Skin Cancer and Nutrition  
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The largest organ in the human body, skin serves as an outer layer of protection, defending the body against light, extreme heat or cold, injury, and infection and also regulating water and lipid stores and body temperature. Both external influences (eg, sun exposure) and internal influences (eg, an individual’s nutritional status) can compromise the skin’s ability to perform these functions and can lead to cutaneous diseases such as skin cancer, or the abnormal growth of skin cells. Skin cancer is the most common form of cancer in the United States, affecting nearly one in five Americans. In recent years, skin cancer has been diagnosed more than all other types of cancers combined.¹

Basal cell carcinoma (BCC), the most common type of skin cancer, rarely is fatal. Basal cells are located beneath squamous cells and are responsible for the production of new skin cells.

Actinic keratosis is a common precancerous scaly growth or lesion that strongly predicts all major types of skin cancer, with nearly 10% of actinic keratoses leading to squamous cell carcinoma (SCC). SCC is the second most common type of skin cancer.² Squamous cells lie just below the skin’s surface (epidermis) and function as its inner lining. Fortunately, there was a 98% survival rate among SCC patients in the United States in 2012.¹

Melanocytes are located in the lower part of the epidermis and produce the pigments that give skin its unique color. Cancer of melanocytes, or melanoma, is the rarest type of skin cancer, accounting for less than 5% of all cases, but it’s also the most dangerous and most fatal.¹ If detected early, the survival rate for melanoma is 98%, but once it metastasizes or spreads to the lymph nodes, the survival rate drops to 62%.¹ The average age at which melanoma is diagnosed is 63 for men and 56 for women.³

From an economic standpoint, skin cancer costs American taxpayers millions in health care dollars. In 2008, allowable charges paid to physicians by Medicare Part B for skin cancer treatment was nearly $633 million, a 137% increase from 1996.⁴

There are several well-established risk factors for skin cancer. The disease is more prevalent in individuals who have fair skin, light eyes, or light hair, possibly because their skin contains less melanin (color pigmentation), which serves as a protective layer from ultraviolet (UV) radiation. Other risk factors include having a family history of skin cancer; having a history of
erythema (sunburns); living in sunny, warm climates or at higher elevations where UV rays are the strongest; and having abnormal moles, called dysplastic nevi, that are irregular in shape and larger than regular moles.

One of the most prominent risk factors for skin cancer is excessive sun or UV exposure. UV radiation can induce premature aging and DNA damage and can act as a tumor initiator to the skin. Nearly 90% of nonmelanoma skin cancers are associated with exposure to UV radiation from the sun.

One of the lesser-known methods for potentially lowering skin cancer risk is diet. There’s promising evidence that dietary interventions may benefit individuals who are at high risk of skin carcinoma.

**Plant-Based Diet**
A plant-based diet rich in antioxidants has been associated with a reduced risk of many types of cancers, such as those of the lung, mouth, throat, stomach, and colon. For other types of cancers, evidence is limited or inconsistent.

Unfortunately, the majority of Americans don’t consume adequate amounts of fruits and vegetables. In fact, only 14.8% to 19.1% of skin cancer survivors are meeting the American Cancer Society’s recommendation to consume at least five servings (or 2 1/2 cups) of fruits and vegetables each day.

Because of this deficiency, vitamin and mineral supplementation may seem like a viable alternative. However, the American Cancer Society also recommends choosing whole foods over dietary supplements since there are many still-unidentified components of fruits and vegetables that haven’t been condensed into pill form.

Table 1 lists some antioxidants and their food sources.
In a 10-year prospective study, subjects who consumed the highest percentage of fruits and vegetables had a 54% reduced risk of SCC. In particular, eating green leafy vegetables was associated with decreased risk. However, the study found that no dietary pattern was associated with BCC tumors.\(^8\)

Another study asked patients who were newly diagnosed with melanoma to complete a food frequency questionnaire. High intake of the following micronutrients was associated with a significantly reduced risk of melanoma compared with low intake: vitamins C and D, retinol (vitamin A), alpha- and beta-carotene, cryptoxanthin, lutein, and lycopene. Compared with the lowest tertiles, high daily intake of the following food groups were associated with a significantly reduced risk of melanoma:\(^9\)

- Fruits/fruit juices: 1.6 or more servings;
- Vegetables: 1.1 or more servings;
- Fruits and vegetables combined: 2.1 or more servings;

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<table>
<thead>
<tr>
<th>TYPES OF ANTIOXIDANTS</th>
<th>FOOD SOURCES</th>
</tr>
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<tbody>
<tr>
<td>Vitamin C</td>
<td>Citrus fruits, tomatoes, melons, peppers, greens, guava, strawberries, pineapple, potatoes, kiwis</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Wheat germ, vegetable oils, green leafy vegetables, egg yolks, milk fat, nuts</td>
</tr>
<tr>
<td>Zinc</td>
<td>Oysters, shellfish, herring, liver, legumes</td>
</tr>
<tr>
<td>Selenium</td>
<td>Grains, onions, meats, milk, vegetable oils (For vegetables, and vegetable oils, this depends on the selenium content of the soil.)</td>
</tr>
<tr>
<td>Carotenoids</td>
<td>Tomatoes and tomato products, carrots, butternut squash, cantaloupe, green vegetables, kale, spinach, corn, eggs, watermelon, grapefruit, avocado, honeydew</td>
</tr>
<tr>
<td>Phenolic acids</td>
<td>Apples, pears, citrus fruits, parsley, carrots, broccoli, cabbages, cucumber, squash, yams, tomatoes, cocoa, cinnamon, peanuts and peanut skins, wine, grapes</td>
</tr>
<tr>
<td>Flavonoids</td>
<td>Dark-colored berries, cherries, red grapes, green tea, cocoa, coffee, onions, apples</td>
</tr>
</tbody>
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- Citrus fruits and juices: 0.6 or more servings;
- Dark green/yellow fruits and vegetables: 0.5 or more servings; and
- Fish: 0.3 or more servings.

In another study, regular consumption (three or more servings per week) of celeriac and pomegranates was associated with a significantly reduced risk of BCC and SCC. Celeriac, more commonly known as celery root, also was associated with a significantly reduced risk of melanoma. Parsnips, red wine, and red berries, however, were associated with an increased risk of melanoma. These results were adjusted for age, sex, skin reaction to the sun, and country of origin.\textsuperscript{10}

Antioxidants found in fruits and vegetables function by eliminating free radicals and reactive oxygen species that can attack DNA and lead to diseases. Vitamins C and E are abundant nutrients in plants that act as antioxidants and may help protect against skin cancer. Vitamin C scavenges free radicals and restores the activity of other antioxidants, enhances the immune system, and hydroxylates lysine and proline in the synthesis of connective tissues proteins, which may alter tumor growth. Vitamin E is an intracellular antioxidant that prevents lipid peroxidation.\textsuperscript{11}

**Plant Components**

**Vitamin A**

Due to its antioxidant properties, vitamin A is sometimes referred to as the “oral skin protectant.” It’s a fat-soluble vitamin that can be consumed in the form of retinols from animal products such as eggs, milk, and liver as well as from plants in the form of alpha- and beta-carotene. Beta-carotene is efficiently converted into retinol, whereas only one-half of alpha-carotene is converted into retinol.

Vitamin A performs many important biological functions, including those involved with vision, reproduction, and immune regulation. Vitamin A also is essential in skin cell proliferation, differentiation, and maintenance and may decrease the amount of UV light that reaches the underlying layers of the skin by increasing epidermal thickness.\textsuperscript{3}

Carotenoid consumption through food and supplements has been shown to decrease the risk of skin cancer. In one study, subjects consumed a 25-mg carotenoid supplement or the same carotenoid supplement plus alpha-tocopherol (vitamin E) daily for 12 weeks. UV light irradiation was used to induce erythema in a small area of the skin. Erythema is redness of the skin and is commonly used in scientific studies as an indicator of sunburn reaction. Researchers found that erythema induced by UV light was significantly reduced in both treatment groups compared with the placebo group, with the greatest photoprotective effect found in the combination of carotenoids plus alpha-tocopherol.\textsuperscript{12}
In a similar study, supplementation with 24 mg of beta-carotene or 24 mg of a mixture of carotenoids daily for 12 weeks were both shown to have photoprotective effects by decreasing UV-induced erythema in human skin, providing protection against exposure to UV radiation.\textsuperscript{13}

In contrast, some studies in which subjects were given carotenoid supplements resulted in no differences in carotenoid-dependent protection against UV radiation.\textsuperscript{14-16}

Lycopene is the major carotenoid in tomatoes and tomato products. It acts as an antioxidant against photo-oxidative stress. Lycopene is more bioavailable from tomato products than from tomato juice or fresh tomatoes. In a study by Stahl and colleagues, nine subjects consumed 40 g of tomato paste for 10 weeks; the paste contained about 16 g of lycopene, 0.5 mg of beta-carotene, and 0.1 mg of lutein. Results found that tomato paste consumption significantly decreased erythema formation by 40% at 10 weeks compared with controls.\textsuperscript{17}

A double-blind, placebo-controlled study found supplementation with retinol (25,000 IU) significantly reduced the incidence of SCC but not BCC.\textsuperscript{18} However, a large prospective study found no association with melanoma and dietary carotenoid or retinol intake through food or the combination of supplement and dietary intake.\textsuperscript{19}

One potential mechanism by which carotenoids may inhibit skin carcinogenesis is their antioxidant abilities; beta-carotene enhances immune system functioning, while provitamin A carotenoids may prevent skin cancer through its conversion to retinoids.\textsuperscript{11} However, there are some concerns about the safety of extremely high doses of carotenoid supplementation due to the results of the Beta-Carotene and Retinol Efficacy Trial, which revealed increased lung cancer incidence and mortality among smokers consuming supplemental beta-carotene. Authors suspect high doses of beta-carotene can act as pro-oxidants and result in secondary reactive oxygen species.\textsuperscript{20}

\textbf{Flavonoids}

Flavonoids are naturally occurring compounds found in fruits and vegetables as well as cocoa, tea, and red wine. More than 5,000 types of flavonoids have been identified and are commonly classified into the following subgroups: anthoxanthins (flavones and flavonols), flavanones, flavanonols, flavanols, and anthocyanidins. These compounds have been found to have antioxidant properties that may be beneficial in the prevention of many types of cancers.

\textbf{Quercetin}

Quercetin, a common flavonoid found in fruits and vegetables such as onions, kale, and broccoli, has many antioxidant and anticarcinogenic properties. In one study, mice fed a quercetin-rich diet had delayed skin tumor development, reduced skin tumor growth, and decreased tumor number and size. Scientists attribute these results to quercetin-fed mice having suppressed insulin-like growth factor-1 (IGF-1) signaling, a protein that regulates cell proliferation, growth, and apoptosis.\textsuperscript{21}
**Apigenin**
Apigenin is a flavone that naturally occurs in fruits such as oranges and grapefruits; vegetables such as onions; herbs such as parsley, chamomile, and wheat sprouts; some seasonings; and plant-based drinks such as tea. Studies have shown that apigenin is effective in reducing skin carcinogenesis by suppressing cyclooxygenase-2 (COX-2) expression and mRNA in mouse and human skin lines. COX-2 is a key enzyme in which overexpression results in carcinogenesis.\(^\text{22}\)

**Flavanols**
In one study, a group of women drank a high flavanol drink made from cocoa powder (326 mg of total flavanols, mostly epicatechin and catechins), comparable to about 100 g of dark chocolate, while another group drank a low flavanol drink (27 mg). After a small area of skin was exposed to UV light, results found that the high-flavanol group had significantly decreased erythema: 15% after six weeks of treatment and 25% after 12 weeks of treatment. This may indicate that the flavanols found in small amounts of cocoa and dark chocolate may reduce the severity of a sunburn and thus could reduce the risk of skin cancer development. However, this was a small study with only 12 subjects in each treatment group.\(^\text{23}\)

**Mediterranean Diet**
The Mediterranean diet, which refers to the dietary patterns of European societies located near the Mediterranean Sea and traditionally consists of fruits, vegetables, fish, olive oil, wine, and fresh herbs, has been shown to lower the risk of overall mortality. For every two-point increase in the score of adherence to a Mediterranean diet, the relative risk of overall mortality decreases by 8%.\(^\text{24}\) However, there have been only a limited number of scientific studies regarding the association between the Mediterranean diet and skin cancer risk.

In one case-control study in a hospital in Rome, 304 patients newly diagnosed with melanoma and 305 control subjects were asked to complete a food frequency questionnaire. After controlling for several confounding factors, such as medical history, sun exposure, and skin pigmentation, results showed that those who consumed a typical Mediterranean diet had a lower incidence of melanoma. Consuming fruits, vegetables, tea, fish, shellfish, and fish rich in omega-3 fatty acids was found to have a protective effect. Fish rich in omega-3 fatty acids include sardines, anchovies, tuna, and salmon. The consumption of cooked vegetables (more than five times per week), cruciferous vegetables (more than three times per week), green leafy vegetables (three times per week), fruits (more than once daily), citrus fruits (more than five times per week), and the use of fresh herbs (four or more regularly) was significantly associated with a decreased risk of melanoma.\(^\text{25}\)
Fat and Red Meat
Many epidemiologic studies have suggested that excessive consumption of red and processed meats is associated with an increased incidence of cancer and risk of all-cause mortality. Processed meats include bacon, sausage, luncheon meats, and hot dogs, and red meats include beef, pork, and lamb. Meat can contain several carcinogens that may raise cancer risk, including heterocyclic amines, polycyclic aromatic hydrocarbons (produced by high temperate/charcoal cooking), and nitrates and nitrites (used as preservatives).  

A high-fat diet has been shown to contribute to oxidative stress, DNA damage, increased inflammatory cytokines in the skin, and decreased cell apoptosis. A high-fat diet may enhance skin carcinogenesis by influencing the composition of cell membrane lipids and intercellular communication.  

There’s suggestive evidence that a high-fat diet and high intakes of red meat and processed meats are associated with skin cancer. One study showed a trend, though not statistically significant, for melanoma with increasing consumption of total fat as a percent of calories and a significant trend for melanoma with increasing consumption of saturated fat and linoleic acid as a percent of calories.  

In a 10-year prospective study, higher consumption of meat and fat was associated with a significantly greater risk of developing SCC. The meat and fat food groups included red meats, processed meats, discretionary fat (habitual consumption of fried foods and visible fat on meat), processed grains, junk food snacks, sweet drinks, and high-fat dairy products. In particular, the consumption of high-fat dairy was associated with an increased risk of SCC. Several studies have shown that dairy consumption is positively associated with increased IGF-1 expression, which may induce SCC. The risk ratio of developing SCC, after adjustment for multiple variables, from the lowest, median, and highest tertile groups of high-fat dairy was 1, 1.84, and 2.38, respectively. However, a case-control study found no association of skin cancer with the consumption of meat, cheese, butter, eggs, or milk.  

A longitudinal study demonstrated that individuals who consumed the highest amounts of eggs and pizza had a 45% and 37% increased risk of actinic keratoses, respectively.  

To investigate nutritional counseling regarding the effects of a low-fat diet on skin cancer risk, more than 48,000 postmenopausal women were randomized to a control or dietary intervention group. The dietary intervention included several educational sessions in which nutritionists educated subjects on how to decrease total fat intake to less than 20% of total calories, consume five or more daily servings of vegetables, and consume six or more daily servings of grains.  

After an eight-year follow-up, there were no differences in the incidence of melanoma or nonmelanoma skin cancer between the two groups of women. Even after sensitivity analysis,
in which participants who may not have fully complied with the trial requirements were excluded, there still was no association between the low-fat intervention and skin cancer risk.\textsuperscript{28}

In another study, a significantly lower risk of nonmelanoma skin cancer was found in the intervention group following a diet consisting of 21\% of calories from fat. The groups successfully maintained the low-fat diet throughout the two-year study. The dietary intervention included weekly and monthly classes in which a dietitian educated subjects about decreasing fat intake by modifying recipes and food preparation techniques, choosing low-fat food options, increasing complex carbohydrates, and increasing fruit and vegetable intake. Because of this increase in fruit and vegetable consumption, dietary analysis revealed vitamin C, beta-carotene, and fiber intake was significantly higher in the intervention group compared with control subjects.\textsuperscript{29} However, maintaining total fat consumption of less than 20\% of calories may be difficult since Americans typically consume an average of 34\% of calories from fat.\textsuperscript{30}

\textbf{Omega-3 Fatty Acids}

There’s strong evidence that omega-3 polyunsaturated fatty acids (PUFAs), more specifically the ratio between omega-3 and omega-6 fatty acids, have a protective effect on overall cancer risk. The primary omega-3 fatty acids include EPA (20:5-n3) and DHA (22:6-n3). Omega-3 fatty acids commonly are found in fatty fish such as salmon and mackerel, and the USDA recommends consuming about two servings of fish per week, with an emphasis on fatty fish.\textsuperscript{30}

In a longitudinal study, individuals who consumed the highest amounts of oily fish (one serving every five days) had a 28\% lower risk of actinic keratosis.\textsuperscript{27} In a meta-analysis of five research studies, dietary omega-3 consumption wasn’t associated with BCC.\textsuperscript{31} High levels of omega-3 PUFAs were inversely associated with SCC, but the association wasn’t statistically significant.\textsuperscript{31} However, Fortes and colleagues found the consumption of fish, shellfish, and fish rich in omega-3 fatty acids was significantly associated with a decreased risk of melanoma.\textsuperscript{25}

In a population, case-control study in Arizona, there was a trend of lower SCC risk with higher omega-3 fatty acid intake but no significant associations between SCC and total energy, fat, and cholesterol intake. There also was a consistent pattern for lower SCC risk with increasing intakes of EPA, DHA, and arachidonic acid, but these results weren’t statistically significant. The protective effect against SCC also was found with increasing omega-3 to omega-6 ratios.\textsuperscript{32}

In a small study of 20 subjects, 4 g/day of fish oil supplementation (containing 2.8 g of EPA and 1.2 g of DHA) for four weeks was associated with a small but statistically significant increase in minimal erythema dose compared with a placebo. Minimal erythema dose is known as the minimum amount of UV exposure that produces sunburn.\textsuperscript{33}

Potential mechanisms by which omega-3 fatty acids may prevent skin carcinogenesis include COX-2 inhibition (high levels are found during inflammation), prostaglandin synthesis
deregulation, membrane fluidity alterations, transcription factor activation, and oxidative stress modulation.25,34

Coffee and Caffeine
In one study, caffeine intake from all dietary sources was inversely associated with BCC risk but not SCC or melanoma risk. After adjusting for multiple variables, individuals who drank more than three cups of coffee per day had the lowest risk of BCC compared with individuals who drank less than one cup per month. The consumption of caffeinated coffee (100 mg/day) was associated with a decreased risk of BCC, but decaffeinated coffee didn’t have this effect. Caffeine (100 mg/day) from other dietary sources, such as tea, cola, and chocolate, wasn’t significantly associated with a decreased risk of BCC. The authors suggested that caffeine might promote elimination of UV-damaged keratinocytes via apoptosis.35

In a study of more than 50,000 individuals, coffee consumption was associated with a decreased risk of melanoma in women but not in men.36 A 36% decrease in nonmelanoma skin cancer was found in women who drank six or more cups of coffee per day compared with nondrinkers.37

In a population from the southwestern United States, no association was found between tea consumption and SCC. However, adjusted odds ratios for hot tea and iced black tea were 0.63 and 1.02, respectively. After adjustment for brewing time, a significant association was found for hot tea consumption and a decreased risk of skin SCC compared with nontea drinkers.38

In a rodent study, the administration of green tea and caffeine has been found to inhibit UVB-induced carcinogenesis in mice. The cancer-preventing caffeine doses in mice were considered equivalent to two to five cups of coffee per day in humans. Green tea, caffeinated coffee, and a caffeine solution, but not decaffeinated green tea, significantly increased apoptosis of the UVB-treated skin.39

Alcohol
While moderate alcohol consumption has been associated with a lower risk of cardiovascular disease, heavy or excessive drinking has been well established as increasing the risk of mouth, throat, liver, colon, and female breast cancers.7 Heavy drinking for women is defined as more than three drinks per day or more than seven per week, and for men is more than four drinks per day or 14 per week.30

There have been mixed results regarding alcohol consumption and skin cancer. In one study, the risk of melanoma was significantly increased in those who consumed 1.4 or more alcoholic drinks per week compared with nondrinkers.9 On the other hand, in a population, case-control study of men from Montreal, Canada, no significant association was found between excessive alcohol consumption and melanoma risk. Interestingly, of the men with melanoma, 31.8% reported drinking one to six alcoholic beverages per week, and 48.6% reported drinking seven
or more per week.\textsuperscript{40} Another study found that regular alcohol use was associated with a significantly increased risk of BCC and melanoma but not of SCC.\textsuperscript{10}

On the other hand, it also has been suggested that individuals who consumed the highest amounts of wine had a 27\% decrease in actinic keratoses compared with the lowest consumers. The highest consumers drank an average of one half-glass of wine every day. There was no association with beer or spirits consumption with actinic keratoses.\textsuperscript{27}

In a large Danish study of more than 50,000 people, there was no association between cumulative alcohol intake and the risk of SCC and BCC, but the specific type of alcoholic beverage did appear to play a role. A dose-responsive effect for wine and spirits was found to be associated with BCC, whereas beer consumption was found to be inversely associated with BCC. The authors concluded that alcohol may promote skin cancer by interfering with normal DNA replication and mitosis in the skin, altering oncogenes and tumor-suppressor genes, inducing skin inflammation, and enhancing the accumulation of UV-damaged cell DNA and mutations. In addition, the by-product of ethanol metabolism, acetaldehyde, is believed to be carcinogenic.\textsuperscript{41}

**Practice Applications**

For clients and patients who want to protect themselves from harmful UV rays, it’s important to emphasize environmental protection from the sun, such as using sunscreen and wearing protective clothing. However, a secondary line of defense from the sun’s harmful UV rays may be diet related.

Research shows dietary factors may play a role in the prevention of skin cancer in both rodents and humans. However, the results of these research studies are mixed and conflicting. A plant-based diet rich in fruits and vegetables and low in fat has shown promising results in altering skin cancer development. The American Cancer Society recommends consuming at least five servings of fruits and vegetables per day for overall cancer prevention. Dietitians can recommend that clients and patients increase their intake of the foods listed in Table 2 and also suggest decreasing fat intake to less than 20\% of calories.
Another beneficial strategy for dietitians is to have clients and patients keep a food diary or complete a food frequency questionnaire. If certain nutrients through food sources are lacking, such as vitamin A and omega-3s, clients and patients may want to consider supplementation, and dietitians can provide guidance.

The dietary strategies with implications in skin cancer prevention also are conducive to an overall healthful lifestyle. A diet high in fruits and vegetables and low in fat may prevent other types of cancers and chronic diseases such as obesity, heart disease, and diabetes, and therefore have an added benefit above skin cancer prevention.

—Mary Rodavich, MS, RD, LDN, is a clinical dietitian and freelance writer based in Pittsburgh.
References


Examination

1. What is the most fatal type of skin cancer?
   A. Actinic keratosis
   B. Squamous cell
   C. Basal cell
   D. Melanoma

2. Which of the following is a major risk factor for skin cancer?
   A. Living at lower elevations
   B. Dark skin, eyes, and hair
   C. Younger age
   D. Excessive sun exposure

3. Skin cancer is the most common form of cancer in the United States.
   A. True
   B. False

4. The American Cancer Society recommends at least how many servings of fruits and
   vegetables per day for cancer prevention?
   A. Three
   B. Four
   C. Five
   D. Six

5. In a case-control study of the Mediterranean diet, which food (or foods) didn't protect
   against skin cancer?
   A. Fatty fish
   B. Meat, eggs, and milk
   C. Fruits and vegetables
   D. Fresh herbs

6. A low-fat diet may increase the risk of skin cancer because it may contain several
   carcinogens and has been shown to contribute to oxidative stress, DNA damage,
   increased inflammatory cytokines in the skin, and decreased cell apoptosis.
   A. True
   B. False

7. For skin cancer prevention, research has suggested that fat should be limited to less
   than what percentage of calories?
   A. 15
   B. 20
   C. 25
   D. 30
8. What component of tomatoes positively affects skin cancer risk?
A. Lycopene  
B. Vitamin A  
C. Vitamin C  
D. Zinc

9. Which of the following foods has been associated with an increased risk of skin cancer?
A. Citrus fruits  
B. Alcohol  
C. Green leafy vegetables  
D. Caffeinated coffee

10. Antioxidants found in fruits and vegetables function by eliminating free radicals and reactive oxygen species.
A. True  
B. False