

ALTERNATIVE THERAPIES IN WOMEN'S HEALTH

Science-based Information for Clinicians

AHC Media LLC Home Page—www.ahcmedia.com

CME for Physicians—www.cmeweb.com

AHC Media LLC

INSIDE

*Not too
WHEL:
Diet and
breast cancer
recurrence*
page 93

*Green tea
prevents
colorectal
cancer in
women*
page 94

*African-
Americans
often use
CAM to treat
conditions,
not to prevent
them*
page 96

*Alternative Therapies in
Women's Health* is available on-
line. For more information, go to
www.ahcmedia.com/online.html
or call (800) 688-2421.

Pomegranate Juice for the Prevention of Cardiac Disease and Cancer

Dónal P. O'Mathúna

Dr. O'Mathuna is a lecturer in Health Care Ethics, School of Nursing, Dublin City University, Ireland; he reports no financial relationship relevant to this field of study.

POMEGRANATES HAVE NOT BEEN WELL KNOWN IN THE WEST, except for those encountering references to them in the Bible and other ancient literature. Native to Iran, the small tree *Punica granatum* is cultivated in parts of the Mediterranean, the Middle East, Russia, India, China, and Japan.¹ The tree is now being grown in parts of the United States, in particular Arizona and California.² The edible fruit is relatively small, sometimes viewed as no more than a large berry.³ It has a leathery orange skin when ripe, topped by a crown and the remains of its red flower. When the fruit is opened, many shiny ruby-shaped seeds spill forth in the midst of its intense red juice. For this reason, pomegranates have long been seen as a symbol of human fertility.⁴ In many cultures, different parts of the fruit and tree have long been used in traditional medicine. Since scientists from Israel published data in 2000 showing pomegranate's beneficial effects on cardiovascular health,⁵ interest in the exotic fruit has been growing. The interest has primarily centered on its possible beneficial effects on cardiovascular health and in cancer prevention and treatment.

Pharmacology

About 20% of a typical pomegranate fruit is made up of its seeds — a relatively large proportion. These contain about 20% pomegranate seed oil made up primarily of polyunsaturated fatty acids.² Among these, 80% is a rare fatty acid called puniic acid. Also present in the oil is the isoflavone genistein (also found in soy), the phytoestrogen coumestrol, and the sex steroid estrone.⁵ This combination of compounds is unique in nature, giving testimony to the plant's unique botanical heritage. Pomegranate juice has an intense red color and is composed of 85% water, 10% sugar, and a large variety of other compounds.¹ Vitamin C is present in large quantities, as are numerous minerals, with iron being particularly prevalent.² The juice's red color arises from several anthocyanins, which are potent

EDITORIAL ADVISORY BOARD

**Judith Balk, MD, MPH,
FACOG**
Assistant Professor
Magge-Womens Hospital
University of Pittsburgh
Pittsburgh, PA

**Kay Ball, RN, MSA,
CNOR, FAAN**
Perioperative Consultant/
Educator
K & D Medical
Lewis Center, OH

Mary Hardy, MD
Director,
Integrative Medicine
Ted Mann Center
University of California-
Los Angeles
Co-Director
Simms/Mann Health
and Wellness Programs
Venice Family Clinic
Venice, CA

**Lynn Keegan, RN, PhD,
HNC-BC, FAAN**
Director,
Holistic Nursing
Consultants
Port Angeles, WA

Felise B. Milan, MD
Associate Professor
of Clinical Medicine
Albert Einstein
College of Medicine
Montefiore Medical Center
Bronx, NY

**Dónal P. O'Mathúna, BS
(Pharm), MA, PhD**
Lecturer in Health Care
Ethics
School of Nursing
Dublin City University
Ireland

Dr. Balk (peer reviewer) reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

antioxidant flavonoids. These, along with several polyphenolics and tannins (which contribute to the juice's tart taste), contribute to pomegranate's antioxidant activity.⁶

Mechanism of Action

Pomegranate juice is believed to work via its significant antioxidant activity, higher than most other fruit juices, red wine, and green tea.⁷ Oxidative stress is associated with poor cardiac health. The body naturally seeks to neutralize various compounds that cause oxidation and can contribute to cardiac disease. Supplemental antioxidants are widely used in the belief they will lower oxidative stress and may thus prevent cardiac disease and some forms of cancer. Laboratory tests have also shown that various components of pomegranate have anti-proliferating, apoptotic (causing cell death), and anti-angiogenic (preventing growth of new blood vessels essential for cancer cell growth) activities, or can inhibit different growth factors involved in cancer cell growth.⁸

Clinical Studies

Cardiovascular Disease

Early tests with healthy humans found that pomegranate juice increased serum total antioxidant levels, thus reducing oxidative stress.⁹ Nineteen patients with 70-90% stenosis of the carotid arteries were randomized

to either receive pomegranate juice (50 mL/day) or no intervention.⁶ Ten patients were in the pomegranate group and consumed the juice for one year, with 5 patients agreeing to continue for an additional 2 years. Outcomes were measured using echo Doppler ultrasound and blood tests. The mean intima-media thickness (IMT) of the carotid arteries in the control group increased significantly by 9% over one year ($P < 0.01$). In the pomegranate juice group, the mean IMT decreased significantly by 13, 22, 26, and 35% after 3, 6, 9, and 12 months, respectively. No significant changes were found in serum glucose, cholesterol (HDL or LDL), or triglyceride levels. Significant reductions in systolic blood pressure (by 12% after one year; $P < 0.05$), unlike diastolic blood pressure, occurred in the pomegranate group, with no changes in the control group. A number of blood tests showed significantly lowered oxidative stress in the pomegranate group. LDL oxidation was significantly reduced by samples taken from the pomegranate group (by 32% after one year; $P < 0.01$) compared to the control group.

Another clinical trial involved 45 patients with coronary heart disease and myocardial ischemia.¹⁰ The randomized, double-blind trial assigned people to receive either pomegranate juice (240 mL/day) or a modified sports beverage of similar color, flavor, and caloric content. Patients underwent myocardial perfusion imaging while exercising to assessed levels of stress-induced myocardial ischemia. At baseline, the two groups did not differ significantly. After 3 months, those consuming pomegranate juice had reduced stress-induced ischemia while those in the control group had increased ischemia ($P < 0.05$). No differences existed in the medications taken by either group and serum lipid levels did not vary between the groups.

Cancer

Naturally occurring antioxidants have been recommended as part of a general strategy in cancer prevention. Given the relatively high levels of antioxidants in pomegranate, it has been tested against several cancers. In lung cancer, an extract of pomegranate juice was tested in cell cultures and mice. The results have been better than those produced by green tea, which is also believed to have potential anti-cancer activity.⁸ Several pomegranate extracts, as well as juice have been tested against breast cancer cell lines, producing beneficial results. With colon cancer cells, pomegranate juice has been shown to be more potent than any pomegranate extract. Preliminary studies have found that rats fed pomegranate seed oil showed less proliferation of colon cancer. All these results warrant further research, but do not as yet

Alternative Therapies in Women's Health,
ISSN 1522-3396, is published monthly by AHC Media LLC, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.
SENIOR VICE PRESIDENT/PUBLISHER: Brenda L. Mooney.
ASSOCIATE PUBLISHER: Lee Landenberger.
MANAGING EDITOR: Leslie Hamlin
EDITOR: Leslie G. Coplin.
GST Registration Number: R128870672.
Periodicals postage paid at Atlanta, GA 30304.
POSTMASTER: Send address changes to *Alternative Therapies in Women's Health*, P.O. Box 740059, Atlanta, GA 30374.
Copyright © 2007 by AHC Media LLC. All rights reserved. No part of this newsletter may be reproduced in any form or incorporated into any information-retrieval system without the written permission of the copyright owner.
Back issues: \$45. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.
This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman.

Subscriber Information
Customer Service: 1-800-688-2421. Customer Service E-Mail: customerservice@ahcmedia.com Editorial E-Mail: paula.cousins@ahcmedia.com World-Wide Web: www.ahcmedia.com
Subscription Prices
United States \$349 per year (Student/Resident rate: \$180). Add \$12.95 for shipping & handling. Multiple Copies Discounts are available for group subscriptions. For pricing information, call Tria Kreutzer at (404) 262-5482. Outside the United States \$379 per year plus GST (Student/Resident rate: \$195 plus GST).
Accreditation
AHC Media LLC is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. AHC Media LLC designates this educational activity for a maximum of 20 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. This CME publication is intended for the women's health physician. It is in effect for 36 months from the date of the publication. For CME credit, add \$50.



Questions & Comments
Please call Leslie Hamlin, Managing Editor, at (404) 262-5416 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

Table 1

Health Benefits of Pomegranate

Providing 16% of an adult's daily vitamin C requirement per 100 mL serving, pomegranate juice is also a good source of vitamin B, pantothenic acid, potassium, and antioxidant polyphenols. Overall, however, pomegranate is not a significant source of nutrients.¹

The most abundant polyphenols in pomegranate juice are the hydrolyzable tannins called punicalagins, shown, in 39 peer-reviewed research publications over 1990-2007 (August), to have potent free-radical scavenging ability in laboratory studies.² The antioxidant punicalagins absorb into the human body after consumption of pomegranate extracts,³ and an *ex vivo* study of human plasma after consumption of a pomegranate extract standardized to punicalagins indicated an average 32% increase in plasma antioxidant capacity.⁴

Many food and dietary supplement makers have found the advantages of using pomegranate extracts (which have no sugar, calories, or additives), instead of the juice, as healthy ingredients in their products. Many pomegranate extracts are essentially ellagic acid, which may only be absorbed into the body after consumption of punicalagins.⁵

In preliminary laboratory research and human pilot studies, juice of the pomegranate has been found effective in reducing heart disease risk factors, including LDL oxidation, macrophage oxidative status, and foam cell formation, all of which are steps in atherosclerosis and cardiovascular disease. Tannins such as punicalagins have been identified as the primary components responsible for the reduction of oxidative stress which led to these risk factors.² Pomegranate has been shown to reduce systolic blood pressure by inhibiting serum angiotensin-converting enzyme (ACE).³

Metabolites of pomegranate juice ellagitannins have been shown to localize specifically in the prostate gland, colon and intestinal tissues of mice⁴ Other research indicates that pomegranate juice may be effective against prostate cancer^{6,7} and osteoarthritis.⁸

In 2007, six clinical trials in the United States, Israel and Norway have been approved to examine the effects of

pomegranate juice consumption on parameters of prostate cancer or prostatic hyperplasia, diabetes or lymphoma.⁹

The juice may also have antiviral¹⁰ and antibacterial effects against dental plaque.¹¹ ■

References

1. Nutrition Data. www.nutritiondata.com/facts
2. Gross PM. Pomegranate punicalagins
3. Aviram M, Dornfeld L. Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure *Atherosclerosis*. 2001;158: 195-198.
4. Seeram NP et al. Pomegranate ellagitannin-derived metabolites inhibit prostate cancer growth and localize to the mouse prostate gland. *J Agric Food Chem*. 2007;55:7732-7737.
5. Mertens-Talcott SU, et al. Absorption, metabolism, and antioxidant effects of pomegranate (*Punica granatum* L.) polyphenols after ingestion of a standardized extract in healthy human volunteers. *J Agric Food Chem*. 2006; 54:8956-8961.
6. Can pomegranates prevent prostate cancer? A new study offers promise 26 September 2005
7. BBC Juice 'can slow prostate cancer' 1 July 2006
8. Pomegranate Fruit Shown To Slow Cartilage Deterioration In Osteoarthritis
9. NIH-listed human clinical trials on pomegranate
10. Neurath AR, et al. *Punica granatum* (Pomegranate) juice provides an HIV-1 entry inhibitor and candidate topical microbicide. *BMC Infect Dis*. 2004;4:41.
11. Menezes SM, et al. *Punica granatum* (pomegranate) extract is active against dental plaque. *J Herb Pharmacother*. 2006; 6:79-92.

Source: Accessed November 7, 2007

<http://en.wikipedia.org/wiki/Pomegranate>

demonstrate that pomegranate or any of its components will prevent or treat cancer in humans.

Anticancer studies with pomegranate have progressed furthest with prostate cancer. An open-label, single-arm phase II clinical trial was reported in 2006.¹¹ This was conducted with men whose prostate cancer had been treated surgically and/or with radiotherapy. In spite of this treatment, the men's prostate specific antigen (PSA) levels were continuing to rise. Forty-eight patients were

enrolled, with two withdrawing early in the study. Among the remaining 46 patients, pomegranate juice (8 oz/day) significantly increased the mean PSA doubling time from 15 to 54 months ($P < 0.001$). Controversy exists regarding the reliability of PSA levels as indicators of prostate cancer mortality, although PSA doubling time is increasingly accepted as a reliable surrogate biomarker. Although this study had limitations, these are being addressed in a randomized, dou-

Table 2

Pomegranate values per 100 g of edible portion

Calories	63-78
Moisture	72.6-86.4 g
Protein	0.05-1.6 g
Fat	Trace only to 0.9 g
Carbohydrates	15.4-19.6 g
Fiber	3.4-5.0 g
Ash	0.36-0.73 g
Calcium	3-12 mg
Phosphorous	8-37 mg
Iron	0.3-1.2 mg
Sodium	3 mg
Potassium	259 mg
Carotene	None to trace
Thiamine	0.003 mg
Riboflavin	0.012-0.03 mg
Niacin	0.180-0.3 mg
Ascorbic Acid	4-4.2 mg
Citric Acid	0.46-3.6 mg
Boric Acid	0.005

Source: Accessed: November 6, 2007

www.hort.purdue.edu/newcrop/morton/pomegranate.html

ble-blind, three-arm trial that began in 2006.⁸ This study is comparing two doses of pomegranate juice against a placebo and will evaluate the reliability of the biomarkers used in the phase II trial.

Adverse Effects

Pomegranate juice consumption (50 mL/day) for 3 years showed no adverse effects in several blood chemistry analyses of liver, heart, and kidney function.⁶ Among these patients, 60% were taking statin drugs for high cholesterol levels. However, a number of in vitro studies have found that pomegranate juice inhibits human cytochrome CYP450 enzyme.¹² The degree of inhibition is similar to that produced by grapefruit juice, which has been demonstrated to impact metabolism of statins. Although a drug-food interaction involving pomegranate has not been demonstrated in humans, people taking statins should be carefully monitored if they start taking pomegranate juice.

Conclusion

The long history of pomegranate's medicinal use is starting to draw attention from medical researchers. Most of the research to date has been carried out in cell cultures and animals. Among the few studies conduct-

ed in humans, the results are encouraging. In spite of these positive results, caution is needed. A review published in October 2007 by researchers working in this area concluded, "Although the evidence on pomegranate is very promising, extensive studies are required to fully understand its contribution to human health, before recommending its regular consumption in human diets."⁸ The early excitement about vitamin E supplementation is a good example here. While preliminary research results were positive, properly controlled clinical trials did not bear out these findings.¹³ What is known for sure is that diets should contain a range of antioxidants from a variety of plants. Pomegranates may contribute to daily fruit intake, but the evidence that they might prevent any particular disease is preliminary at this stage. ■

References

1. Pomegranates for the prostate and the heart: Seeds of hope. *Harv Mens Health Watch*. 2007;11:4-5.
2. Syed DN, et al. Pomegranate derived products for cancer chemoprevention. *Semin Cancer Biol*. 2007; 17:377-385.
3. Lansky EP, Newman RA. *Punica granatum* (pomegranate) and its potential for prevention and treatment of inflammation and cancer. *J Ethnopharmacol*. 2007;109:177-206.
4. Southgate MT. The cover. Pomegranate Jars. *JAMA*. 2007;297:781.
5. Longtin R. The pomegranate: Nature's power fruit? *J Natl Cancer Inst*. 2003;95:346-348.
6. Aviram M, et al. Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common intima-media thickness, blood pressure and LDL oxidation. *Clin Nutr*. 2004;23:423-433.
7. Malik A, Mukhtar H. Prostate cancer prevention through pomegranate fruit. *Cell Cycle*. 2006;5:371-373.
8. Syed DN, et al. Pomegranate derived products for cancer chemoprevention. *Semin Cancer Biol*. 2007;17:377-385.
9. Aviram M, et al. Pomegranate juice consumption reduces oxidative stress, atherogenic modifications of LDL, and platelet aggregation: Studies in humans and in atherosclerotic apolipoprotein E-deficient mice. *Am J Clin Nutr*. 2000;71:1062-1076.
10. Sumner MD, et al. Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. *Am J Cardiol*. 2005;96:810-814.
11. Pantuck AJ, et al. Phase II study of pomegranate juice for men with rising prostate-specific antigen following surgery or radiation for prostate cancer. *Clin Cancer Res*. 2006;12:4018-4026.

12. Summers KM. Potential drug-food interactions with pomegranate juice. *Ann Pharmacother.* 2006;40:1472-1473.
13. O'Mathúna D, Larimore W. *Alternative medicine*, rev. ed. Grand Rapids, MI: Zondervan; 2007.

Not Too WHEL: Diet and Breast Cancer Recurrence

ABSTRACT & COMMENTARY

By Russell H. Greenfield, MD

Dr. Greenfield is Clinical Assistant Professor, School of Medicine, University of North Carolina in Chapel Hill, and Visiting Assistant Professor, University of Arizona, College of Medicine in Tucson; he reports no financial relationships relevant to this field of study.

Source: Pierce JP, et al: Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer. The Women's Healthy Eating and Living (WHEL) Randomized Trial. *JAMA.* 2007;298:289-298.

IN A LARGE, MULTI-INSTITUTIONAL (7 SITES), RANDOMIZED, controlled study of dietary change, researchers sought to determine whether a significant increase in vegetable, fruit, and fiber intake, together with a decrease in total dietary fat intake, reduces risk of recurrent and new primary breast cancer and all-cause mortality among women with previously treated early stage breast cancer (aged 18-70 years). The intervention group (n = 1537) was assigned to a telephone counseling program supplemented with 12 cooking classes during the first year, and then monthly newsletters during the second year that promoted daily targets of 5 vegetable servings plus 16 oz of vegetable juice; 3 fruit servings; 30 g of fiber; and 15-20% of energy intake from fat. The comparison group (n = 1551) was provided with print materials describing "5-A-Day" dietary guidelines that also emphasized > 20 g fiber per day and < 30% total energy intake from fat. Dietary intake was assessed with 4 prescheduled 24-hour dietary recalls conducted by telephone on random days over a 3-week period, stratified for weekend vs weekdays, that occurred at baseline, 1 year, 4 years, and 6 years, and on 50% random samples at 6, 24, and 36 months. Clinic visits occurred at baseline, 1, 2, or 3 years (randomly determined), and 4 and 6 years. Prior to clinic visits, subjects were mailed questionnaires that included measures of physical activity and psychosocial functioning. The principle outcomes of

interest were invasive breast cancer events (recurrence or new primary) or death from any cause. Two independent oncologists reviewed the medical records of subjects diagnosed with recurrent or new primary breast cancer. Throughout the study, women in both groups received similar medical care.

Data analysis and laboratory studies confirmed that subjects in the intervention groups had maintained a significantly increased intake of fruits, vegetables, and fiber as compared with the comparison group, where intakes changed but modestly, except for a 13% increase in total fat intake. Over a mean follow-up period of 7.3 years, a total of 256 women in the intervention group (16.7%) and 262 subjects in the comparison group (16.9%) experienced an invasive breast cancer event; 155 women in the intervention group (10.1%) died, as compared with 160 in the comparison group (10.3%). Over 80% of all deaths were related to breast cancer. Disease-free survival curves were virtually identical across groups. No between-group differences were found for depression, social support, or quality of life during the most intensive period of intervention (year 1). Pierce and colleagues concluded that among survivors of early stage breast cancer, adoption of a diet that is very high in vegetables, fruit, and fiber and low in fat does not reduce additional breast cancer events or mortality.

■ COMMENTARY

For years, many of us have relied upon a wealth of preclinical data and the smattering of clinical research strongly suggesting that high intakes of fruit, vegetables, and fiber, and a lessened reliance upon high fat foods, constitute an effective preventive strategy against development of breast cancer. Our belief was so strong that this position assumed the station of fact in many circles. Unfortunately, results of this extremely well done trial serve as a sobering reminder that things are rarely as linear or as simple as we would like.

The methodology employed was strong, with a formidable sample size (n = 3,088), as well as significant length and completeness of follow-up. While participants did not attend the majority of classes and may not have read all the newsletters, the approach parallels what might be seen in real life, and the results thus seem generalizable. It is notable that only 14% of subjects could be classified as minorities. Even more notable, the fact that at baseline women in both groups were consuming an average of more than 7 servings of fruits and vegetables a day (likely in response to the diagnosis of breast cancer). Lastly, it is important to remember that the trial did not address carcinoma in situ or stage I tumors < 1 cm in size.

It appears that the dietary manipulation described herein does not have the desired breast cancer chemopreventive effect hoped for in women previously treated for breast cancer. However, the trial did not address the effect of dietary intervention on primary prevention of breast cancer. It is possible that similar dietary interventions might mitigate circumstances associated with other forms of cancer. In addition, diets high in fruits, vegetables, fiber, and omega-3 fatty acids are heart healthy.

Is it time to ditch the farmer's market and hit the burger joint? No. The results of this trial are disappointing, but the evidence of health benefits associated with a diet high in fruits, vegetables, and fiber and low in total fat remain compelling. We can and should continue to recommend such a diet to our patients, even those with a history of breast cancer, though we cannot point to a direct breast cancer-related benefit for women in this group. ■

Green Tea Prevents Colorectal Cancer in Women

ABSTRACT & COMMENTARY

By Donald Brown, ND

Dr. Brown is Founder and Director, Natural Product Research Consultants, Inc.; he serves on the Advisory Board of the American Botanical Council and the President's Advisory Board, Bastyr University, Seattle, WA; and is an Advisor to the Office of Dietary Supplements at the National Institutes of Health; he is a consultant for Nature's Way, Inc.

Source: Yang G, et al. Prospective cohort study of green tea consumption and colorectal cancer risk in women. *Cancer Epidemiol Biomarkers Prev.* 2007;16:1219-1223.

IN A POPULATION-BASED, PROSPECTIVE COHORT STUDY (The Shanghai Women's Health Study), Japanese women were studied for the possible association between green tea consumption and colorectal cancer. The study recruited 74,942 women (aged 40 to 70 years) between 1996 and 2000 from 7 urban communities of Shanghai, with a participation rate of 92.7%. This study excluded subjects who reported a history of cancer (n = 1490), diabetes (n = 3302), or familial adenomatous polyposis (n = 86) at baseline, subjects with an extreme total energy intake (< 500 or > 3,500 kcal/day; n = 132), subjects lost to follow-up since enrollment (n = 10), or

subjects who drank black or oolong tea regularly and exclusively (n = 381). After these exclusions, a total of 69,710 women remained for the study. The study lasted 6 years.

Biennial follow-ups determined the occurrence of cancer and other chronic diseases during home visits with the cohort members or next of kin for those who were deceased. The majority of cases of cancer (n = 246; 96.1%) were pathologically confirmed, with the remainder (n = 10; 3.9%) diagnosed with endoscopy, radiography, or ultrasound. Tea consumption was assessed at the baseline survey and reassessed 2 to 3 years later for more than 91.4% of the participants at the first follow-up survey. Each subject was asked whether she drank green tea regularly (at least 3 times per week for at least 6 months) and at what age she started. This was followed by questions on the type and amount of tea consumed during the past year, as well as the current level of consumption.

The multivariate relative risk of colorectal cancer (CRC) was 0.63 (95% confidence interval, 0.45-0.88) for women who reported drinking green tea regularly at baseline compared with non-regular tea drinkers. A significant dose-response relationship was found for both the amount of green tea consumed (*P* trend = 0.001) and the duration in years of lifetime tea consumption (*P* trend = 0.006). Compared with non-drinkers, each 1.67 g increase (approximately equal to the amount of tea in one tea bag) in daily green tea consumption was associated with a 10% reduction in CRC risk (RR, 0.90; CI: 0.80-1.00). Additional 5-year consumption of green tea was also associated with a 10% reduction in CRC risk (RR, 0.90; 95% CI: 0.83-0.97) after fully adjusting for potential confounding variables (eg, cigarette smoking, alcohol consumption, exercise). The reduction in risk was most evident for those women who reported to drink tea regularly at both baseline and during follow-up surveys (RR, 0.43; 95% CI: 0.24-0.77).

■ COMMENTARY

The data on the chemopreventive benefits of green tea continue to grow with this large, prospective cohort study of women in Shanghai. The results demonstrate an inverse correlation between green tea consumption and the risk of CRC — most notably those women who regularly consumed green tea over a longer period of time.

With research showing protection against ovarian cancer^{1,2} and breast cancer,^{3,4} as well as a reduction in mor-

tality due to cardiovascular disease in women,⁵ it's time for practitioners to begin advising their female patients to drop the coffee and start adding green tea to their daily regimen.

Conclusion

As noted in an earlier review, large population studies in women continue to suggest that risk of cardiovascular disease, ovarian cancer, breast cancer, and now colorectal cancer are all reduced with increased intake of green tea. As previously noted, it's important to remember that these studies were looking at women consuming green tea as a beverage and not in capsules. While studies have suggested possible weight loss benefits for concentrated green tea extracts,⁶ case studies suggesting a possible link between a few of these encapsulated extracts and hepatotoxicity suggest the need for more safety studies before recommending them as a substitute for a few cups of green tea each day.⁷ ■

References

1. Larsson SC, Wolk A. Tea consumption and ovarian cancer risk in a population-based cohort. *Arch Intern Med.* 2005;165:2683-2686.
2. Zhang M, et al. Green tea consumption enhances survival of epithelial ovarian cancer. *Int J Cancer.* 2004;112:465-469.
3. Wu AH, et al. Green tea and risk of breast cancer in Asian Americans. *Int J Cancer.* 2003;106:574-579.
4. Nakachi K, et al. Influence of drinking green tea on breast cancer malignancy among Japanese patients. *Jpn J Cancer Res.* 1998;89:254-261.
5. Kuriyama S, et al. Green tea consumption and mortality due to cardiovascular disease, cancer, and all causes in Japan: The Ohsaki study. *JAMA.* 2006;296:1255-1265.
6. Nagao T, et al. A green tea extract high in catechins reduces body fat and cardiovascular risks in humans. *Obesity (Silver Spring).* 2007;15:1473-1483.
7. Bonkovsky HL. Hepatotoxicity associated with supplements containing Chinese green tea (*Camellia sinensis*). *Ann Intern Med.* 2006;144:68-71.

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

41. **The types of antioxidants in pomegranate juice are:**
 - a. anthocyanins.
 - b. polyphenolics.
 - c. tannins.
 - d. All of the above
42. **There is preliminary evidence that pomegranate juice may interact with certain drugs in the same way as:**
 - a. apple juice.
 - b. orange juice.
 - c. grapefruit juice.
 - d. tomato juice.
43. **Among common nutrient antioxidants, the one with the highest antioxidant activity is:**
 - a. green tea.
 - b. pomegranate juice.
 - c. red wine.
 - d. None of the above

Answers: 41. (d); 42. (c); 43. (b)

African-Americans often use CAM to treat conditions, not to prevent them

A recent study found that a substantial number of African-Americans use complementary and alternative medicine (CAM), most often to treat specific conditions as opposed to preventing them.

Researchers in the study wanted to determine patterns of CAM use in African-Americans. Specifically, they wanted to know: 1) characteristics of CAM users in the African-American population; 2) the prevalence of CAM use; and 3) CAM use for treatment and prevention of disease.

They analyzed data from the 2002 National Health Interview Survey (NHIS), which included 4,256 African-American adults representing 23,828,268 African-American adults nationwide. Chi-squared tests based on weighted data were used to examine differences in CAM users and nonusers, the researchers say. CAM use was categorized as CAM Ever, CAM Past 12 Months, and CAM for Treatment.

Of the African-Americans identified in the NHIS dataset, 67.6% used CAM in the past 12 months, when prayer for health was included. Users were more likely older, female, college educated, and insured compared to nonusers. Prayer was the most common CAM used by more than 60% of respondents, followed by herbals (14.2%) and relaxation (13.6%).

Overall, a majority used CAM to treat illness. The use of CAM was significantly higher across all the disease states common in African-Americans as compared to nonuse. For more information on this study, see the September issue of the *Journal of Alternative and Complementary Medicine*.

NCCAM expands Centers of Excellence in CAM research program

The National Center for Complementary and Alternative Medicine (NCCAM) in Bethesda, MD, has added three new Centers of Excellence for Research on Complementary and Alternative Medicine (CAM) to its centers program. These centers will explore the biological effects of a number of plant-derived compounds and preparations found in CAM products on pancreatic diseases, autoimmune and inflammatory diseases, and Alzheimer's disease.

The Centers of Excellence apply cutting-edge technology to basic and clinical research on a wide range of CAM practices and products, and are one part of NCCAM's larger research centers program. The program also includes

Developmental Centers for Research on CAM, which are partnerships between CAM institutions and established research institutions to conduct exploratory research, and International Centers for Research on CAM, which are collaborations of United States and foreign teams studying traditional medical systems.

The new Centers of Excellence for Research on CAM are:

- **UCLA Center of Excellence in Pancreatic Diseases**

This center will study plant-derived compounds found in a variety of dietary and herbal supplements and traditional herbal medicines, including antioxidants such as curcumin (a component of the spice turmeric) and lycopene (the component that gives tomatoes their color), and preparations of green tea and *Scutellaria baicalensis* (a plant used in traditional Chinese medicine). Using animal models, the investigators will study the mechanisms and effects of these plant compounds on the prevention and/or treatment of pancreatic cancer and pancreatitis (inflammation of the pancreas).

- **Center for CAM Research on Autoimmune and Inflammatory Diseases; Institution; University of South Carolina Research Foundation, Columbia, SC**

This center will focus on the effects of plant and herbal products on preventing or arresting inflammation in diseases caused by immune system breakdown. Using an animal model, researchers will investigate the mechanisms by which resveratrol, a compound found in the skin of red grapes, might aid in the treatment of multiple sclerosis. The center will also examine anti-inflammatory mechanisms of the herb American ginseng in colitis and the actions of a compound from hemp in treating autoimmune hepatitis.

- **Institution: Mount Sinai School of Medicine, New York, NY**

This center will conduct preclinical studies to identify natural compounds extracted from grapes, known as polyphenols, that might have a protective role in Alzheimer's disease. Using an animal model, the research team will then investigate the biological mechanisms by which these grape-derived compounds may affect changes in the brain that are characteristic of Alzheimer's disease and associated with cognitive decline.

These center grants, which provide five years of support, bring the total number of Centers of Excellence for Research on CAM to 11. The existing Centers of Excellence look at a range of CAM practices, such as acupuncture and meditation. To learn more about NCCAM's Research Centers program, visit: <http://nccam.nih.gov/training/centers/>. ■

In Future Issues:

Medicinal Properties of Tea

Herbs and Breast Cancer

Herbs and Urinary Tract Infections

ALTERNATIVE THERAPIES IN WOMEN'S HEALTH

Science-based Information for Clinicians

CUMULATIVE INDEX

Volume 9, Numbers 1-12, Pages 1-96

January 2007–December 2007

A

acupuncture

- depression, 7:49
- IVF, 11:81
- CAM use, 12:96

Asian-Americans

- CAM use, 3:24

B

benefits

- exercise, 8:62

black cohosh

- menopausal symptoms, 4:29

botanicals

- dietary supplements, 6:47

breast cancer recurrence

- diet, 12:93

C

calcium

- osteoporosis, 3:24

CAM treatments

- counseling, 2:16

CAM use

- African-Americans, 12:96
- Asian-Americans, 3:24
- depression, 4:32
- diabetes, 2:15
- health behaviors, 10:80
- infertile couples, 5:39
- menopause, 11:88
- menopause, 2:15
- non-caucasian CAD patients, 5:39
- older Americans, 3:23
- weight loss, 5:39
- women in midlife, 6:45

cardiovascular disease and cancer

- pomegranate juice, 12:89
- folate, 3:22
- garlic, 5:33
- green tea, 2:13
- soy, 10:73

childhood eczema

- maternal stress, 10:77

colorectal cancer

- green tea, 12:94

concerns

- oral health, 1:1

counseling

- CAM treatments, 2:16

cranberries

- urinary tract infections, 2:9

cranberry juice

- warfarin, 5:36

D

depression

- acupuncture, 7:49
- CAM use, 4:32
- exercise, 8:57

DHEA therapy

- review, 9:65

diabetes

- CAM use, 2:15

diet

- breast cancer recurrence, 12:93

dietary supplements

- botanicals, 6:47
- FDA, 8:64
- regulation, 7:56

E

exercise

- benefits, 8:62
- depression, 8:57

F

FDA

- dietary supplements, 8:64

folate

- cardiovascular disease, 3:22

G

garlic

- cardiovascular disease, 5:33

genistein

- osteopenia, 11:85

glucomannan

- review, 6:41

green tea

- cardiovascular disease, 2:13
- colorectal cancer, 12:94

H

health behaviors

- CAM use, 10:80

health promotion

- herbs, 6:47

herbs

- health promotion, 6:47

horse chestnut seed extract

- venous insufficiency, 4:25

I

infertile couples

- CAM use, 5:39

IVF

- acupuncture, 11:81

M

maternal stress

childhood eczema, 10:77

menopause

black cohosh, 4:29
CAM use, 2:15, 11:88

metabolic syndrome

soda, 10:76

N

non-caucasian CAD patients

CAM use, 5:39

O

older Americans

CAM use, 3:23

optimal levels

vitamin D, 3:22

oral health

concerns, 1:1

osteopenia

genistein, 11:85

osteoporosis

calcium, 3:24
soda, 6:46

P

pomegranate juice

cardiovascular disease and cancer,
12:89

pregnancy

seafood consumption, 5:37

R

reflexology

relaxation, 3:17

regulation

dietary supplements, 7:56

relaxation

reflexology, 3:17
yoga, 9:70

review

DHEA therapy, 9:65
glucomannan, 6:41

S

seafood consumption

pregnancy, 5:37

soda

metabolic syndrome, 10:76
osteoporosis, 6:46

soy

cardiovascular disease, 10:73

study

weight loss, 7:53

U

urinary lignan excretion

uterine fibroids, 1:7

urinary tract infections

cranberries, 2:9

uterine fibroids

urinary lignan excretion, 1:7

V

venous insufficiency

horse chestnut seed extract, 4:25

vitamin D

optimal levels, 3:22

W

warfarin

cranberry juice, 5:36

weight loss

CAM use, 5:39
study, 7:53

women in midlife

CAM use, 6:45

Y

yoga

relaxation, 9:70

CME Evaluation

Please take a moment to answer the following questions to let us know your thoughts on the CME program. Fill in the appropriate space and return this page in the envelope provided. **You must return this evaluation to receive your credit letter.** Thank you.

CORRECT ● **INCORRECT** ○ ✎ ✖ ✕ ✗

1. Please indicate the appropriate credential: MD DO Other

	Strongly Disagree	Disagree	Slightly Disagree	Slightly Agree	Agree	Strongly Agree
After participating in this program, I am able to:						
2. Evaluate alternative medicine and complementary therapies for women's health concerns.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. Identify risks and interactions associated with alternative therapies.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. Discuss options with patients and offer guidance based on the latest science and clinical studies regarding alternative and complementary therapies.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. The test questions were clear and appropriate.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. I am satisfied with customer service for the CME program.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. This activity reaffirmed my clinical practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. This activity has changed my clinical practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

If so, how? _____

9. How many minutes do you estimate it took you to complete this entire semester (6 issues) activity? Please include time for reading, reviewing, answering the questions, and comparing your answers to the correct ones listed. _____ minutes.

10. I detected no commercial bias in this activity. Yes No

11. Do you have any general comments about the effectiveness of this CME program?

I have completed the requirements for this activity.

Name (printed) _____ **Signature** _____

Please make label address corrections here or
PRINT address information to receive a credit letter.

PLEASE NOTE: If your correct name and address do not appear below, please complete the section at left.

Account # _____

Name: _____

Company: _____

Address: _____

City: _____ State: _____ Zip _____

Fax: _____ Phone: _____

E-mail: _____