SPOTLIGHT D

# Dietary Supplements

## LEARNING OBJECTIVES

- Identify the types of products or substances that might be classified as dietary supplements **(Infographic D.1)**
- Identify at least three situations or conditions for which specific supplementation may be warranted **(Infographic D.2)**
- Provide an overview of the regulatory policies in the United States for dietary supplements compared with those for prescription or conventional drugs **(Infographic D.3)**
- Describe the type of information provided on a Supplement Facts Panel **(Infographic D.4)**
- Describe how approved health claims differ from structure/function claims for dietary supplements, and provide at least two examples of each **(Infographic D.5 and Infographic D.6)**
- Identify at least three considerations before choosing a multivitamin supplement **(Infographic D.7 and Infographic D.8)**
- Provide an example of an herbal supplement, and explain its possible benefits and adverse effects **(Infographic D.9)**
- Describe what might make a food or dietary constituent "functional" and how these foods might affect health, dietary quality, and overall nutrient intake **(Infographic D.10)**

Gilbert Omenn swallowed hard. It was April 1993, and he had just been called into an emergency breakfast meeting with two scientists from the National Cancer Institute (NCI), a division of the United States National Institutes of Health. "We have a very serious problem. We would like to tell you all about it," the NCI scientists told Omenn, who at the time was Dean of the University of Washington's School of Public

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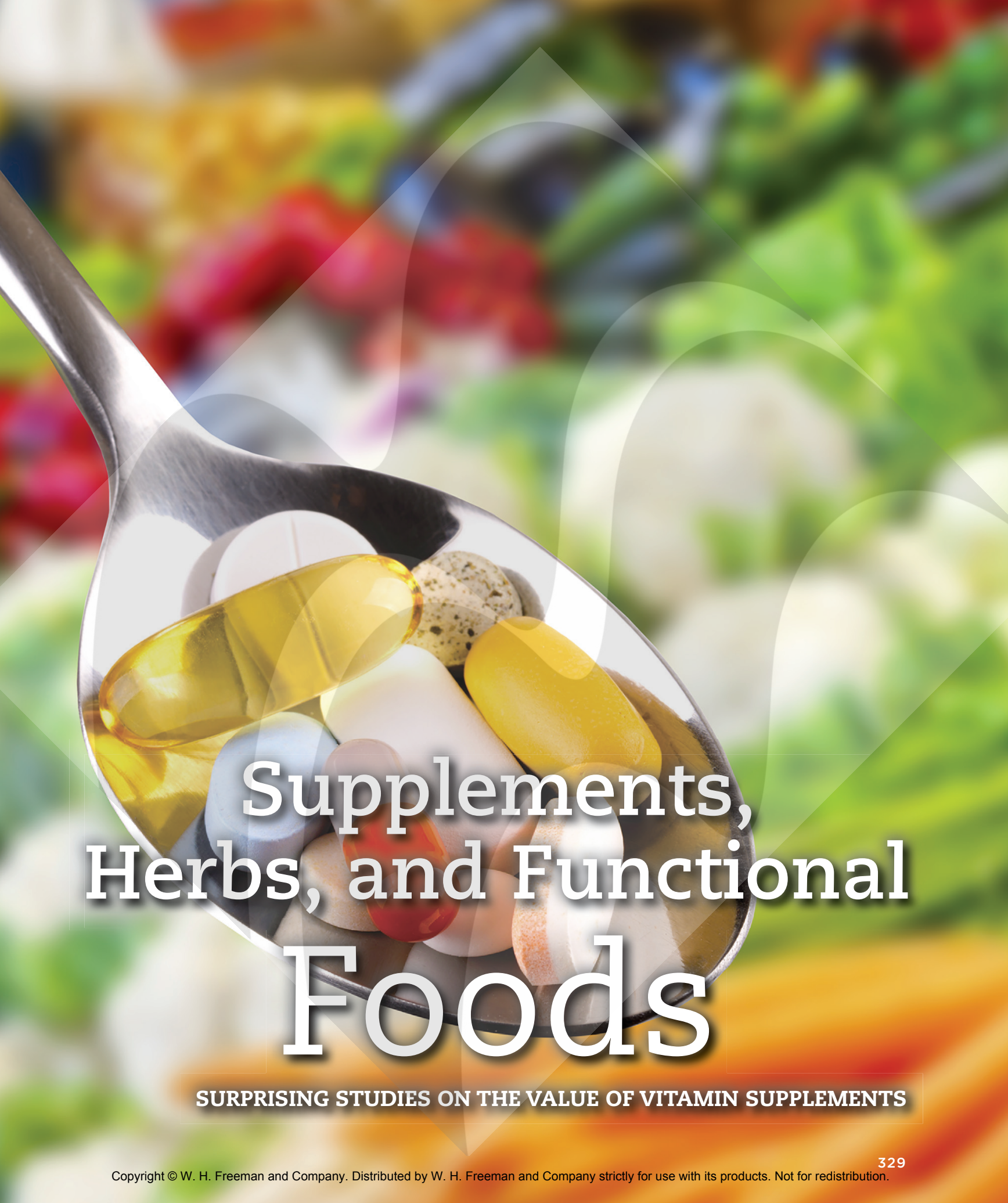
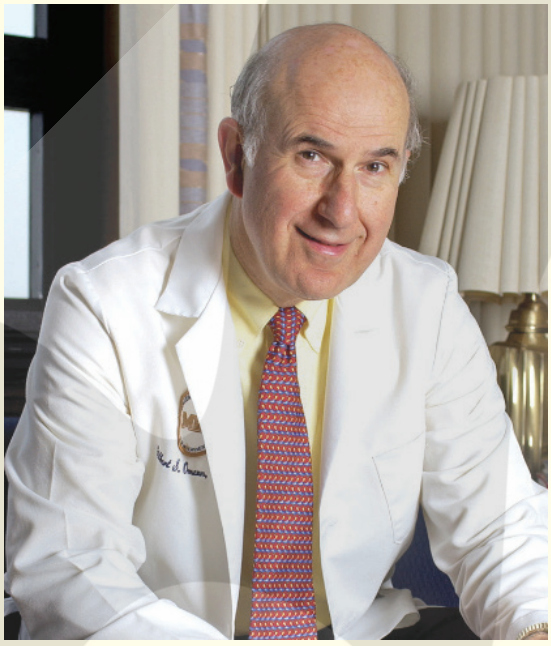


# Supplements, Herbs, and Functional Foods

## SURPRISING STUDIES ON THE VALUE OF VITAMIN SUPPLEMENTS

***Gilbert Omenn, Professor of Internal Medicine, Human Genetics, and Public Health at the University of Michigan.*** *Omenn was principal investigator of the Beta-Carotene and Retinol Efficacy Trial (CARET), which explored potential lung cancer and heart disease preventatives.*



Gilbert Omenn, M.D., Ph.D

Health and Community Medicine. "On one critical condition: You must not tell anybody else."

Omenn didn't like secrets, but he agreed—not least because he wanted to know if their concerns had anything to do with the large NCI-funded clinical trial he was leading called Beta-Carotene and Retinol Efficacy Trial (CARET). He was testing whether large doses of beta-carotene in addition to vitamin A could prevent lung cancer in more than 18,000 people who currently smoked, had smoked in the past, or had been exposed to asbestos. As it turned out, the NCI scientists were worried about a different ongoing antioxidant trial being conducted by researchers at the NCI and in Finland. The scientists pulled out some of the preliminary Finnish trial data and laid it out in front of him.

Omenn was looking at the lung cancer rates of people in the Finnish trial who had taken beta-carotene in addition to either vitamin E supplements or sugar pills. "What it showed was a difference in cancer incidence in the two treatment groups of the study that received beta-carotene, starting a year or two after the beginning, getting bigger and bigger," Omenn recalls. That made sense: Beta-carotene was probably preventing cancer, but the placebo wasn't. But when Omenn saw the data labels, he froze. The study participants who were developing cancer were the ones taking the beta-carotene—not the ones taking placebos.

"This was a big shock," Omenn recalled—so much so that he didn't believe it. The labels must have been switched accidentally, he said. The NCI scientists assured him that they hadn't.

In closed meetings that Omenn attended over the course of the next few weeks, the cancer agency confirmed that beta-carotene had increased lung cancer risk by 18% compared with the placebo in the Finnish trial, although vitamin E seemed to have no effect. All the while Omenn's own trial continued. A year later, in late spring 1994, the NCI gave Omenn the green light to tell his colleagues and his 18,314 trial participants about the Finnish findings. Only 606 of his participants chose to drop out of the study. By January 1996, Omenn had enough data to crunch numbers, and what he discovered was distressing: The combination of beta-carotene and vitamin A was increasing his participants' risk of lung cancer by a whopping 28% compared with sugar pills. For the safety of everyone enrolled, Omenn immediately stopped the trial, 21 months ahead of schedule. Looked at another way, Omenn's results, which were published in the *Journal of the National Cancer Institute* later that year, suggested that the people had a 1 in 1000 increased chance of developing cancer each year as a direct result of taking the beta-carotene /vitamin A supplements.

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Chances are if you opened the medicine cabinet in your bathroom or the cabinets in your kitchen, you would find a multivitamin mineral supplement bottle or a nutritional supplement drink powder or perhaps a

***Does vitamin A supplementation prevent cancer?*** *Observational studies had shown that people eating more fruits and vegetables, which are rich in beta-carotene (that the body can convert into retinol, or vitamin A), had lower rates of lung cancer. The Beta-Carotene and Retinol Efficacy Trial (CARET) tested the combination of beta-carotene and vitamin A supplements in men and women at high risk of developing lung cancer. The CARET intervention was stopped 21 months early because of clear evidence of no benefit and substantial evidence of possible harm.*


StockImages/Alamy

protein energy bar of some sort. *Dietary supplements* are a more than a $35 billion a year industry, more than 65,000 varieties are sold in the United States today, and more than half of all Americans take supplements in an attempt to stay healthy or prevent disease. Globally, it is estimated that the growing supplement market will exceed 200 billion in U.S. dollars by 2022. The most common supplements are multivitamin mineral supplements, followed by vitamin D, calcium, omega-3 fatty acid supplements (fish oil), and vitamin C. Yet fewer than a quarter of Americans who take supplements do so at the recommendation of a qualified health-care provider.

Supplements can be beneficial for some individuals, particularly those who cannot meet their nutritional requirements because of disease, increased need, or restricted diets. But many people take supplements despite

***Dietary supplements are a big business in the United States.*** *According to NHANES data, the percentage of the U.S. population who used at least one dietary supplement increased from 42% in 1988–1994 to 52% in 2011–2012.*

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**DIETARY SUPPLEMENT**
*a food or substance that supplements the diet and contains one or more dietary ingredients (including vitamins, minerals, herbs, amino acids, and certain other substances) or their constituents*

the fact that they are already in good health and likely get adequate nutrients through their diet. Women are more likely to take supplements to keep their bones healthy, whereas men tend to pop pills in the hope of preventing heart problems. But do these supplements actually help? A growing body of research, including the results of those National Cancer Institute trials from the 1990s, suggests that supplementation with single vitamins or other dietary components, especially in amounts above recommended intake levels, may offer little benefit at best and may pose health risks at worst. The majority of studies have found that multivitamin/mineral (MVM) supplement use does not decrease the risk of death or chronic disease and has little benefit, if any, for those who already meet nutrient needs through their regular diet. People who take supplements tend to have healthier habits and more favorable health indicators (for example, has normal blood pressure, has a healthy body weight, and is a nonsmoker) than those who do not take supplements. So those who might benefit the most from supplementation are, ironically, often the ones who are least likely to take them.

## WHAT ARE DIETARY SUPPLEMENTS?

As defined by Congress in the 1994 Dietary Supplement Health and Education Act (DSHEA), **dietary supplements** are intended to be taken by mouth and contain one or more dietary ingredients or their constituents: vitamins, minerals, herbs or other botanicals; amino acids; or other dietary substances such as enzymes. The diverse array of products containing these ingredients and constituents are grouped together and called "dietary supplements" because they are regulated by a common set of regulations. Essentially any substance that is found in any food, even if present only in minute quantities, can be extracted or concentrated in the form of pills, capsules, tablets, liquids, powders, and bars and then sold as a dietary supplement. Therefore, these substances are commonly being consumed at levels far exceeding those ever achieved from the intake of food alone. **(INFOGRAPHIC D.1)**

**INFOGRAPHIC D.1 What Are Dietary Supplements?** *Dietary supplements are a diverse array of products meant to "supplement the diet." They include vitamins, minerals, herbals, botanicals, amino acids, and enzymes.*


Eli Ensor

*Women who are pregnant or plan to become pregnant are advised to take a folic acid supplement to help prevent neural tube defects.*

SpeedKingz/Shutterstock

**Who Benefits from Taking Supplements?**

For the average person, the Academy of Nutrition and Dietetics recommends that the best nutrition-based strategy for health is to eat a wide variety of foods. However, some populations may benefit from using dietary supplements. For example, women who have heavy menstrual bleeding may need supplemental iron, and people who have had procedures that interfere with nutrient absorption, such as gastric bypass surgery, may need particular nutrient supplements. Nutrient supplementation of some specific nutrients may also be warranted during certain life stages (for instance, the increased nutrient demands of pregnancy and lactation as well as the impact of physiological changes associated with aging that impact nutrient intake and absorption). **INFOGRAPHIC D.2** lists additional circumstances that might benefit from the use of a dietary supplement.

## REGULATION OF DIETARY SUPPLEMENTS

The Food and Drug Administration (FDA) regulates both dietary supplement products and the ingredients found within them, and it does so under a different set of regulations than those governing "conventional" foods and drugs. Unlike drug regulation, the FDA does not approve dietary supplements for their effectiveness or safety before they are made available to consumers. Dietary supplements do not undergo the rigorous testing for effectiveness, interaction, or safety requirements that prescription and over-the-counter drugs do. In fact, as DSHEA dictates, the *manufacturer* of a dietary supplement or ingredient is responsible for ensuring that the product is safe, unadulterated, produced with good manufacturing practices, and properly and truthfully marked with a label that identifies the product as a dietary supplement and that the product includes specific information about the supplement and its use.

Although dietary *ingredients* found in supplements are federally regulated, ingredients and additives that were already in the food supply prior to when DSHEA went into effect on October 15, 1994, were grandfathered in as **"generally recognized as safe" (GRAS)**. GRAS substances don't need FDA approval before being marketed, so many long-standing

**GENERALLY RECOGNIZED AS SAFE (GRAS)**
*any substance intentionally added to food that is generally recognized among qualified experts as having been adequately shown to be safe under the conditions of its intended use; not subject to premarket review and approval by the FDA*

***The FDA does not approve dietary supplements for their effectiveness or safety.*** *The manufacturer of a dietary supplement or ingredient is responsible for ensuring product safety.*

H. Mark Weidman Photography/Alamy

## INFOGRAPHIC D.2 Circumstances That May Warrant Nutrient Supplementation

*Nutrient supplements may be useful in some circumstances, but they cannot replace a healthy diet.*

| **Population Group** *Do you fit into one of these categories?* | **Dietary Concerns** |
|---|---|
| **Infants and children** | Breastfed children and any child consuming less than 1 qt/day of vitamin D–fortified milk should receive a vitamin D supplement. |
| **Women who may become pregnant** | Supplemental folic acid reduces the occurrence of neural tube defects. |
| **Pregnant women** | A folic acid supplement is recommended during pregnancy. A multivitamin/mineral (MVM) supplement is recommended for anemia, women carrying multiple fetuses, or women consuming little or no animal proteins. |
| **Vegans** | The only source of $B_{12}$ is animal proteins and fortified foods, so vegans who eat no animal products may need a supplement as well as supplementary calcium, iron, and zinc. |
| **Those who do not consume dairy products** | Because milk and other dairy products are an important source of vitamin D and calcium, a supplement providing these nutrients may improve bone health. |
| **Adults older than 50 years** | $B_{12}$ and vitamin D supplements are recommended because $B_{12}$ absorption tends to decline with age and older individuals synthesize less vitamin D when exposed to UV light. |
| **Those with dark skin** | Vitamin D supplements are recommended because skin pigments block UV light and decrease the synthesis of vitamin D. |
| **Individuals on restricted diets** | Those with low food intake or limited food choices may benefit from an MVM supplement. |
| **Individuals who smoke, alcohol-dependent individuals, and those taking some medications** | Nutrient absorption, utilization, and excretion can be affected by prescription or recreational drug use. Therefore, an MVM supplement may be warranted. |
| **Women who are pregnant; women with heavy menstrual periods; individuals who frequently donate blood, as well as those with some stomach and intestinal conditions (food sensitivity, hookworms)** | Iron supplementation may be necessary. |

J Am Diet Assoc. 109: 2073–2085, 2009.

? *Identify at least three underlying reasons supplements might be necessary in these circumstances.*

supplement ingredients have not undergone FDA scrutiny for safety.

For new dietary ingredients, DSHEA requires that manufacturers must notify the FDA 75 days before the product is to be introduced and provide the agency with evidence that the supplement is "reasonably expected to be safe." Unfortunately, it is common for supplement distributors and manufacturers to ignore this requirement as well as other regulations.

Because the FDA does not regulate dietary supplements as rigorously as it does drugs, supplements are sometimes sold contaminated with banned substances or prescription drugs. In 2010, for instance, the agency warned consumers not to take the Chinese weight-loss supplement Fruta Planta, because FDA testing had revealed it contained sibutramine, a drug that had been withdrawn from the U.S. market earlier that year for safety reasons. And in a 2013 study, Pieter Cohen, an assistant professor of medicine at Harvard Medical School who studies dietary supplement safety, and his colleagues found traces of a methamphetamine-like substance in a popular workout supplement. In April 2017, the FDA sent warning letters to 14 companies that were marketing their supplements using illegal claims that their product treated cancer.

## INFOGRAPHIC D.3 FDA Regulations Governing the Introduction of New Dietary Ingredients in Supplements

*Many dietary ingredients legally present in supplements have not been reliably demonstrated to be safe. The 2011 Food Safety Modernization Act expands the authority of the FDA to oversee new dietary ingredients, but the new recommendations are not currently being enforced.*

| Current Enforced Regulations | Current FDA Recommendations—Unenforced |
|---|---|
| • Manufacturers must submit information to the FDA regarding the "safety and efficacy" of a dietary supplement containing a new dietary ingredient.<br>• The manufacturer need only demonstrate that the new dietary ingredient can "reasonably be expected to be safe" by providing *some* evidence of safety but not actually proving safety.<br>• The FDA does not approve new dietary ingredients or supplements—they are free to be marketed 75 days after the information was submitted to the FDA. | • Safety must be established by a documented history of use at the same or higher dosage, frequency, and duration of use.<br>• Laboratory or animal studies would be required for products marketed for consumption at higher than historical intakes.<br>• No human studies are required, even for substances without any documented historical use. |

New Eng J Med. 366: 289–391, 2012.

https://www.fda.gov/food/guidanceregulation/guidancedocumentsregulatoryinformation/dietarysupplements/ucm257563.htm

? *Give an example of "some evidence of safety" that would NOT actually prove that the ingredient is safe.*

The FDA is responsible for taking action against unsafe or improperly labeled dietary supplements after they go to market, but this is not easy to do: The agency must *prove* that the product is unsafe to restrict its use or remove it, and "there's no effective system that the FDA has to identify these supplements, so hazardous supplements stay on the marketplace for years," Cohen says. Even when the FDA announces that a supplement is unsafe, it may not cease being sold. In a 2011 study, Cohen and his colleagues found that after the FDA recalled a popular weight-loss supplement called Pai You Guo in 2009, women were able to continue buying it for years. That being said, the 2011 Food Safety Modernization Act expanded some of the FDA's authority over supplement manufacturers. **(INFOGRAPHIC D.3)**

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### UNDERSTANDING SUPPLEMENT LABELS

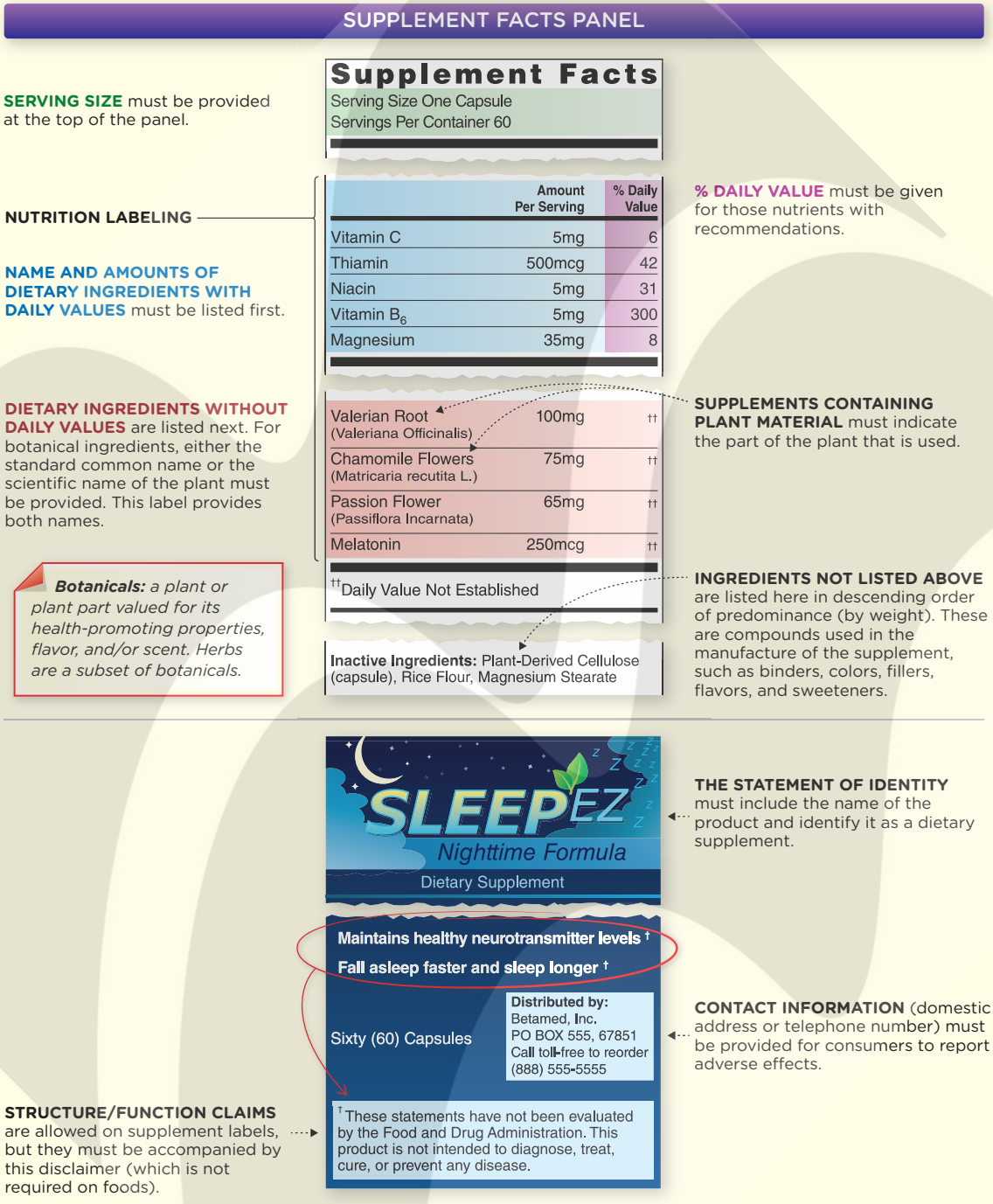
The FDA requires that dietary supplement manufacturers list certain details about their products on product labels. The general information required on the package includes the name of the product; the word *supplement* or a statement that the product is a supplement; the quantity of the package contents; the name and location of the manufacturer, packer, or distributor; and directions for using the product.

In addition to the general information, a supplement must also have what is called a **Supplement Facts Panel**. This panel must include information on serving size and amount of product per serving size (by weight), the percent of Daily Value (%DV) that a particular ingredient or nutrient provides per serving (if this is known), and a list of the product's dietary ingredients. **(INFOGRAPHIC D.4)** If a dietary ingredient is a botanical, the panel must list the scientific name of the plant or the common name that has been standardized in the reference book *Herbs of Commerce* (2000 edition). The panel must also include the name of the plant part that has been used. If the dietary ingredient is a proprietary blend, meaning a blend that is exclusive to the manufacturer, the Supplement Facts Panel must list the total weight of the blend and its components in descending order of predominance by weight.

**SUPPLEMENT FACTS PANEL**
*a package label that must indicate that the product is a supplement and not a conventional food and must include serving size and the amount of the product per serving size, the percent of Daily Value that a particular ingredient or nutrient provides per serving, and a list of the product's dietary ingredients*

## INFOGRAPHIC D.4 Dietary Supplement Labeling Requirements

*One of the most significant differences between the "Facts Panel" for a supplement versus a food is that substances and ingredients that do not have recommendations are allowed on the supplement panel.*




*Must all ingredients be declared on the label of a dietary supplement?*

Supplements must also include another ingredients panel. This lists all nondietary components found in the product, such as fillers, water, artificial colors, sweeteners, flavors, and processing aids such as binders, gelatin, and stabilizers. These ingredients are listed by common name or proprietary blend in descending order of predominance by weight. The ingredients listed in this panel may include the sources of the dietary ingredients if they are not identified on the Supplement Facts Panel—for instance, a label might list rose hips as the source of vitamin C.

Finally, supplement labels may also contain cautionary statements about potential side effects, but if a supplement does not have a cautionary statement, it does not mean that the product is completely safe. Unlike conventional drugs, supplement manufacturers do not have to list known adverse effects on their labels.

### Health Claims

As introduced in Chapter 2, supplement labels can also include *health claims* that describe a relationship between a dietary ingredient and a reduced risk of a disease or condition. The FDA must preapprove these claims based on Significant Scientific Agreement (SSA) about the publicly available scientific evidence. A supplement containing calcium and vitamin D can legally claim that it reduces the risk of osteoporosis, for instance, and a folic acid supplement can say that it may prevent fetal neural tube defects, for example. **(INFOGRAPHIC D.5)** The FDA also allows the use of *qualified* health claims for conventional foods and dietary supplements when the evidence linking a food, food component, or supplement to a reduced risk of a disease is emerging but not well enough established to meet the SSA standard for a true health claim. For example, the number of studies demonstrating a beneficial effect may be limited, or the results of studies may be inconsistent. Qualifying language is included to indicate that the evidence supporting the relationship is limited—for instance, you might read on a label that "supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease." But even qualified claims must be approved by the FDA based on the quality and strength of the scientific evidence.

### Structure/Function Claims

Supplement manufacturers can't make claims that their product treats, prevents, or cures disease unless it has been approved for a health claim or qualified health claim. However, companies can make a *structure/function claim* on the label about how that product could affect the body's structure or function. **(INFOGRAPHIC D.6)** "Calcium builds strong bones" is an example of a structure-related claim, whereas "fiber maintains bowel regularity" or "antioxidants maintain cell integrity" are function-related claims. Alternatively, these claims may state that consuming a nutrient or dietary ingredient may improve general well-being or describe a benefit related to a nutrient deficiency disease. Labels containing these claims must state in a disclaimer that the FDA has not evaluated the claim and that the product is not intended to diagnose, treat, cure, or prevent any disease. Still, "more times than not, the label is going to be misleading, and the claims are going to be overly positive," Cohen says.

### Supplement Quality

How do we know if supplements on the market are pure and of high quality? The FDA does not monitor supplements for quality assurance, potency, purity, or efficacy (effectiveness)—there are far too many supplements for the agency to handle—but the FDA does track reports of illness, injury, or reactions that might occur in consumers who have taken supplements. Supplement manufacturers are now required to report serious harmful effects to the FDA, too.

Supplements may be labeled as "pure," "natural," or "quality-assured," but because the FDA does not regulate these terms, these claims may not be true. Supplements that claim to be "all natural," for instance, are not always better or safer than refined or synthetic substances, because natural and synthetic forms generally have the same chemical structure and do not differ in terms

## INFOGRAPHIC D.5 FDA-Approved Health Claims and Qualified Health Claims

*When there is significant scientific agreement that evidence supports a link between a diet or nutrient and a disease, the FDA establishes approved health claims. When the evidence is not as strong, the FDA allows qualified health claims.*

**Selected Approved Health Claims**

| Nutrient and Disease | Claim Statement |
|---|---|
| Calcium and Osteoporosis | Adequate calcium throughout life, as part of a well-balanced diet, may reduce the risk of osteoporosis. |
| Dietary Fat and Cancer | Development of cancer depends on many factors. A diet low in total fat may reduce the risk of some cancers. |
| Sodium and Hypertension | Diets low in sodium may reduce the risk of high blood pressure, a disease associated with many factors. |
| Dietary Saturated Fat and Cholesterol and Risk of Coronary Heart Disease | Although many factors affect heart disease, diets low in saturated fat and cholesterol may reduce the risk of this disease. |
| Fiber-Containing Grain Products, Fruits, and Vegetables and Cancer | Low-fat diets rich in fiber-containing grain products, fruits, and vegetables may reduce the risk of some types of cancer, a disease associated with many factors. |
| Fruits, Vegetables, and Grain Products That Contain Fiber, Particularly Soluble Fiber, and Risk of Coronary Heart Disease | Diets low in saturated fat and cholesterol and rich in fruits, vegetables, and grain products that contain some types of dietary fiber, particularly soluble fiber, may reduce the risk of heart disease, a disease associated with many factors. |
| Folate and Neural Tube Defects | Healthful diets with adequate folate may reduce a woman's risk of having a child with a brain or spinal cord defect. |
| Potassium and the Risk of High Blood Pressure and Stroke | Diets containing foods that are a good source of potassium and that are low in sodium may reduce the risk of high blood pressure and stroke. |
| Whole Grain Foods and Risk of Heart Disease and Certain Cancers | Diets rich in whole grain foods and other plant foods and low in total fat, saturated fat, and cholesterol may reduce the risk of heart disease and some cancers. |

**Selected Qualified Health Claims**

| Nutrient and Disease | Eligible Foods | Claim Statement |
|---|---|---|
| Green Tea and Cancer | Green tea and conventional foods and dietary supplements that contain green tea | Green tea may reduce the risk of breast or prostate cancer. The FDA has concluded that there is very little scientific evidence for this claim. |
| Selenium and Cancer | Dietary supplements containing selenium | Selenium may produce anticarcinogenic effects in the body. Some scientific evidence suggests that consumption of selenium may produce anticarcinogenic effects in the body. However, the FDA has determined that this evidence is limited and not conclusive. |
| Antioxidant Vitamins and Cancer | Dietary supplements containing vitamin E and/or vitamin C | Vitamin C may reduce the risk of gastric cancer. The FDA has concluded that there is very little scientific evidence for this claim.<br><br>Vitamin E may reduce the risk of colorectal cancer. The FDA has concluded that there is very little scientific evidence for this claim. |
| Omega-3 Fatty Acids and Coronary Heart Disease | Conventional foods and dietary supplements that contain EPA and DHA omega-3 fatty acids | Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease. |

? *Which one of the sample qualified health claims has the strongest supporting evidence?*

## INFOGRAPHIC D.6 Examples of Structure/Function Claims on Dietary Supplements


? *What is the difference between the statements "calcium builds strong bones" and "calcium reduces the risk of osteoporosis"?*

of how they are absorbed or used by the body. They may, however, differ in price—the "natural" forms are often costlier.

Consumers do have some ways of gauging supplement quality, though. Independent labs test supplements that manufacturers voluntarily submit; some labs also do product reviews. Organizations such as the United States Pharmacopeial Convention (USP)—a scientific nonprofit organization that sets standards for the identity, strength, quality, and purity of medicines, food ingredients, and dietary supplements distributed and consumed

***Meaningless words.*** *Supplements may be labeled with words that are meant to make a product seem trustworthy, such as* quality, pure, *or* natural, *but these terms have no legal meaning.*


Vadim.Petrov/Shutterstock

***Look at the label.*** *Independent labs such as the United States Pharmacopeial Convention (USP) and NSF International (NSF) can evaluate and set standards for dietary supplements.*


Editorial Image, LLC/Alamy

worldwide—provide seals of quality that companies can display on their products. Another independent lab that provides quality labels is NSF International (NSF).

## ARE DIETARY SUPPLEMENTS HARMFUL?

Of course, purity is not the only important quality. The question that is much harder to answer is whether a particular supplement will actually improve the health of the general population. The National Cancer Institute studies led by Omenn and his colleagues suggest that some supplements not only are ineffective but also can be harmful.

A small subset of studies, however, suggests that supplements may be beneficial for preventing certain conditions. **(INFOGRAPHIC D.7)** For instance, in 1997, researchers at Harvard University and its affiliated hospitals and schools began a clinical trial as part of the Physicians Health Study II to test whether moderate doses of multivitamins might prevent cancer or heart disease. "When you think about individual vitamin supplements tested in trials, there's been an emphasis on high doses," explains Howard Sesso, one of the study's leaders and an associate professor of epidemiology at the Harvard School of Public Health. "We thought it would be interesting to have the opposite approach: It might be more appropriate to test a standard common multivitamin that has all the essential vitamins and minerals in combination, but in lower, more usual, doses that you would get in your diet." To do this, the Harvard researchers tracked the health of nearly 15,000 physicians older than 50 years who had been randomly assigned to take either a standard multivitamin or a sugar pill every day for an average of 11 years.

## INFOGRAPHIC D.7 Effects of Long-Term Use of Multivitamin/Mineral Supplements on Mortality

*Neither the long-term use of full-spectrum multivitamin/mineral supplements nor the administration of more narrowly formulated vitamin/mineral supplements decrease the risk of death.*

**Studies Examining Multivitamin/Mineral Supplements**

- Of eight observational studies that examined the effect of long-term multivitamin/mineral (MVM) supplements on mortality, six studies found no effect of MVM use, whereas two studies observed an increased risk of death in those taking MVM supplements.
- In a recent randomized clinical trial, approximately 10 years of MVM administration caused no decrease in deaths from cardiovascular disease or cancer. MVM supplements did not affect the occurrence of CVD, although there was a slight decrease in the occurrence of all cancers.
- An earlier randomized clinical trial found no decrease in mortality following the administration of an MVM supplement to a poorly nourished population for six years, nor was there any affect on mortality 20 years later.
- Analysis of data pooled from 78 clinical trials involving nearly 300,000 participants found no benefit of antioxidant vitamins and minerals on the risk of death; however, consuming supplements of beta-carotene and vitamin E were found to increase the risk of death.
- The analysis of pooled data from 21 studies that had administered supplements containing three or more vitamins and minerals to more than 90,000 participants found no effect on mortality risk.

? *From the research findings summarized here, identify perhaps the best reason NOT to use vitamin/mineral supplements.*

Although the multivitamin takers did not end up with a reduced risk for heart disease, they were 8% less likely to develop cancer during the follow-up period than the doctors who did not take multivitamins. A separate arm of the study that evaluated the effects of taking a 400 mg dose of vitamin C every day and a 400 IU dose of vitamin E every other day did not, however, find that the two vitamins reduced cancer risk. It seemed to be the combination of many vitamins at lower doses that made a positive difference.

Sesso and his colleagues were very pleased with their study results, "but what we were immediately trying to think through was: How do you explain the findings?" Indeed, one major question is exactly *how* vitamins may protect against cancer. Another question is whether a person is better off getting vitamins through whole foods or through pills. "I think a lot of people would argue that the natural approach through food is the way to go," Sesso says, but more research is needed to prove this.

Supplements seem to pose the highest risks when they are what are known as "high-potency supplements," which include one or more nutrients or ingredients in amounts significantly in excess of recommendations. These supplements include the megadoses of beta-carotene (30 mg) and vitamin A (7500 mcg) that the participants were taking as part of Omenn's CARET trial. Sometimes these supplements also exceed the established Tolerable Upper Intake Limit (UL), the maximum level of daily intake that is likely to cause no risk of adverse health effects to almost all individuals in the population. No laws establish or cap potency for any supplements except potassium because of potential side effects on heart rate and rhythm. But high doses of some supplements can cause fatigue, diarrhea, hair loss, kidney stones, liver and nerve damage, and birth defects. They can lead to nutrient imbalances or unwanted interactions, reducing the absorption and utilization of other nutrients. And taking high doses of many minerals—as well as the fat-soluble vitamins A, D, and E—can be toxic. Even high doses of the water-soluble vitamin $B_6$ are toxic, potentially causing permanent nerve damage. It's important to remember that even if you don't exceed the UL for a nutrient through supplement use, you may exceed it when you combine the amount you're getting from a

## INFOGRAPHIC D.8 Tips for Choosing a Multivitamin Supplement

*If you are in a category that might benefit from taking a multivitamin supplement (see INFOGRAPHIC D.2), these guidelines can help you.*

### Tips for Choosing a Multivitamin Supplement

- **Read the label carefully**. Examine which nutrients are included and the amounts contained within each serving. In general, choose a supplement that provides 100% of the Daily Value (DV) for most of the vitamins and minerals in that supplement. Some nutrients, such as calcium and magnesium, are rarely included at 100% because the pill would be too large to swallow.
- **Look for quality products.** The initials USP stand for U.S. Pharmacopeial Convention, and NSF stands for NSF International; both are reputable organizations that test dietary supplements for quality.
- **Look for the expiration date.** Select products that will have a long shelf life.
- **Consider formulas for men, women, and age groups.** Choose a multivitamin designed for your age and sex so that the nutrients included will be right for you.
- **Don't overdo it.** Avoid multivitamins that exceed 100% of daily recommended values.

*Rudchenko Liliia/ Shutterstock*

#### SPECIAL CAVEATS

- **Beware of interactions.** Taking a combination of supplements together with medications could produce adverse effects. For example, Coumadin (a prescription drug), ginkgo biloba (an herbal supplement), aspirin (an OTC drug), and vitamin E (a vitamin supplement) can each thin the blood, and taking any of these products together can increase the potential for internal bleeding. The herbal supplement St. John's wort may also reduce the effectiveness of prescription drugs for heart disease, depression, seizures, certain cancers, and oral contraceptives.
- **Some supplements may interfere with surgeries.** Before elective surgery, you may be asked to stop taking vitamins, minerals, or herbal supplements to avoid potentially dangerous supplement/drug interactions—such as changes in heart rate, blood pressure, and increased bleeding—that could adversely affect the outcome of your surgery.

**STAY TUNED**
for more on the nutritional considerations for the aging adult in Spotlight G.

supplement with the amount you're getting from food. **(INFOGRAPHIC D.8)**

The potential benefits or risks of choosing to take dietary supplements warrants special consideration for the aging adult. Not only are older adults (> 60 years of age) more likely to take dietary supplements than younger adults but they are also more likely to take one or more medications. Concurrent use of supplements and medications (whether prescribed or over-the-counter) increases the risk for interactions, with herbal (botanical) supplements being the most likely to cause adverse effects when taken with medications. It is important for all individuals to alert their healthcare providers of any supplements they take, especially when other medications are prescribed or new medical conditions arise. Multivitamin/mineral supplements may help meet recommended intake levels by providing nutrients that may be lacking or inadequate in the diet of older adults and can help meet recommended intake targets. However, adverse effects are possible if the additional nutrients provided by supplements push intake above the UL.

**Pros and Cons of Herbal Supplements**

Botanical supplements are valued for their medicinal or therapeutic properties to treat disease or maintain health. Botanicals include any supplement that is derived from plants and may include liquid extracts, oils, or herbs. **Herbal supplements** are a subset of botanicals that are typically dried preparations of flowers, leaves, roots, bark, or seeds. They are less popular in the United States than vitamin and mineral supplements, but more than one-fifth of U.S. adults take them. There are 550 primary herbs with 1800 names, but examples of some of the most common herbs sold in this country include echinacea, flaxseed, ginseng, ginkgo, saw palmetto, St. John's wort, black cohosh, milk thistle, and garlic. **(INFOGRAPHIC D.9)** From a medicinal perspective, herbs are less potent crude drugs and can have druglike effects, yet they do not undergo the same stringent approval process as drugs do. Sometimes herbal supplements can contain biologically active ingredients and toxins in addition to their active "useful"

**HERBAL SUPPLEMENT**
*a type of dietary supplement that includes plants (botanicals), singly or in combination; typically dried preparations of flowers, leaves, roots, bark, and seeds*

## INFOGRAPHIC D.9 Possible Adverse Effects and Benefits Associated with the Use of Herbal Supplements

**Potentially Effective Botanical Supplements and Possible Adverse Effects**

| | Supplement | Possible Benefits | Adverse Effects |
|---|---|---|---|
|  | Senna | Laxative | Liver failure with excessively high doses |
|  | Licorice root | Protection against liver damage, anti-ulcer effects | Hypertension |
|  | Hawthorn | Cardiovascular benefits | None |
|  | Ginger | Reduction of nausea and vomiting | None |
|  | Garlic | Reduction of hypertension and cardiovascular benefits | Decreased clotting |
|  | Black cohosh | Relief of menopausal symptoms | Possible liver injury with long-term use |
|  | Holy basil | Anti-inflammatory, anticarcinogenic effects | None |
|  | Fenugreek | Lower blood glucose and improved insulin sensitivity | Diarrhea, low blood glucose |
|  | St. John's wort | Treatment of mild to moderate depression | Hypertension |
|  | French maritime pine bark (Pycnogenol) | Antioxidant, decreased hypertension, improved cardiovascular function | May cause mild dizziness, nausea, headache |

*A recent study found that bottles labeled as St. John's wort from two manufacturers contained none of the medicinal herb; one contained only rice powder, and the other contained senna.*

? *What adverse effects might you experience if you had taken a supplement containing senna?*

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*Even though herbal supplements are called "natural," they can cause drug interactions and exacerbate medical conditions.*


Mario Tama/Getty Images

components. Even though herbal supplements are often considered natural, they can still cause drug interactions and serious adverse effects and even exacerbate medical conditions; there is no legal definition for the term *natural*, and it certainly does not mean that a product is safe or effective. Athletes should be particularly cautious when contemplating the use of any sports-enhancing dietary supplement as they are often contaminated, intentionally or through poor manufacturing processes, with banned substances that can result in disqualification or adverse effects.

**STAY TUNED**
Sports-enhancing dietary supplements are covered in Chapter 12 Nutrition and Fitness.

**FUNCTIONAL FOOD**
*a food that provides health benefits or improved physical performance beyond the traditional vitamins, minerals, or other nutrients it contains; also known as nutraceuticals*

## FUNCTIONAL FOODS

Food manufacturers may opt to add other nutrients to food products to boost nutritional value and potential health benefits. These products fall under a class of foods called **functional foods** (also called *nutraceuticals*). A functional food contains nutrients or other constituents, such as phytochemicals, that

***Nutritional products for athletes.*** *Energy gels, bars, and powders are often used by athletes to improve performance or help them endure a grueling workout.*


B Christopher/Alamy

may enhance a food's contribution to health and disease prevention beyond its basic nutritional content. Functional foods may be whole foods or processed foods that have been touted to decrease the risk of cancer, heart disease, diabetes, or obesity or to slow the aging process. Some of these claims may be overhyped, but some may be valid.

Functional foods include whole foods such as vegetables, whole grains, and berries that may provide health benefits due to the abundance of phytochemicals they contain. Functional foods are also those foods that have been fortified with nutrients not traditionally found in the food, such as the addition of calcium to orange juice and the fortification of breakfast cereals with higher levels of vitamins and minerals. They may also be "engineered foods," such as sports bars and sports drinks, that are designed to help you exercise longer or play sports more intensely.

In its 2013 position statement on functional foods, the Academy of Nutrition and Dietetics noted that "all food is essentially functional at some level, as it provides energy and nutrients needed to sustain life. However, there is growing evidence that some food components, not considered nutrients in the traditional sense, may provide positive health benefits." **(INFOGRAPHIC D.10)**

## INFOGRAPHIC D.10 Examples of Functional Foods

*Functional foods have health benefits beyond those provided by the vitamins and minerals they traditionally contain.*


Orange juice has added calcium to improve bone health.

Blueberries and blackberries contain high amounts of anthocyanins that promote cardiovascular health.


Yogurt has live bacterial cultures to promote gastrointestinal health.


Margarine has plant sterols added to lower blood cholesterol.

Tomatoes are naturally an excellent source of the phytochemicals lutein and lycopene that are associated with a reduced risk of eye disease and some cancers, respectively.

? *Why is the orange juice pictured here considered a functional food?*

*Photo credits (all photos): Eli Ensor*

# DIETARY SUPPLEMENTS

Nutrient-dense plant-based functional foods may, for instance, contain disease-fighting phytochemicals, or phytonutrients, which are biologically active constituents in foods. More than 2000 phytochemicals have been found in plant-based foods, and many have antioxidant or hormonelike actions and may help to reduce the risk of certain types of cancer and other chronic diseases. (Refer to Spotlight C.) Functional foods also might contain *prebiotics*, which are nondigestible carbohydrates broken down by bacteria in the large intestine, or *probiotics*, which are live beneficial microorganisms found in fermented foods. (Refer to Chapter 3.) Prebiotics foster the growth of healthy bacteria in the gut. Probiotics, when consumed in sufficient amounts, may confer gastrointestinal and other health benefits.

The United States currently has no statutory legal definition for functional foods, nor does it have any specific regulatory policies for them, so they can be categorized as conventional foods, dietary supplements, or medical foods. Functional foods are common, representing the largest percentage of new food products introduced to the market over the past decade. Many packaged functional foods include health claims on their labels that are regulated by the FDA, and most are high in nutrients in relation to calories. So they can contribute to dietary quality, optimal health, and disease prevention when consumed as part of a varied balanced diet and healthy lifestyle.

Dietary supplements can be important and potentially life-saving products for individuals who cannot get enough nutrients through foods—for instance, vegans, whose only source of vitamin $B_{12}$ is fortified foods, may not get enough through diet alone. But because supplements are not as tightly regulated as drugs and because in some cases scientists do not fully understand their potential effects, supplements do not come without risks. "The great majority of the time people are taking supplements, and it's just a waste of money," Cohen says. "And a small percentage of the time, they're taking something that's actually dangerous."

SPOTLIGHT D **BRING IT HOME**

# Functional foods: What's in this food?

Food manufacturers are expanding the range of nutrients they add to foods as well as the types of foods to which nutrients are added. The increasing presence of fortified and enhanced foods in supermarkets has the potential to affect the nutrient intake and health of individuals. What role do functional foods play in your diet?

1. Choose a functional food product (one that has one or more added nutrients or dietary constituents) that you typically consume.
2. What nutrients or dietary constituents have been added to this product?
3. Are there any health claims on the food label? If so, list them.
4. Would you consider the added nutrients to be ones that most people need more of in their diets? Explain.
5. Why do you use this particular food product? Do you purchase it for the taste, the added nutrients, the potential health benefits, or other reasons?
6. Is this particular type of product available without the added nutrients or extra fortification? For example, if you chose orange juice with added calcium, the answer would be "yes, this product is available as orange juice without added calcium." Do you know if there is a cost difference between the regular product and the functional food version? Are you willing to pay more for the enhanced product? Why or why not?
7. What role do you think functional foods should play in the food market and in the overall population's diet?
8. Do you see any potential for misuse or excessive nutrient intake through the use of this or a similar product? What if an individual is also taking a dietary supplement that includes the same nutrient?


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# KEY IDEAS

- Dietary supplements, including vitamins, minerals, herbs, botanicals, amino acids, and enzymes, are meant to "supplement the diet," not replace nutrients that are best obtained through a varied and balanced diet.
- Under the 1994 Dietary Supplement Health and Education Act (DSHEA) and more recently the 2011 Food Safety Modernization Act, the U.S. Food and Drug Administration (FDA) is responsible for regulating the sale, labeling, and manufacturing of dietary supplements, as well as approving any health claims made by manufacturers or producers of the supplements.
- Current regulations do not require dietary supplements, including botanical supplements, to undergo the same rigorous testing for effectiveness, interaction, or safety requirements as conventional drugs.
- Supplement manufacturers are responsible—and accountable to the FDA—for ensuring that supplements are safe, unadulterated, and produced with good manufacturing practices.
- Manufacturers must provide specific product information and ingredients on the Supplement Facts Panel.
- Supplements may also include health claims on the label that describe a relationship between a dietary supplement ingredient and a reduced risk of a disease or condition. These claims must be preapproved for use on supplement labels by the FDA using Significant Scientific Agreement (SSA).
- Manufacturers are also able to make certain claims about how a product affects the body's structure or function. These structure/function claims must include a disclaimer that the claim has not been evaluated by the FDA.
- Current evidence does not demonstrate that dietary supplements provide significant health benefits. They may, in some cases, increase the risk of disease and mortality. However, some individuals and groups may benefit from using supplemental nutrients to help meet their nutritional needs.

The use of high-potency supplements may result in nutrient intakes above the Tolerable Upper Intake Level (UL) and cause adverse effects.

Some foods may have a positive effect on health beyond that of basic nutrition. These are called functional foods, and the group includes whole foods as well as fortified food products.

# NEED TO KNOW

## Review Questions

1. In the United States, nutrition surveys indicate that the people who are most likely to use dietary supplements:
   a. usually are in poor health with diets deficient in multiple nutrients.
   b. already tend to have healthful diets adequate in most nutrients.
   c. do so based primarily on the advice of their healthcare provider.
   d. experience immediate and significant health benefits.
2. Which of the following would NOT meet the criteria for being called a "dietary supplement" in the United States?
   a. omega-3 fish oil capsule
   b. multivitamin and mineral tablet
   c. chewable children's multivitamin "gummy"
   d. vitamin $B_{12}$ injection or shot
3. Dietary supplements in the United States are monitored by the FDA for:
   a. purity.
   b. potency.
   c. effectiveness.
   d. reports of illness, reactions, or harmful effects.
4. According to the Dietary Supplement Health and Education Act, what is considered a "new" dietary ingredient?
   a. a dietary ingredient that was not sold in a dietary supplement in the United States before 1994
   b. a dietary ingredient that has not been evaluated by the FDA for safety and efficacy
   c. any type of ingredient or supplement other than a vitamin or a mineral
   d. vitamins or minerals added to processed foods for fortification purposes
5. Dietary supplements that have GRAS status:
   a. require the FDA's approval before they can be marketed and sold.
   b. are generally recognized as safe by the FDA.
   c. have undergone rigorous testing by the FDA for safety.
   d. have been banned for use in the United States.
6. Which of the following is an example of an acceptable structure/function claim that might appear on a dietary supplement label?
   a. helps maintain cardiovascular health
   b. prevents heart disease
   c. lowers cholesterol to prevent heart disease
   d. alleviates chest pain in individuals with heart disease
7. Synthetic vitamins are:
   a. tested for safety and efficacy by the FDA.
   b. significantly less effective than natural vitamins.
   c. generally chemically identical to vitamins labeled "natural."
   d. always classified as a new dietary ingredient by the FDA.
8. The vitamins and minerals found in high-potency supplements:
   a. are proven to improve health and promote longevity.
   b. cannot by law exceed the percent of Daily Value.
   c. may exceed the Tolerance Upper Intake Level.
   d. will not result in toxicity because any excess is excreted through the urine.
9. Herbal supplements include all of the following characteristics, EXCEPT:
   a. the same approval process as drugs.
   b. a label that clearly states the scientific or standardized name of the plant used to make the supplement.
   c. possible toxins in addition to active components.
   d. medicinally considered to be crude drugs.

10. All of the following are true in regard to functional foods, EXCEPT:
    a. they represent the largest percentage of new products introduced to the food marketplace in the United States.
    b. they are generally high in nutrients in relation to calories.
    c. they are only whole foods; processed or packaged foods would not meet the criteria.
    d. if packaged, they often include a health claim or nutrient content claim on their label.

## TAKE IT FURTHER

**A friend shows you the vast array of dietary supplements that he takes each morning in hopes of improving his fitness, boosting his energy, and increasing his immunity. Your friend is in good health, is at a healthy weight, and seems to follow a varied and balanced diet. What are three considerations or cautions that come to mind regarding the use of dietary supplements in this scenario? Do you believe supplementation is warranted? Why or why not?**