

Spinach and Cancer



Introduction

The most effective nutrition education program in history may be a cartoon. Popeye “the sailor man” debuted as a newspaper cartoon in 1929 before moving to the small screen in 1933. Popeye’s popularity is credited with increasing spinach intake in the 1930s by 33 percent, a significant amount, considering it occurred during the Depression, when money was tight and budgeting took center stage.

Spinach deserves the attention it received from Popeye, and it tops many “superfood” lists with good reason. Spinach is packed with a variety of bioactive compounds including vitamins A, C, K, and folate; the minerals potassium and magnesium; and cancer-fighting phytonutrients including carotenoids and flavonoids. Clearly, it deserves its place among the most nutritious foods available.

History

The earliest reports of spinach date to ancient Persia (now Iran). In the 7th century it was introduced to China as the “Persian Green”, and by the 11th century spinach had become popular in Spain before spreading to the rest of Europe. Spinach was reportedly the favorite vegetable of Catherine de Medici, who became Queen of France in the 16th century. When leaving her home in Florence, Italy to get married, she brought along her own cooks to prepare her favorite spinach recipes, inspiring the descriptor “a la Florentine” for dishes served with spinach.

Nutrient Analysis:

Spinach is low in calories and provides a wide range of nutrients, making it a “nutrient dense” food. Table 1 outlines the nutrient profile of spinach, which is a good or excellent source of 75% of listed vitamins and minerals for a ½ cup serving of cooked spinach.

Table 1: Nutrient Analysis of Spinach

Nutrient	Unit of Measure	1 cup Raw Spinach (= 30 grams)	% Daily Value*	½ cup cooked (boiled) Spinach (= 90 grams)	Percent (%) Daily Value*
Energy	Kcalories	7		20	
Protein	Grams	0.86	2%	2.7	5%
Fat	Grams	0.12	<1%	0.23	<1%
Carbohydrate	Grams	1.09	<1%	3.35	<1%
Total Dietary Fiber	Grams	0.7	3%	2.1	8%
Calcium	Milligrams	30	3%	122	12%**
Iron	Milligrams	0.81	4%	3.2	18%**
Magnesium	Milligrams	24	6%	75	19%**
Phosphorus	Milligrams	15	2%	50	5%
Potassium	Milligrams	167	5%	420	42%***
Zinc	Milligrams	0.16	1%	0.7	5%
Vitamin A	IU	1831	36%***	9433	188%***
Vitamin C	Milligrams	8.4	14%**	8.8	15%**
Vitamin E (alpha-tocopherol)	Milligrams	0.61	2%	1.87	6%
Vitamin K (phylloquinone)	Micrograms	144.9	181%***	444.2	555%***
Vitamin B6	Milligrams	0.058	3%	0.218	11%**
Folate	Dietary Folate Equivalents (micrograms)	58	15%**	131.5	33%***

* Daily Values (DVs), developed by the United States Department of Agriculture (USDA), represent the target intake goal for each nutrient (6-7). Percent (%) DV represents the percent of the DV found in a standard serving of each food (6-7).

** A food is considered a "good source" of a nutrient if the food contains 10-19% of the DV (6-7).

*** A food is considered "high" in a nutrient (i.e. an "excellent" source) if it contains more than 20% of the DV (6-7).

Cancer-Fighting Compounds in Spinach

Cancer development and growth involves many steps. Bioactive compounds found in spinach and other plant foods can affect many of these processes in a positive way, and possibly reduce the risk of cancer.

- DNA—the genetic "blueprint" inside nearly all of our cells—damage can result in abnormal cells. When abnormal cells divide, that DNA damage is passed on. Over time, these damaged cells can evolve into cancer. Phytonutrients, vitamins, and minerals can help prevent and repair

DNA damage in cells, thus keeping cells healthy and protecting against cancer development.

- Cell division occurs in phases. Dividing cells rest between these phases, allowing time for the cell to repair any damage. Bioactive compounds, including many phytochemicals, help regulate the cell cycle to allow for more time for repair.
- Cancer cells obtain nutrients and oxygen through their blood supply. Some bioactive compounds in plant foods block blood vessel growth within a tumor, which may help to slow tumor growth by limiting access to nutrients and oxygen.
- Cancer cells are abnormal. Some phytonutrients help the body to recognize cells as being abnormal, and promote their destruction, a process known as apoptosis.
- Free radicals—also called oxidants—are byproducts of energy metabolism. We breathe oxygen, the body uses oxygen to make energy, and free radicals, or oxidants, are created. Some free radical production is normal, however, excess free radical production can damage cells, which may contribute to cancer development. Antioxidants stop free radicals, thus decreasing risk of free radical damage to cells, and protecting against cancer development.
- Inflammation creates an environment in the body friendly to cancer growth. Increased intake of vegetables and fruits reduces inflammation, which is protective against cancer development.

Cancer-Fighting Vitamins and Minerals in Spinach

Some cancer experts refer to it as a “free radical” disease, and note that free radical damage to cells can accumulate with aging. Spinach is a source of antioxidant vitamins (e.g. vitamins C and E), which can help lower cancer risk by controlling levels of free radicals. Spinach is a source of folate as well, a nutrient important for cell division. Population studies following large groups of people have found an association between higher dietary folate intake and lower risk of colorectal cancer. However, it’s important to note that getting this nutrient through supplements, which is a slightly different version of this nutrient called folic acid, may not protect against colorectal cancer. In fact, some studies have suggested getting too much folic acid from dietary supplements may increase colorectal cancer risk. For this reason, food sources of folic acid are the best option for most people. Other spinach nutrients, including vitamin A, B6, and folate, promote a healthy

immune system, which is essential for disease prevention. And magnesium, found in abundance in spinach, is important to hundreds of vital processes in the body, and helps manage inflammation. Not getting enough magnesium has been associated with inflammatory stress, which may increase risk of chronic diseases including some forms of cancer. Over 40% of Americans do not consume recommended amounts of magnesium, and spinach is one of the best dietary sources available.

Cancer-Fighting Phytonutrients in Spinach

Phytonutrients are bioactive compounds found in fruits, vegetables, whole grains, beans, nuts, seeds, tea, coffee, and even herbs and spices. Thousands of phytonutrients have been identified, and researchers believe that many more have yet to be discovered. Phytonutrients infuse vegetables and fruits with many of their cancer-fighting benefits. The ideal amount of most phytonutrients is unknown. However, researchers agree that as fruit and vegetable intake increases, so does phytonutrient intake. Table 2 summarizes phytonutrients in spinach, and their cancer-fighting benefits.

Evidence suggests that nutrients and phytochemicals complement each other, and perhaps work synergistically, which may help explain why studies providing individual bioactive compounds in supplements have failed to show health benefits. Randomized, clinical trials do not support a role for dietary supplements of vitamins, minerals, and phytochemicals for cancer prevention. For example, two widely reported intervention studies examining effects of beta-carotene supplements on prostate cancer risk found either no effect or an increased risk of cancer from beta-carotene in supplement form.

Some studies (though not all) have suggested dietary intake of phytonutrients in spinach and other plant foods are linked with lower risk of colon cancer, breast cancer (particularly Estrogen Receptor (ER) negative), advanced prostate cancer, and esophageal adenocarcinoma. Table 3 summarizes studies suggesting that phytonutrients may help protect against risk of some cancers.

Table 2: Phytochemicals in Spinach

Class of Phytonutrients	Individual Phytonutrients	Cancer-Fighting Benefits
Flavonones	Luteolin	Helps prevent and repair DNA damage, regulates cell cycle (more DNA repair time) Inhibits angiogenesis (blood vessel growth in tumors) Encourages apoptosis (abnormal cell death)
Flavonoids	Kaempferol	Helps prevent and repair DNA damage
	Myricetin	Limits DNA damage by preventing free radical formation (antioxidant activity), Reduces inflammation
	Quercetin	Reduces inflammation Encourages apoptosis (abnormal cell death)
Carotenoids	Beta-carotene	Limits DNA damage by preventing free radical formation (antioxidant activity)
	Lutein	Helps prevent and repair DNA Limits DNA damage by preventing free radical formation (antioxidant activity)
	Zeaxanthin	Inhibits angiogenesis (blood vessel growth in tumors) Encourages apoptosis (abnormal cell death) Limits DNA damage by preventing free radical formation (antioxidant activity)

Table 3: Nutrients/Phytochemicals in Spinach and Cancer Risk

Research Study	Summary of Results
Screening arm of the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial	No association between prostate cancer risk and fruit and vegetable intake. Risk of Stage III and IV prostate cancer decreased with increasing (predominantly cruciferous) vegetable intake. Risk of aggressive prostate cancer decreased as spinach intake increased (not statistically significant).
Case control review: 2000 cases and 2410 controls	Men and women consuming the most lutein were less likely to develop colon cancer compared with people consuming the least lutein. Spinach was found to be a major dietary source of lutein in this case review.
Pooled analysis of eight prospective studies	Women with the highest plasma carotenoid levels had 15-20 percent reduced risk of breast cancer compared with women with the lowest blood levels.
Pooled analysis of NHS, NHS II, and 16 other studies (with ~1 million and 30,000 cases of breast cancer)	Higher intakes of alpha-carotene, beta-carotene, and lutein/zeaxanthin was associated with a significantly lower risk of ER- breast cancer.
Six-year study of 58,000 Dutch men	Dietary intakes of lutein and zeaxanthin were associated with a decreased risk of lung cancer.
National Institutes of Health (NIH)-AARP Diet and Health Study (500,000 participants)	Higher vegetable and fruit intake was associated with lower risk of Esophageal Squamous Cell Cancer (ESCC); fruit was more protective against cancer than vegetables. Higher spinach intake was associated with lower risk of Esophageal Adenocarcinoma..
Case-control study	Eating more quercetin-rich foods (including spinach) was associated with reduced risk of lung cancer in a case-control study in the Lombardi region of Italy.
Case-control study in Sweden with 505 cases of gastric cancer and 1116 controls	People in the highest quintile (top quarter) of quercetin intake had a lower risk of noncardia gastric cancer compared with people in the lowest quintile intake.

Incorporating Spinach in a Diet

Spinach is a good choice for a cancer-fighting diet, which should include a minimum of 2½ cups of vegetables and fruit each day. Popeye may have preferred canned spinach, but over the past decade, consumer demand for fresh spinach has increased, and now accounts for almost 75% of all spinach that we eat. Here are a few of the ways you can get more spinach into your diet.

- Salads
- Side dishes (e.g. steamed and sautéed with garlic and other herbs/spices)
- Dips (combined with artichokes and other veggies)
- Salsa prepared with cooked spinach and combined with commercial salsa
- Quiche and Tarts
- Spanakopita (traditional Greek dish prepared with Spinach and Feta Cheese)
- Spinach Stuffed Salmon or Chicken Breasts
- Soufflés and Omelets
- Lasagna and other casseroles; add it to vegetarian and non-vegetarian lasagnas

Here are a few resources providing tips on additional ways to eat more spinach, and to grow spinach in a home or community garden:

<http://www.ksre.ksu.edu/HumanNutrition/doc16211.ashx>

<http://content.ces.ncsu.edu/spinach/>

<http://www.uaex.edu/publications/PDF/FSA-6077.pdf>

<https://www.udc.edu/docs/causes/online/Spinach%2014.pdf>

Potential Health Concerns About Spinach

There are three main concerns regarding spinach:

1. Does the oxalic acid found in spinach affect nutrient absorption?

Oxalic acid binds to calcium, iron, and other minerals in food, thus reducing their absorption by the body.. Spinach, tea, rhubarb, and parsley are major sources of oxalic acid. Calcium is of particular concern because some vegans rely on spinach and other greens to meet their calcium needs. Calcium absorption from spinach is 5%, as compared to approximately 32% from a similar load of milk, however, calcium absorption from other vegetables is high. For broccoli, 60% of the calcium is absorbed. If a person is consuming large amounts of high oxalate foods and inadequate amounts of calcium, they may need to increase their calcium intake from other sources, or discuss the need for a calcium supplement with their registered dietitian nutritionist (RDN).

2. Can someone taking the blood thinning medication Warfarin (brand name Coumadin) eat spinach?

Coumadin is a blood thinning medication often prescribed for people at increased risk of blood clots and stroke. It works by interfering with vitamin K, which is essential for blood clotting, and this means dietary sources of

vitamin K can influence the activity of Coumadin. The National Institutes of Health (NIH) Clinical Center (CC) Drug-Nutrient Interaction Task Force advises people taking Coumadin to keep their vitamin K intake consistent from day to day. To do that, it is important to keep intake of foods high in vitamin K about the same from day to day. This handout, developed by RDNs and other members of the NIH CC Drug-Nutrient Interaction Task Force, provides dietary guidelines for consuming a consistent vitamin K intake, which will help coumadin work properly.

3. Does fresh spinach pose any food safety risks?

In response to rare salmonella and E. coli outbreaks (in 2006) from fresh spinach, the FDA allows growers to irradiate conventionally grown fresh spinach, but does not require it. The FDA considers this irradiation safe and will not affect the taste of spinach; it has only limited effect on nutrient content. In addition, some states have adopted food safety practices targeted at preventing contamination of leafy greens. The program allows government inspectors to monitor compliance with established food safety practices.

References:

1. Sutton M. Spinach, iron and Popeye: Ironic lessons from biochemistry and history on the importance of healthy eating, healthy skepticism and adequate citation. *Internet Journal of Crimonology*. 2010.
2. Clifford A. Wright.com. A premier source for Italian and Mediterranean food, cooking, food history, and traditional recipes. Accessed 1/15/2015. <http://www.cliffordawright.com/caw/food/entries/display.php/id/15/>
3. U.S. Department of Agriculture, Agricultural Research Service. 2014. USDA National Nutrient Database for Standard Reference, Release 27. Nutrient Data Laboratory Home Page. Accessed 1/10/2015. <http://www.ars.usda.gov/nutrientdata>
4. Gibellini L, Pinti M, Nasi M, et al. Quercetin and cancer chemoprevention. *Evid Based Complement Alternat Med*. 2011;2011:591356.
5. Canterro G, Campanella C, Mateos S, Cortes F. Topoisomerase II inhibition and high yield of endoreduplication induced by the flavonoids luteolin and quercetin. *Mutagenesis*. 2006;21(5):321-325.
6. Ribaya-Mercado JD and Blumberg, JB. Lutein and zeaxanthin and their potential roles in disease prevention. *First International Scientific Symposium on Eggs and Human Health: The Transition from Restrictions to Recommendation*. U.S. Department of Agriculture, Washington, D.C., 2003.
7. Chen AY, Chen YC. A review of the dietary flavonoid, kaempferol on human health and cancer chemoprevention. *Food Chemistry*. 2013;138(4):2099-2107. doi:10.1016/j.foodchem.2012.11.139.

8. Bishayee K, Ghosh S, Mukherjee A, Sadhukhan R, Mondal J, Khuda-Bukhsh AR. Quercetin induces cytochrome-c release and ROS accumulation to promote apoptosis and arrest the cell cycle in G2/M, in cervical carcinoma: signal cascade and drug-DNA interaction. *Cell Prolif.* 2013;46(2):153-163. doi: 10.1111/cpr.12017.
9. Yong L, Shi R, Wang X, Shen H-M. Luteolin, a flavonoid with potentials for cancer prevention and therapy. *Current Cancer Drug Targets.* 2008;8(7):634-646.
10. Wang Z (Wang Z, Dabrosin C, Yin X, et al. Broad targeting of angiogenesis for cancer prevention and therapy. *Semin Cancer Biol.* 2015 Jan 16. pii: S1044-579X(15)00002-4. doi: 10.1016/j.semcancer.2015.01.001. [Epub ahead of print]
11. Thakur VS, Deb G, Babcook MA, Gupta S. Plant phytochemicals as epigenetic modulators: role in cancer chemoprevention. *Am Assoc Pharmaceutical Scientists J.* 2014;16(1):151-163. doi: 10.1208/s12248-013-9548-5.
12. Cheng S, Gao N, Zhang Z, et al. Quercetin induces tumor-selective apoptosis through down-regulation of Mcl-1 and Bax. *Clin Cancer Res.* 2010;16(23):5679-5691. doi: 10.1158/1078-0432.CCR-10-1565.
13. Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: impact on human health. *Pharmacogn Rev.* 2010;4(8):118-126.
14. Sanjoaquin MA, Allen NA, Couto E, Roddam AW, Key TJ. Folate intake and colorectal cancer risk: a meta-analytical approach. *Int J Cancer.* 2005;113(5):825-838.
15. Volpe SL. Magnesium in disease prevention. *Adv Nutr.* 2013;4(3):378S-383S.
16. Agarwal S, Reider C, Brooks JR, Fulgoni VL 3rd. Comparison of prevalence of inadequate nutrient intake based on body weight status of adults in the United States: Ana Analysis of NHANES 2001-2008. *J Am Coll Nutr.* 2015. Jan 7:1-9 (Epub ahead of print).
17. Small E. Top 100 Food Plants: The World's Most Important Culinary Crops. National Research Council Press Canada, 2009;487-488.
18. American Cancer Society. Phytochemicals. Last revised 01/17//2013. Accessed 01/20/2015.
19. Gescher AJ, Steward WP, Brown K. Phytochemicals in Cancer Prevention In Schwab M, ed. *Encyclopedia of Cancer.* Heidelberg: Springer Berlin Heidelberg; 2012:2882-2885. 10.1007/978-3-642-16483-5_4564.
20. González-Vallinas M, González-Castejón M, Arantxa Rodríguez-Casado A, Ramírez de Molina A. Dietary phytochemicals in cancer prevention and therapy: a complementary approach with promising perspectives. *Nutr Rev.* 2013;71(9):585-599.
21. Shankar S, Kumar D, Srivastata RK. Epigenetic modifications by dietary phytochemicals: implications for personalized nutriyiton. *Pharmacol Ther.* April 2013;138(1):1-17.
22. Rajendran P, Ho E, Williams ED, Dashwood RH. Dietary phytochemicals, HDAC inhibition, and DNA damage/repair defects in cancer cells. *Clin Epigenetics.* 2011;3(1):4.

23. Heinonen OP and Koss L. Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: incidence and mortality in a controlled trial. *J Natl Cancer Inst.* 1998;90(6):440-446.
24. Ohno Y, Yoshida O, Oishi K, Okada K, Yamabe H, Schroeder FH. Dietary beta-carotene and cancer of the prostate: a case-control study in Kyoto, Japan. *Cancer Res.* 1988;48(5):1331-1336.
25. Kirsh VA, Peters U, Mayne ST, Subar AF, Chatterjee N, Johnson CC, Hayes RB. Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. Prospective study of fruit and vegetable intake and risk of prostate cancer. *J Natl Cancer Inst.* 2007;99(15):1200-1209.
26. Slattery ML, Benson J, Curtin K, Ma KN, Schaeffer D, Potter JD. Carotenoids and colon cancer. *Am J Clin Nutr.* 2000;71(2):575-582.
27. Eliassen AH, Hendrickson SJ, Brinton LA, et al. Circulating carotenoids and risk of breast cancer: pooled analysis of eight prospective studies. *J Natl Cancer Inst.* 2012;104(24):1905-1916.
28. Zhang X, Spiegelman D, Baglietto L, et al. Carotenoid intakes and risk of breast cancer defined by estrogen receptor and progesterone receptor status: a pooled analysis of 18 prospective cohort studies. *Am J Clin Nutr.* 2012;95(3):713-725.
29. Voorrips LE, Goldbohm A, Brants HAM, et al. A prospective cohort study on antioxidant and folate intake and male lung cancer risk. *Cancer Epidemiol Biomarkers Prev.* 2000;9(4):357-365.
30. Freedman N, Park Y, Subar AF, et al. Fruit and vegetable intake and esophageal cancer in a large prospective cohort study. *Int J Cancer.* 2007;121(12):2753-2760.
31. Lam TK, Ruczinski I, Helzlsouer KJ, Shugart YY, Caulfield LE, Alberg AJ. Cruciferous vegetable intake and lung cancer risk: a nested case control study matched on cigarette smoking. *Cancer Epi Bio Prev.* 2010;19(10):2545-2540. doi: 10.1158/1055-9965
32. Ekstrom AM, Serafini M, Nyren O, Wolk A, Bosetti C, Bellocco R. Dietary quercetin intake and risk of gastric cancer: results from a population-based study in Sweden. *Ann Oncol.* 2011;22(2):438-443.
33. Borris H and Kreith, Agricultural Issues Center, University of California (updated June 2013 by Diane Huntrods). AgMRC, Iowa State University. Agricultural Marketing Resource Center. http://www.agmrc.org/commodities_products/vegetables/spinach-profile/ Created February 2006 and updated June 2013. Accessed 1/20/2015.
34. Weaver CM and Heaney RP. Food Sources, Supplements, and Bioavailability in Weaver CM and Heaney RP, eds. *Calcium in Human Health.* New Jersey: Humana Press; 2006:135.
35. Weaver CM and Proulx W. Choices for achieving adequate dietary calcium with a vegetarian diet. *Am J Clin Nutr.* 1999;70(suppl):543S-548S.

36. National Institutes of Health (NIH) Clinical Center (CC) Drug-Nutrient Interaction Task Force. Warfarin and Vitamin K. Revised 2012. Accessed 1/20/2015.

37. U.S. Food and Drug Administration. Irradiation: A Safe Measure for Safer Iceberg Lettuce and Spinach. Last Updated 10/7/2014. Accessed 1/15/2015.
<http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm093651.htm>

38. Leafy Greens Marketing Agreement. www.lgma.org. Copyright 2014. Accessed 1/10/2015.

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