

Phytochemicals' Role in Good Health **By Densie Webb, PhD, RD**

Suggested CDR Learning Codes: 2010, 2020, 4030, 4040

Much of early medicine relied on the prescription of specific plants and herbs for healing, a practice still supported by contemporary research. One of the principle recommendations from the 2010 Dietary Guidelines is to eat more fruits, vegetables, and whole grains by having fruits and vegetables represent one-half of the food on Americans' plates and making whole grains account for one-half of the recommended six or more daily servings of grains.¹ That recommendation was developed based on several population studies suggesting diets rich in fruits, vegetables, and whole grains may offer some degree of protection against cancer, cardiovascular disease, type 2 diabetes, and neurodegeneration.²⁻⁵

Consumption of tea, wine, and cocoa, which also are plant based (tea comes from the dried leaves of the *Camellia sinensis* bush, wine from grapes, and cocoa from the dried and fermented seed of the *Theobroma cacao* tree), has been associated with reduced risk of these diseases as well.⁶⁻⁹

Naturally occurring compounds, known as phytochemicals (phyto means plant in Greek) are thought to be largely responsible for the protective health benefits of these plant-based foods and beverages, beyond those conferred by their vitamin and mineral contents. These phytochemicals, which are part of a large and varied group of chemical compounds, also are responsible for the color, flavor, and odor of plant foods, such as blueberries' dark hue, broccoli's bitter taste, and garlic's pungent odor. Research strongly suggests that consuming foods rich in phytochemicals provides health benefits, but not enough information exists to make specific recommendations for phytochemical intake.

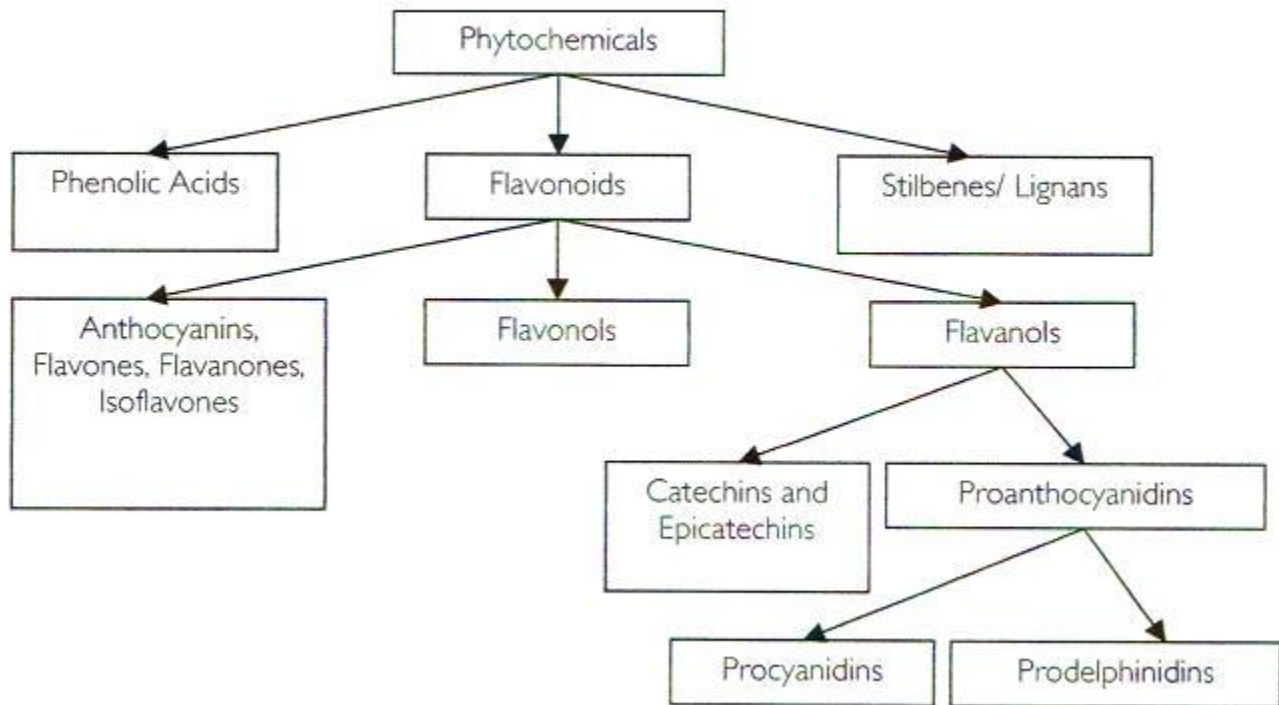
This continuing education course discusses the classification and mechanisms of action of phytochemicals; explores research concerning their role in the prevention of cardiovascular disease, cancer, and diabetes as well as neurological diseases such as Parkinson's and Alzheimer's; and provides suggestions RDs can share with clients for consuming phytochemical-rich foods.

Phytochemicals Defined

Phytochemicals, also referred to as phytonutrients, are found in fruits, vegetables, whole grains, legumes, beans, herbs, spices, nuts, and seeds and are classified according to their chemical structures and functional properties. The terminology used to describe phytochemicals (flavonoids, flavonols, flavanols, proanthocyanidins, procyanidins) can be confusing. Phytochemicals include compounds such as salicylates, phytosterols, saponins, glucosinolates, polyphenols, protease inhibitors, monoterpenes, phytoestrogens, sulphides,

terpenes, lectins, and many more. The Phytochemical Family Tree shows the major groups of phytochemicals found in foods.

Phytochemical Family Tree



Source: Heneman K, Zidenberg-Cherr S. Some facts about phytochemicals. UC Cooperative Extension Center for Health and Nutrition Research Nutrition and Health Info Sheet. <http://nutrition.ucdavis.edu/content/infosheets/fact-pro-phytochemical.pdf>. October 2008

Tens of thousands of phytochemicals have been identified, and researchers speculate that there are likely many more they haven't yet discovered in the foods we eat. Though the broadest groups of phytochemicals, such as flavonoids, isoflavones, or anthocyanidins, often are referred to as if they were a homogenous group, the individual compounds within each group have different chemical structures, are metabolized differently by the body, and may have different health effects.¹⁰

Flavonoids are the largest, most varied, and most studied group of phytochemicals. In fact, more than 6,000 flavonoids that occur in plant foods have been described.¹¹ Plants typically produce several phytochemicals that act as a protective mechanism against environmental stressors; the more environmental stressors, the more phytochemicals a plant produces.¹² As a result, phytochemical content can vary with growing conditions.

There's little information on the average intake of phytochemicals among Americans. However, it shouldn't be surprising that the intake of phytochemicals is higher among people consuming the recommended amounts of fruits and vegetables.¹³ Though recommendations suggest

consuming a variety of fruits, vegetables, and whole grains, for example, single foods often account for the majority of the total intake of some phytochemicals.¹³

Phytochemical Research

As mentioned, research on specific phytochemicals in foods and their effects on disease risk is limited, but there's enough evidence—mostly from looking at the association between foods rich in phytochemicals and disease risk—to strongly suggest that consuming foods and beverages rich in these compounds may help prevent disease. However, it isn't known whether the health benefits are the result of individual phytochemicals, the interaction of various phytochemicals, the fiber content of plant foods, or the interaction of phytochemicals and the vitamins and minerals found in the same foods.

Cardiovascular Disease

There's evidence to suggest that consuming foods rich in phytochemicals may reduce the risk of cardiovascular disease.¹⁴ One meta-analysis found that increasing fruit and vegetable consumption from fewer than three to more than five servings per day was associated with a 17% reduction in risk.¹⁵ Another meta-analysis suggested that the risk of coronary heart disease would decrease by 4% for each portion per day of fruits and vegetables added to the diet.¹⁴

When studies have attempted to identify a relationship between specific fruit polyphenols and cardiovascular disease risk, the findings have been limited, but there's support for the current recommendations to eat a variety of fruits and vegetables daily.¹³ Most studies concerning cardiovascular disease, however, have looked at the consumption of soy (rich in isoflavones) and/or cocoa (rich in polyphenols). Soy, cocoa, and black and green teas have been studied extensively, and consumption of each one is associated with a reduced risk of cardiovascular disease. There's a wide range of benefits associated with the phytochemical content of these foods and beverages, including lowering blood pressure, reducing inflammation, increasing HDL cholesterol while decreasing LDL oxidation, dilating blood vessels, and decreasing the tendency of the blood to form clots.^{9,16,17} Cocoa was found to improve endothelial function by dilating blood vessels; it was more effective among those older than the age of 50.¹⁸

A meta-analysis and a systematic examination of prospective cohort studies and randomized controlled trials found that an average of 2.5 to five servings of whole grains per day was associated with a 21% lower risk of cardiovascular disease compared with consuming fewer than 0.2 servings per day.^{19,20} The range of phytochemicals, including anthocyanins, phytosterols, phenolic acids, lignans, and carotenoids, that are present in wheat, rye, oats, rice, and other grains is believed to contribute to these cardioprotective effects.²¹

The consumption of whole grains rich with phytochemicals also is associated with lower blood pressure, which aids in the prevention of cardiovascular disease. Consuming four or more servings of whole grains daily is associated with a 23% lower risk of high blood pressure. As consumption of whole grains increases, blood pressure generally decreases.²² Intervention studies, while inconsistent, also have found a positive association between whole grain intake and blood pressure.^{23,24}

Cancer

The consumption of fruits, vegetables, and whole grains, as well as dietary patterns such as the Mediterranean diet that emphasize these foods, have been associated with a reduced risk of several types of cancer, including breast, lung, and colon.²⁵⁻²⁷ A systematic review of 25 prospective studies found that an increase of three servings per day of whole grains was associated with a 17% lower risk of colorectal cancer.²⁸ But not all studies on fruit, vegetable, and whole grain consumption have found the same reduction in risk.²⁹

Studies also have looked at the intake of specific phytochemicals and found a link to reduced cancer risk.^{3,25,30} One study found that only specific flavonoid subgroups were associated with a decreased risk of breast cancer.²⁵ Others have found the reduced risk of cancer wasn't as strong for individual phytochemicals as for the foods rich in phytochemicals.^{25,30}

The consumption of cruciferous vegetables such as broccoli, cabbage, and cauliflower has been associated with a decreased risk of prostate, lung, breast, and colon cancers.³¹ Isothiocyanate phytochemicals found in cruciferous vegetables, especially sulforaphane in broccoli, which has been studied extensively, are believed to offer some degree of prevention.

Therapeutic combinations of foods rich in phytochemicals that have yet to be identified could be effective for both cancer prevention and treatment.²² There's also evidence that some phytochemicals may have varying effects with respect to cancer risk, depending on an individual's age and genetic makeup. Isoflavones, for example, have estrogenlike effects and either may increase or decrease risk of breast cancer, depending on genetics and menopausal status.³² Some phytochemicals, such as resveratrol, sulforaphane, curcumin, quercetin, and genistein, may enhance the action of chemotherapeutic agents used to treat cancer.³³⁻³⁵ However, it's too early to recommend phytochemicals or specific combinations of foods as a way to prevent cancer or increase the effectiveness of chemotherapy.

There's a large volume of laboratory and animal research showing preventive effects of tea polyphenols against cancer of the skin, lung, oral cavity, esophagus, stomach, liver, pancreas, small intestine, colon, bladder, prostate, and mammary gland.^{36,37} Tea polyphenols have been shown to affect tumor suppression and cancer cell replication and also alter gene regulation.³⁸ These effects usually are attributed to tea's catechin polyphenols.³⁸ However, studies in humans haven't demonstrated a clear connection. The lack of a consistent effect in humans could be due to the fact that they don't consume the larger doses typically used in animal studies, the difficulty in obtaining accurate measurements of tea intake among human subjects, and genetic diversity among the human population that isn't present in research animals.^{36,37}

The polyphenols in cocoa have been found in laboratory studies to interfere with the initiation, promotion, and progression of cancer cells.³⁹ While chocolate, especially dark chocolate, is rich in these polyphenols, it isn't known whether the same cancer-preventive effects would apply in the body and what an effective dose may be.³⁹

Type 2 Diabetes

Research suggests that phytochemical-rich foods may directly decrease the risk of type 2 diabetes, most likely by reducing inflammation and improving insulin sensitivity, and indirectly by preventing weight gain, the most important risk factor of the disease.^{26,40-42}

Positive effects on fasting blood glucose levels and insulin sensitivity have been found specifically with the consumption of polyphenols both in laboratory and animal studies.⁴³ Dietary polyphenols may inhibit carbohydrate digestion and glucose absorption in the intestine, stimulate insulin secretion from the pancreas, modulate glucose release from the liver, activate insulin receptors and glucose uptake in insulin-sensitive tissue, and modulate intracellular signaling pathways and gene expression.⁴³ Some studies have found that a reduced risk was strongest with the consumption of green leafy vegetables, which are rich sources of phytochemicals.⁴²

In the Nurses' Health Studies I and II and the Health Professionals Follow-Up Study, higher intakes of anthocyanins and anthocyanin-rich fruits were linked with a lower risk of developing type 2 diabetes.⁴⁴ However, the Women's Health Study didn't find the same connection, although the researchers suggested that apple and tea intake may have a modest risk-reducing effect.⁴⁵

The polyphenols in tea and cocoa also may contribute to improved insulin sensitivity and lower type 2 diabetes risk. In a large population study from eight European countries, tea intake was associated with a significantly decreased risk of developing type 2 diabetes.⁴⁶ Specifically, those who drank more than four cups of tea per day had a 16% lower risk compared with non-tea drinkers.

In a placebo-controlled trial with diabetes patients, those given flavonoid-enriched chocolate and supplemental isoflavones for one year experienced significantly reduced insulin levels, improved insulin sensitivity, and decreased total cholesterol, HDL ratio, and LDL cholesterol.⁴⁷

A systematic examination of 45 prospective cohort studies found a 26% lower risk of type 2 diabetes among those who consumed 48 to 80 g of whole grains per day (three to five servings) compared with those who never or rarely ate whole grains.²⁰ A review of the prospective Nurses' Health Studies I and II, which included almost 162,000 US women enrolled without a history of diabetes, found a 37% lower risk of developing type 2 diabetes among those with the highest intake of whole grains compared with those with the lowest intake.⁴⁸

The 2010 Dietary Guidelines Committee concluded that limited evidence exists associating whole grain consumption with a reduced risk of type 2 diabetes.⁵ However, the German Nutrition Society determined there's probable evidence that it decreases the risk of type 2 diabetes.⁴⁹

Neurodegeneration

Phytochemicals may provide protection against neurodegenerative diseases such as Alzheimer's and Parkinson's.⁵⁰ Research has suggested that phytochemicals such as capsaicin (found in red pepper), curcumin (found in the spice turmeric), epigallocatechin gallate (a catechin in tea known as EGCG), and resveratrol (found in grapes, wine, and peanuts) may have neuroprotective effects.^{51,52}

Flavonoids in general are thought to help reverse age-related declines in cognitive function by increasing the number of connections among neurons and improving blood flow to the brain,^{53,54} which protects vulnerable neurons and enhances the functioning of existing neurons.⁵³ The consumption of flavonoid-rich foods such as berries and cocoa throughout life may hold the potential to limit, prevent, or reverse normal or abnormal deterioration in cognitive function in the aging brain.⁵³

Several studies have found an association between tea consumption and a lower risk of developing Parkinson's disease or delaying its onset by several years.⁵⁵⁻⁵⁷ It has been suggested that the association is due to its caffeine content, which also is a naturally occurring phytochemical, but flavonoid intake in general, and berries in particular, also have been linked to a reduced risk of Parkinson's disease.⁵⁸

Combining specific dietary flavonoids that are absorbed well and can penetrate the blood/brain barrier (which exists to prevent many substances in the blood from reaching the brain), thus preventing or slowing the production of damaging free radicals in the body, could help prevent and treat a variety of neurodegenerative disorders.⁵⁹ But this uniquely effective combination of phytochemicals hasn't yet been identified.

The consumption of flavanol-rich cocoa has been found to improve cerebral blood flow, which is critical for optimal brain function and decreases in dementia and Alzheimer's disease.^{53,60,61} It's been suggested that consuming flavonoid-rich foods such as cocoa and berries throughout life may limit neurodegeneration and prevent cognitive decline.⁵³

Phytoestrogens, which have estrogenlike activity and are found in soy and whole grains, may help prevent cognitive decline that can occur following menopause.⁶²

Mechanism of Action

Researchers have found that phytochemicals have the potential to stimulate the immune system, prevent toxic substances in the diet from becoming carcinogenic, reduce inflammation, prevent DNA damage and aid DNA repair, reduce oxidative damage to cells, slow the growth rate of cancer cells, trigger damaged cells to self-destruct (apoptosis) before they can reproduce, help regulate intracellular signaling of hormones and gene expression, and activate insulin receptors.^{3,43} In addition, there likely are health effects of phytochemicals that researchers haven't yet recognized.³

Much laboratory research has focused on the antioxidant function of phytochemicals. However, their antioxidant activity is reduced in the body during metabolism, and the levels present in blood and tissue are fleeting and quite low.^{63,64} For many of the phytochemicals in

food, their antioxidant effects on cell signaling and gene expression may be more important for health benefits than direct antioxidant activity,⁶³ effects that can be seen even with low concentrations of phytochemicals in plasma and tissues.

In addition to being rich sources of phytochemicals, plant foods also are sources of fiber, vitamins, and minerals whose mechanisms have been more clearly elucidated. But identifying which individual compounds are responsible for the benefits associated with phytochemical-rich foods is difficult, if not impossible, because of the interactions that occur with vitamins, minerals, and fiber as well as among the phytochemicals themselves. The unique combination of these compounds may be the key to reduced disease risk, but that formula hasn't yet been identified and tested.

Factors That Affect Metabolism

The bioavailability of phytochemicals varies greatly and can range from less than 0.03% of what's consumed (certain flavonols) to 50% (isoflavones).⁶³ While evidence is limited regarding how phytochemicals are stored, research suggests there are no long-term stores of polyphenols in the body.¹⁰ Aside from inherent differences in the bioavailability of these compounds, absorption also is affected by the gut microflora and individuals' genetic makeup, both of which vary greatly.⁶⁵ In addition, processing, such as steaming, drying, freezing, and boiling, can reduce the levels of some phytochemicals found in the final food product.⁶⁶

Unidentified Therapeutic Intakes

Even though many phytochemicals are believed to have disease-preventing properties, the lack of food composition data and the incomplete understanding of their absorption, metabolism, and interaction have prevented the Institute of Medicine from creating a Dietary Reference Intake (DRI) for any of them. In addition, unlike vitamins and minerals, these compounds aren't essential and are therefore not considered nutrients.³

The research regarding phytochemicals is complicated by the fact that the effects of consuming phytochemical-rich foods may be most beneficial for people with more severe metabolic abnormalities, such as elevated blood lipids, type 2 diabetes, or obesity, and may not be as apparent in otherwise healthy populations. The complexity of the family of phytochemicals, their potential interactions, and the possible variations in levels found in any given food make it currently impossible to issue specific phytochemical guidelines. In addition, people eat a variety of foods and nutrients every day, each combination holding the potential for unique interactive effects, again making it extremely difficult to link a particular food, nutrient, or phytochemical to a specific health or disease outcome.⁴

More information is needed before dietary recommendations can be made.¹⁰ However, researchers have suggested that once sufficient data are established, a DRI should be developed for one or more of the groups of flavonoids.¹⁰

Potential Risks

Phytochemicals are widely distributed in the food supply, yet because of the lack of an accurate, comprehensive database, estimating intake remains difficult. This affects

researchers' ability to determine what level of phytochemical intake is optimal or what level of intake could potentially pose a health risk.

One of the major functions of phytochemicals is their role as antioxidants. However, as with all antioxidant compounds, once they've carried out their antioxidant function, they become oxidizing compounds themselves. While it would be difficult to get excessive amounts of antioxidant phytochemicals from the diet, large doses of antioxidants in the form of supplements have the potential to be harmful.

The long-term effects of large amounts of phytochemicals on health aren't known, and therefore supplements aren't recommended. While taking large amounts of phytochemicals as supplements could theoretically pose a risk, the risks of consuming high intakes aren't well understood because of the sheer volume of these compounds found in foods, the lack of accurate information regarding dietary intake, and the lack of studies evaluating their safety.¹⁰

Recommendations for Practice

While the associations found regarding a diet rich in fruits, vegetables, tea, whole grains, and other plant foods are consistent and strong, they don't demonstrate a clear cause and effect relationship. However, experts such as the 2010 Dietary Guidelines for Americans Committee¹ and the American Institute for Cancer Research³ agree that consuming a variety of plant-based foods is important for health. Research shows that those who meet the recommendations for fruit and vegetable consumption have considerably higher intakes of phytochemicals.

The best advice for clients and patients is to consume a wide variety of plant-based foods, using MyPlate, which recommends three to five servings of fruits and vegetables per day, at least three daily servings of whole grains, and including beans, legumes, roasted soybeans ($\frac{1}{4}$ cup cooked), and nuts or seeds ($\frac{1}{2}$ oz) as protein choices.⁶⁷ There are no guidelines for coffee, tea, or cocoa consumption, but as long as their intake is factored into the day's intake of calories, moderate consumption of all three may offer additional health benefits. Bear in mind that dark chocolate is richer in phytochemicals than milk chocolate, and tea varieties (white, green, oolong, and black) have different amounts and types of phytochemicals that may provide different health benefits.

—*Densie Webb, PhD, RD is a freelance writer, editor, and industry consultant based in Austin, Texas.*

Phytochemicals in Foods and Possible Health Benefits

Foods	Phytochemicals	Possible Health Benefits
Soybeans, soy milk, tofu	Isoflavones (genistin, daidzein), types of flavonoids	Reduction in blood pressure and increased blood vessel dilation
Strawberries, red wine, blueberries	Anthocyanins, a type of flavonoid	Blood vessel dilation, induction of cancer cell death, improved insulin sensitivity, neuroprotective effects
Red wine, grape juice, grape extracts, cocoa, peanuts	Proanthocyanidins, a type of flavonoid; resveratrol	Inhibition of LDL oxidation and inflammation
Garlic, onions, leeks, olives, scallions	Sulfides, thiols	Decreased LDL cholesterol, anticancer effects
Carrots, tomatoes and tomato products, other orange, yellow, and red fruits and vegetables	Carotenoids, such as lycopene, and beta-carotene	Neutralization of free radicals that cause cell damage
Cruciferous vegetables such as broccoli and kale, horseradish	Isothiocyanates (sulforaphane)	Neutralization of free radicals that cause cell damage and protection against some types of cancer
Green and black tea, cocoa	Catechins, epicatechins, types of flavonoids	Vasodilation, improved blood flow to the brain, improved insulin sensitivity

References

1. US Department of Agriculture, US Department of Health and Human Services. ***Dietary Guidelines for Americans, 2010***. 7th ed. Washington, DC: US Government Printing Office; 2010.
2. Hung HC, Joshipura KJ, Jiang R, et al. Fruit and vegetable intake and risk of major chronic disease. ***J Natl Cancer Inst***. 2004;96(21):1577-1584.
3. World Cancer Research Fund/American Institute for Cancer Research. ***Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective***. Washington, DC: American Institute for Cancer Research, 2007.
4. Slavin JL, Lloyd B. Health benefits of fruits and vegetables. ***Adv Nutr***. 2012;3(4):506-516.
5. US Department of Agriculture Nutrition Evidence Library. <http://www.nel.gov/search.cfm?keywords=fruits+and+vegetables>
6. Bohn SK, Ward NC, Hodgson JM, Croft KD. Effects of tea and coffee on cardiovascular disease risk. ***Food Funct***. 2012;3(6):575-591.
7. Cano-Marquina A, Tarin JJ, Cano A. The impact of coffee on health. ***Maturitas***. 2013; 75(1):7-21.

8. Kokubo Y, Iso H, Saito I, et al. The impact of green tea and coffee consumption on the reduced risk of stroke incidence in Japanese population: The Japan Public health center-based study cohort. **Stroke**. 2013;44(5):1369-1374.
9. Andujar I, Recio MC, Giner RM, Rios JL. Cocoa polyphenols and their potential benefits for human health. **Oxid Med Cell Longev**. 2012; 2012:906252.
10. Erdman JW Jr, Balentine D, Arab L, et al. Flavonoids and heart health: Proceedings of the ILSI North America Flavonoids Workshop, May 31-June 1, 2005, Washington, DC. **J Nutr**. 2007;137(3 Suppl 1):718S-737S.
11. Arts IC, Hollman PC. Polyphenols and disease risk in epidemiologic studies. **Am J Clin Nutr**. 2005;81(1 Suppl):317S-325S.
12. Chalker-Scott L. Environmental significance of anthocyanins in plant stress responses. **Photochem Photobiol**. 1999;70(1):1-9.
13. Murphy MM, Barraj LM, Herman D, Bi X, Cheatham R, Randolph RK. Phytonutrient intake by adults in the United States in relation to fruit and vegetable consumption. **J Acad Nutr Diet**. 2012;112(2):222-229.
14. Dauchet L, Amouyel P, Hercberg S, Dallongeville J. Fruits and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies. **J Nutr**. 2006;136(10):2588-2593.
15. He FJ, Nowson CA, Lucas M, MacGregor GA. Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies. **J Hum Hypertens**. 2007;21(9):717-728.
16. Suzuki Y, Miyoshi N, Isemura M. Health-promoting effects of green tea. **Proc Jpn Acad Ser B Phys Biol Sci**. 2012;88(3):88-101.
17. Bahorun T, Luximon-Ramma A, Neergheen-Bhujju V, et al. The effect of black tea on risk factors of cardiovascular disease in a normal population. **Prev Med**. 2012;54 Suppl:S98-102.
18. Fisher ND, Hollenberg NK. Aging and vascular responses to flavanol-rich cocoa. **J Hypertens**. 2006;24(8):1575-1580.
19. Mellen PB, Walsh TF, Herrington DM. Whole grain intake and cardiovascular disease: a meta-analysis. **Nutr Metab Cardiovasc Dis**. 2008;18(8):283-290.
20. Ye EQ, Chacko SA, Chou EL, Kugizaki M, Liu S. Greater whole-grain intake is associated with lower risk of type 2 diabetes, cardiovascular disease, and weight gain. **J Nutr**. 2012;142(7):1304-1313.

21. Fardet A. New hypotheses for the health-protective mechanism of whole-grain cereals: what is beyond fibre? **Nutr Res Rev.** 2010;23(1):65-134.
22. Wang L, Gaziano JM, Liu S, Manson JE, Buring JE, Sesso HD. Whole- and refined-grain intakes and the risk of hypertension in women. **Am J Clin Nutr.** 2007;86(2):472-479.
23. Tighe P, Duthie G, Vaughan N, et al. Effect of increased consumption of whole-grain foods on blood pressure and other cardiovascular risk markers in healthy middle-aged persons: a randomized controlled trial. **Am J Clin Nutr.** 2010;92(4):733-740.
24. Bodinham CL, Hitchen KL, Youngman PJ, Frost GS, Robertson MD. Short-term effects of whole-grain wheat on appetite and food intake in healthy adults: a pilot study. **Br J Nutr.** 2011;106(3):327-330.
25. Hui C, Qi X, Qianyong Z, Xiaoli P, Jundong Z, Mantian M. Flavonoids, flavonoid subclasses and breast cancer risk: a meta-analysis of epidemiologic studies. **PLoS One.** 2013;8(1):e54318.
26. Boeing H, Bechthold A, Bub A, Ellinger S, Haller D, et al. Critical review: vegetables and fruit in the prevention of chronic diseases. **Eur J Nutr.** 2012;51:637-663.
27. Wakai K, Matsuo K, Nagata C, et al. Lung cancer risk and consumption of vegetables and fruit: an evaluation based on a systematic review of epidemiological evidence from Japan. **Jpn J Clin Oncol.** 2011;41(5):693-708.
28. Aune D, Chan DS, Lau R, et al. Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. **BMJ.** 2011;343:d6617.
29. McCullough ML, Robertson AS, Chao A, et al. A prospective study of whole grains, fruits, vegetables and colon cancer risk. **Cancer Causes Control.** 2003;14(10):959-970.
30. Romagnolo DF, Selmin OI. Flavonoids and cancer prevention: a review of the evidence. **J Nutr Gerontol Geriatr.** 2012;31(3):206-238.
31. Juge N, Mithen RF, Traka M. Molecular basis for chemoprevention by sulforaphane: a comprehensive review. **Cell Mol Life Sci.** 2007;64(9):1105-1127.
32. Bondesson M, Gustafsson JA. Does consuming isoflavones reduce or increase breast cancer risk? **Genome Med.** 2010;2(12):90.
33. Sak K. Chemotherapy and dietary phytochemical agents. **Chemother Res Pract.** 2012;2012:282570.

34. Kaminski BM, Steinhilber D, Stein JM, Ulrich S. Phytochemicals resveratrol and sulforaphane as potential agents for enhancing the anti-tumor activities of conventional cancer therapies. ***Curr Pharm Biotechnol***. 2012;13(1):137-146.
35. Vinod BS, Maliekal TT, Anto RJ. Phytochemicals as chemosensitizers: from molecular mechanism to clinical significance. ***Antioxid Redox Signal***. 2013;18(11):1307-1348.
36. Yang CS, Lambert JD, Ju J, Lu G, Sang S. Tea and cancer prevention: molecular mechanisms and human relevance. ***Toxicol Appl Pharmacol***. 2007;224(3):265-273.
37. Yang CS, Ju J, Lu G, et al. Cancer prevention by tea and tea polyphenols. ***Asia Pac J Clin Nutr***. 2008;17(Suppl 1):245-248.
38. Thakur VS, Gupta K, Gupta S. The chemopreventive and chemotherapeutic potentials of tea polyphenols. ***Curr Pharm Biotechnol***. 2012;13(1):191-199.
39. Martin MA, Goya L, Ramos S. Potential for preventive effects of cocoa and cocoa polyphenols in cancer. ***Food Chem Toxicol***. 2013;56:336-351.
40. Gonzalez-Castejon M, Rodriguez-Casado A. Dietary phytochemicals and their potential effects on obesity: a review. *Pharmacol Res*. 2011;64(5):438-455.
41. Cooper AJ, Forouhi NG, Ye Z, et al. Fruit and vegetable intake and type 2 diabetes: EPIC-InterAct prospective study and meta-analysis. ***Eur J Clin Nutr***. 2012;66(10):1082-1092.
42. Carter P, Gray LJ, Troughton J, Khunti K, Davies MJ. Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis. ***BMJ***. 2010;341:c4229.
43. Hanhineva K, Torronen R, Bondia-Pons I, et al. Impact of dietary polyphenols on carbohydrate metabolism. ***Int J Mol Sci***. 2010;11(4):1365-1402.
44. Wedick NM, Pan A, Cassidy A, et al. Dietary flavonoid intakes and risk of type 2 diabetes in US men and women. ***Am J Clin Nutr***. 2012;95(4):925-933.
45. Song Y, Manson JE, Buring JE, Sesso HD, Liu S. Associations of dietary flavonoids with risk of type 2 diabetes, and markers of insulin resistance and systemic inflammation in women: a prospective study and cross-sectional analysis. ***J Am Coll Nutr***. 2005;24(5):376-384.
46. The InterAct Consortium. Tea consumption and incidence of type 2 diabetes in Europe: the EPIC-InterAct case-cohort study. ***PLoS One***. 2012;7(5):e36910.
47. Curtis PJ, Sampson M, Potter J, Dhatariya K, Kroon PA, Cassidy A. Chronic ingestion of flavan-3-ols and isoflavones improves insulin sensitivity and lipoprotein status and attenuates estimated 10-year CVD risk in medicated postmenopausal women with type 2 diabetes: a 1-year, double-blind, randomized, controlled trial. ***Diabetes Care***. 2012;35(2):226-232.

48. de Munter JS, Hu FB, Spiegelman D, Franz M, van Dam RM. Whole grain, bran, and germ intake and risk of type 2 diabetes: a prospective cohort study and systematic review. *PLoS Med*. 2007;4(8):e261.
49. Hauner H, Bechthold A, Boeing H, et al. Evidence-based guideline of the German Nutrition Society: carbohydrate intake and prevention of nutrition-related diseases. *Ann Nutr Metab*. 2012;60 Suppl 1:1-58.
50. Lee JG, Yon JM, Lin C, Jung AY, Jung KY, Nam SY. Combined treatment with capsaicin and resveratrol enhances neuroprotection against glutamate-induced toxicity in mouse cerebral cortical neurons. *Food Chem Toxicol*. 2012;50(11):3877-3885.
51. Davinelli S, Sapere N, Zella D, Bracale R, Intrieri M, Scapagnini G. Pleiotropic protective effects of phytochemicals in Alzheimer's Disease. *Oxid Med Cell Longev*. 2012;2012:386527.
52. Mythri RB, Bharath MM. Curcumin: a potential neuroprotective agent in Parkinson's disease. *Curr Pharm Des*. 2012;18(1):91-99.
53. Spencer JP. Flavonoids and brain health: multiple effects underpinned by common mechanisms. *Genes Nutr*. 2009;4(4):243-250.
54. Williams RJ, Spencer JP. Flavonoids, cognition, and dementia: actions, mechanisms, and potential therapeutic utility for Alzheimer disease. *Free Radic Biol Med*. 2012;52(1):35-45.
55. Kandinov B, Giladi N, Korczyn AD. Smoking and tea consumption delay onset of Parkinson's disease. *Parkinsonism Relat Disord*. 2009;15(1):41-46.
56. Hu G, Bidel S, Jousilahti P, Antikainen R, Tuomilehto J. Coffee and tea consumption and the risk of Parkinson's disease. *Mov Disord*. 2007;22(15):2242-2248.
57. Tanaka K, Miyake Y, Fukushima W, et al. Intake of Japanese and Chinese teas reduces risk of Parkinson's disease. *Parkinsonism Relat Disord*. 2011;17(6):446-450.
58. Gao X, Cassidy A, Schwarzschild MA, Rimm EB, Ascherio A. Habitual intake of dietary flavonoids and risk of Parkinson disease. *Neurology*. 2012;78(15):1138-1145.
59. Jones QR, Warford J, Rupasinghe HP, Robertson GS. Target-based selection of flavonoids for neurodegenerative disorders. *Trends Pharmacol Sci*. 2012;33(11):602-610.
60. Fisher ND, Sorond FA, Hollenberg NK. Cocoa flavanols and brain perfusion. *J Cardiovasc Pharmacol*. 2006;47 Suppl 2:S210-S214.
61. Francis ST, Head K, Morris PG, Macdonald IA. The effect of flavanol-rich cocoa on the fMRI response to a cognitive task in healthy young people. *J Cardiovasc Pharmacol*. 2006;47 Suppl 2:S215-S220.

62. Zhao L, Mao Z, Brinton RD. A select combination of clinically relevant phytoestrogens enhances estrogen receptor beta-binding selectivity and neuroprotective activities in vitro and in vivo. **Endocrinology**. 2009;150(2):770-783.
63. Gordon MH. Significance of dietary antioxidants for health. **Int J Mol Sci**. 2012;13(1):173-179.
64. Tsao R. Chemistry and biochemistry of dietary polyphenols. **Nutrients**. 2010;2(12):1231-1246.
65. Da Costa LA, Garcia-Bailo B, Badawi A, El-Sohemy A. Genetic determinants of dietary antioxidant status. **Prog Mol Biol Transl Sci**. 2012;108:179-200.
66. Mahn A, Reyes A. An overview of health-promoting compounds of broccoli (*Brassica oleracea* var. *italica*) and the effect of processing. **Food Sci Technol Int**. 2012;18(6):503-514.
67. US Department of Agriculture Choose MyPlate. <http://www.choosemyplate.gov/food-groups>

Examination

1. Which of the following best defines phytochemicals?

- A. Phytochemicals are foods that contain chlorophyll.
- B. Phytochemicals are compounds found only in fruits and vegetables.
- C. Phytochemicals are compounds found in all plant foods.
- D. Phytochemicals are compounds found only in supplements.

2. Which group of foods below is not a rich source of phytochemicals?

- A. Butter, margarine, low-fat milk, cheddar cheese
- B. Oranges, blueberries, strawberries, apples
- C. Brown rice, oatmeal, kashi, whole wheat couscous
- D. Peanuts, pecans, walnuts, cashews

3. Research conclusively has shown that diets rich in certain phytochemicals can reduce the risk of several common diseases.

- A. True
- B. False

4. Studies have found that diets rich in phytochemicals may help prevent which of the following?

- A. Cardiovascular disease
- B. Carpal tunnel syndrome
- C. Endometriosis
- D. Gluten intolerance

5. What is the best dietary advice for consuming phytochemicals?

- A. Eliminate animal products from the diet.
- B. Eat raw phytochemical-rich foods.
- C. Take probiotics along with phytochemical-rich foods.
- D. Consume at least three to five servings of fruits and vegetables and three servings of whole grains per day.

6. What is the largest and most varied group of phytochemical compounds found in food?

- A. Isothiocyanate
- B. Isoflavones
- C. Flavonoids
- D. Carotenoids

7. If the diet provides few phytochemical-rich foods, phytochemical supplements are recommended.

- A. True
- B. False

8. Which of the following foods has not been linked to a reduced risk of type 2 diabetes?

- A. Tea
- B. Whole grains
- C. Cocoa
- D. White rice

9. Studies on the effects of phytochemicals on health have been hindered the most by which of the following?

- A. Lack of phytochemical nutrient databases
- B. Lack of knowledge of the interactions among phytochemicals
- C. Lack of available funding for phytochemical research
- D. Dangers in eating too much phytochemical-rich food

10. Phytochemicals are thought to be involved in which of the following?

- A. Preventing DNA damage
- B. Antihistamine effects
- C. Antibiotic effects
- D. Anti-HIV effects