have worse socioeconomic status than nonusers, we found no evidence that they were less compliant with evidence-based therapies."

NCCAM to Hold Informational Teleconference on May 17

The National Center for Complementary and Alternative Medicine (NCCAM) in Bethesda, MD, will hold an informational conference call on Thursday, May 17, 2007, from 2:00 to 3:30 pm ET to review requirements of the Developmental Centers for Research (DCRC) I funding opportunity announcement (FOA) and criteria for DCRC I applications. During the call, NCCAM staff will also answer applicants' questions.

Applicants wishing to register for the call should send an e-mail including name, department, institution, e-mail address, and phone number to nccamdcrcinfo@mail.nih.gov. This information will be used to contact registrants and provide them with information they will need to participate in the phone call. Registration is free, but must be completed no later than 5:00 pm ET on Friday, May 11, 2007.

In advance of the call, applicants planning to submit DCRC I applications are urged to familiarize themselves with the text of the DCRC I FOA, as well as with NCCAM's research funding priorities and NCCAM policies relevant to the research to be proposed.

Use of CAM Therapies Other Than Dietary Supplements Low for Weight Loss

Recent research shows that other than dietary supplements, the use of complementary and alternative medicine (CAM) for adults trying to lose weight is relatively low. Researchers designed their sample to obtain adequate representation of Hispanic and non-Hispanic

black respondents. Data from the total sample of 11,211 were weighted to achieve an estimate of the U.S. population. The research focused on 372 people (3.3%) who had used CAM within the previous 12 months.

Higher adjusted odds ratios for CAM use were found among respondents who were exercising for weight control; using a lower carbohydrate, higher protein diet; using a nonprescription weight-loss product(s); overweight; physically active; and not satisfied with their bodies (with adjustments for age, race, gender, education, and city size). The most often used therapies were yoga (57.4%), meditation (8.2%), acupuncture (7.7%), massage (7.5%), and Eastern martial arts (5.9%). CAM users used the therapies on their own (62.6%), in a group setting (26.8%), or with a CAM practitioner (10.6%).

"Persons who had used other weight loss methods had greater odds for using CAM in the previous 12 months, suggesting that CAM use is often added to other weight-loss strategies," the researchers say. For more information, see the March issue of *The Journal of Alternative and Complementary Medicine*. ❖

CME Objectives

After reading *Alternative Therapies in Women's Health*, the health care professional will be able to:

1. evaluate alternative medicine and complementary therapies for women's health concerns;
2. identify risks and interactions associated with alternative therapies;
3. discuss alternative medicine options with patients;
4. offer guidance to patients based on latest science and clinical studies regarding alternative and complementary therapies.

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. 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, you must complete the evaluation form provided and return it in the reply envelope provided at the end of the semester to receive a certificate of completion. Upon receipt of your evaluation, a certificate will be mailed.

CME Questions

16. Garlic is believed to impact cardiovascular disease by:
- a. lowering blood pressure.
- b. lowering serum cholesterol levels.
- c. inhibiting platelet aggregation.
- d. All of the above

17. The particular element believed to be important in garlic's active ingredients is:
- a. sulfur.
- b. calcium.
- c. iron.
- d. sodium.

18. The area of cardiovascular benefit best demonstrated for garlic has been for:
- a. reducing serum cholesterol levels.
- b. preventing platelet aggregation.
- c. lowering blood pressure.
- d. increasing serum antioxidant capacity.

19. Pregnant women should avoid which of the following fish?
- a. shark.
- b. swordfish.
- c. king mackerel.
- d. tilefish.
- e. All of the above

Answers: 16. d, 17. a, 18. b, 19. e.