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## CHAPTER

# 11

# Dietary Supplements

### Time for Completion

Activities: 1½ hours

Optional examination: ½ hour



## OBJECTIVES

Upon completion of this chapter the student should be able to do the following:

1. Describe how the 1994 Dietary Supplements Health and Education Act (DSHEA) changed the regulation of dietary supplements.
2. List the five criteria that define a supplement according to the DSHEA.
3. Explain the difference in a traditional dietary supplement and the present dietary supplement.
4. List three examples of a structure-function claim.
5. Describe how the FDA regulates claims made for advertising dietary supplements.
6. Identify at least five health claims made for ginseng, and five side effects that may be encountered from its use.
7. Identify the major uses of *Ginkgo biloba* and three possible side effects.
8. Describe five major health claims and five possible side effects of saw palmetto.
9. List five proposed benefits for valerian, and five possible side effects that can occur when valerian is taken for more than 2–3 weeks, or in large doses.
10. Discuss the interactions of supplements with medications.
11. Recognize fraudulent products.

12. Provide clients with information on reputable Web sites for information on supplements, and how to recognize unreliable sources.
13. Become familiar with the FDA's enforcement in dealing with manufacturers of dietary supplements that make illegal health claims and pose danger to the consumers who use their products.

## GLOSSARY

**Adulterated:** the addition of inactive ingredients to a food that cause the food to have toxic effects when ingested.

**Dietary supplement:** a product used to provide nutritional support to the human diet.

- a. **Traditional definition:** a product composed of essential nutrients, such as vitamins, minerals, and protein.
- b. **Expanded definition:** product containing not only essential nutrients, but also may be composed of herbs and other botanicals, amino acids, glandulars, metabolites, enzymes, extracts, or any combination of these.

**DSHEA:** Dietary Supplement Health and Education Act. The 1994 amendment to the FD&C Act that included provisions that apply only to dietary supplements and dietary ingredients of supplements.

**FDA:** Food and Drug Administration. Agency responsible for enforcement of federal regulations regarding manufacture and distribution of food, drugs, and cosmetics as protection against sale of impure or dangerous substances.

**FD&C Act:** Federal Food, Drug, and Cosmetic Act. The 1958 act that evaluated the safety of all new ingredients, excluding dietary supplements and dietary ingredients of supplements.

**Food additive:** a new ingredient added to another food. Requires government approval if the ingredient has not been recognized as safe.

**GMP for the FD&C Act:** Good Manufacturing Practices for the FD&C Act. They are umbrella regulations governing the production of safe food, drugs, and cosmetics.

**GMP for the DSHEA:** Good manufacturing practices for the DSHEA. They are umbrella regulations governing the production of safe dietary supplements.

**Health claims:**

- a. **Unapproved:** one that claims to prevent, mitigate, treat, or cure a specific disease, for example, "cures cancer."
- b. **Approved:** one that, if the product substantiates the claim, may be said to improve health status, such as "may lower cholesterol" or "may reduce risk of osteoporosis."

**GRAS:** Generally recognized as safe: Substances used in foods that have been proven safe to use over a period of time.

## BACKGROUND INFORMATION

All information in this chapter is based on documents published by the U.S. Food and Drug Administration, unless otherwise qualified.

Set between a Chinese restaurant and a pizza and sub sandwich eatery, a Rockville health food store offers yet another brand of edible items: bottled herbs such as cat's claw, dandelion root, and blessed thistle; vitamins and minerals in varying doses; and herbal and nutrient concoctions whose labels carry claims about relieving pain, "energizing" and "detoxifying" the body, or providing "guaranteed results."

This store sells dietary supplements, some of the hottest selling items on the market today. Surveys show that more than half of the U.S. adult population uses these products. In 1996 alone, consumers spent more than \$6.5 billion on dietary supplements, according to Packaged Facts, Inc., a market research firm in New York City. But even with all the business they generate, consumers still ask questions about dietary supplements: Can their claims be trusted? Are they safe? Does the Food and Drug Administration (FDA) approve them?

Many of these questions come in the wake of the 1994 Dietary Supplement Health and Education Act, or DSHEA, which set up a new framework for FDA regulation of dietary supplements. It also created an office in the National Institutes of Health to coordinate research on dietary supplements, and it called on President Clinton to set up an independent dietary supplement commission to report on the use of claims in dietary supplement labeling.

### Dietary Supplement Health and Education Act of 1994

For decades, the Food and Drug Administration regulated dietary supplements as foods, in most circumstances, to ensure that they were safe and wholesome, and that their labeling was truthful and not misleading. An important facet of ensuring safety was FDA's evaluation of the safety of all new ingredients, including those used in dietary supplements, under the 1958 Food Additive Amendments to the federal Food, Drug, and Cosmetic Act (FD&C Act). However, with passage of the Dietary Supplements Health and Education Act of 1994, Congress amended the FD&C Act to include several provisions that apply only to dietary supplements and dietary ingredients of dietary supplements. As a result of these provisions, dietary ingredients used in dietary supplements are no longer subject to the premarket safety evaluations required of other new food ingredients or for new uses of old food ingredients. They must, however, meet the requirements of other safety provisions.

The provisions of DSHEA define dietary supplements and dietary ingredients; establish a new framework for

assuring safety; outline guidelines for literature displayed where supplements are sold; provide guidelines for use of claims and nutritional support statements; require ingredient and nutrition labeling; and grant the FDA the authority to establish good manufacturing practice (GMP) regulations. The law also requires formation of an executive-level Commission on Dietary Supplement Labels and an Office of Dietary Supplements within the National Institutes of Health.

These specific provisions of the DSHEA are summarized in Activity 1.

### PROGRESS CHECK ON BACKGROUND INFORMATION

#### TRUE/FALSE

Circle T for True and F for False.

1. T F A traditional definition of dietary supplement is a product composed of essential nutrients, such as vitamins, minerals, and/or proteins.
2. T F The Food and Drug Administration (FDA) is an agency responsible only for enforcement of federal regulations regarding manufacture and distribution of food, drugs, and cosmetics as protection against sale of impure or dangerous substances.
3. T F A food additive is a new ingredient added to another food without government approval.
4. T F A food or supplement is adulterated with the addition of inactive ingredients to a food that cause the food to have toxic effects when ingested.

#### MULTIPLE CHOICE

Circle the letter of the correct answer.

5. Dietary supplements may be which of the following:
  - a. essential nutrients
  - b. herbs and other botanicals
  - c. amino acids
  - d. glandulars
  - e. metabolites
  - f. enzymes
  - g. extracts
  - h. any combination of above

#### FILL-IN

6. The purpose of the 1994 Dietary Supplement Health and Education Act, or DSHEA was to:
  - a. \_\_\_\_\_
  - b. \_\_\_\_\_
  - c. \_\_\_\_\_

7. Define these acronyms:

- a. GRAS \_\_\_\_\_
- b. GMP \_\_\_\_\_
- c. DSHEA \_\_\_\_\_
- d. FD&C \_\_\_\_\_

## ACTIVITY 1:

### DSHE Act of 1994

#### DEFINITION OF DIETARY SUPPLEMENT

The FDA traditionally considered dietary supplements to be composed only of essential nutrients, such as vitamins, minerals, and proteins. The Nutrition Labeling and Education Act of 1990 added “herbs, or similar nutritional substances,” to the term *dietary supplement*. Through the DSHEA, Congress expanded the meaning of the term *dietary supplements* beyond essential nutrients to include such substances as ginseng, garlic, fish oils, psyllium, enzymes, glandulars, and mixtures of these ingredients.

The DSHEA established a formal definition of *dietary supplement* using several criteria:

1. A dietary supplement is a product (other than tobacco) that is intended to supplement the diet and which bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical; an amino acid; a dietary substance for use by humans to supplement the diet by increasing the total daily intake; or a concentrate, metabolite, constituent, extract, or combinations of these ingredients.
2. A dietary supplement is intended for ingestion in pill, capsule, tablet, or liquid form.
3. A dietary supplement is not represented for use as a conventional food or as the sole item of a meal or diet.
4. A dietary supplement is labeled as a “dietary supplement.”
5. A dietary supplement includes products such as an approved new drug, certified antibiotic, or licensed biologic that was marketed as a dietary supplement or food before approval, certification, or license (unless specifically waived).

Dietary supplements come in many forms, including tablets, capsules, powders, softgels, gelscaps, and liquids. Though commonly associated with health food stores, dietary supplements also are sold in grocery, drug, and national discount chain stores, as well as through mail-order catalogs, TV programs, the Internet, and direct sales.

One thing dietary supplements are not is drugs. A drug, which sometimes can be derived from plants used

as traditional medicines, is an article that, among other things, is intended to diagnose, cure, mitigate, treat, or prevent diseases. Before marketing, drugs must undergo clinical studies to determine their effectiveness, safety, possible interactions with other substances, and appropriate dosages, and the FDA must review these data and authorize the drugs' use before they are marketed. The FDA does not authorize or test dietary supplements.

A product sold as a dietary supplement and touted in its labeling as a new treatment or cure for a specific disease or condition would be considered an unauthorized—and thus illegal—drug. Labeling changes consistent with the provisions in DSHEA would be required to maintain the product's status as a dietary supplement.

Another thing dietary supplements are not are replacements for conventional diets, nutritionists say. Supplements do not provide all the known—and perhaps unknown—nutritional benefits of conventional food.

## NUTRITIONAL SUPPORT STATEMENTS

The DSHEA provides for the use of various types of statements on the label of dietary supplements, although claims may not be made about the use of a dietary supplement to diagnose, prevent, mitigate, treat, or cure a specific disease (unless approved under the new drug provisions of the FD&C Act). For example, a product may not carry the claim “cures cancer” or “treats arthritis.” Appropriate health claims authorized by the FDA—such as the claim linking folic acid to reduced risk of neural tube birth defects and the claim that calcium may reduce the risk of osteoporosis—may be made in supplement labeling if the product qualifies to bear the claim. Under the DSHEA, firms can make statements about classical nutrient deficiency diseases—as long as these statements disclose the prevalence of the disease in the United States. In addition, manufacturers may describe the supplement's effects on “structure or function” of the body or the “well-being” achieved by consuming the dietary ingredient. To use these claims, manufacturers must have substantiation that the statements are truthful and not misleading, and the product label must bear the statement “This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.” Unlike health claims, nutritional support statements need not be approved by the FDA before manufacturers market products bearing the statements; however, the agency must be notified no later than 30 days after a product that bears the claim is first marketed.

## INGREDIENT AND NUTRITION INFORMATION LABELING

Like other foods, dietary supplement products must bear ingredient labeling. This information must include the

name and quantity of each dietary ingredient or, for proprietary blends, the total quantity of all dietary ingredients (excluding inert ingredients) in the blend. The label must also identify the product as a “dietary supplement” (e.g., “Vitamin C Dietary Supplement”). Labeling of products containing herbal and botanical ingredients must state the part of the plant from which the ingredient is derived. If a supplement is covered by specifications in an official compendium and is represented as conforming, it is misbranded if it does not conform to those specifications. Official compendia include the U.S. Pharmacopeia, the Homeopathic Pharmacopeia of the United States, or the National Formulary. If not covered by a compendium, a dietary supplement must be the product identified on the label and have the strength it is represented as having.

Labels also must provide nutrition labeling. This labeling must first list dietary ingredients present in “significant amounts” for which the FDA has established daily consumption recommendations, followed by dietary ingredients with no daily intake recommendations. Dietary ingredients that are not present in significant amounts need not be listed. The nutrition labeling must include the quantity per serving for each dietary ingredient (or proprietary blend) and may include the source of a dietary ingredient (for example, “calcium from calcium gluconate”). If an ingredient is listed in the nutrition labeling, it need not appear in the statement of ingredients. Nutrition information must precede ingredient statements on the product label.

An example on the statement of identity (e.g., “ginseng”)

1. Net quantity of contents (e.g., “60 capsules”)
2. Structure-function claim and the statement “This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.”
3. Directions for use (e.g., “Take one capsule daily.”).
4. Supplement Facts panel (lists serving size, amount, and active ingredient).
5. Other ingredients in descending order of predominance and by common name or proprietary blend.
6. Name and place of business of manufacturer, packer, or distributor. This is the address to write for more product information.

## NEW DIETARY INGREDIENTS

Supplements may contain new dietary ingredients—those not marketed in the United States before October 15, 1994—only if those ingredients have been present in the food supply as an article used for food in a form in which the food has not been chemically altered or there is a history of use, or some other evidence of safety exists that establishes that there is a reasonable expectation of



safety when the product is used according to recommended conditions of use. Supplement manufacturers must notify the FDA at least 75 days before marketing products containing new dietary ingredients, providing the agency with the information on which the conclusion that a dietary supplement containing the new dietary ingredient “will reasonably be expected to be safe” was based. Any interested party, including a manufacturer of a dietary supplement, may petition the FDA to issue an order prescribing the conditions of use under which a new dietary ingredient will reasonably be expected to be safe.

## MONITORING FOR SAFETY

The FDA oversees safety, manufacturing and product information, such as claims in a product's labeling, package inserts, and accompanying literature. The Federal Trade Commission regulates the advertising of dietary supplements.

As with food, federal law requires manufacturers of dietary supplements to ensure that the products they put on the market are safe. But supplement manufacturers do not have to provide information to the FDA to get a product on the market. FDA review and approval of supplement ingredients and products is not required before marketing.

Unlike dietary supplements, food additives not generally recognized as safe must undergo the FDA's pre-market approval process for new food ingredients. This requires manufacturers to conduct safety studies and submit the results to the FDA for review before the ingredient can be used in marketed products. Based on its review, the FDA either authorizes or rejects the food additive.

Under DSHEA, once a dietary supplement is marketed, the FDA has the responsibility for showing that a dietary supplement is unsafe before it can take action to restrict the product's use. This was the case when, in June 1997, FDA proposed, among other things, to limit the amount of ephedrine alkaloids in dietary supplements (marketed as ephedra, Ma huang, Chinese ephedra, and ephedronin, for example) and provide warnings to consumers about hazards associated with use of dietary supplements containing the ingredients. The hazards ranged from nervousness, dizziness, and changes in blood pressure and heart rate to chest pain, heart attack, hepatitis, stroke, seizures, psychosis, and death. The proposal stemmed from the FDA's review of adverse event reports it had received, scientific literature, and public comments. The FDA has received many comments on the 1997 proposal and was reviewing them at press time.

Also in 1997, the FDA identified contamination of the herbal ingredient plantain with the harmful herb *Digitalis lanata* after receiving a report of a complete heart block in a young woman. FDA traced all use of the

contaminated ingredient and asked manufacturers and retailers to withdraw these products from the market.

## UNDERSTANDING CLAIMS

Claims that tout a supplement's healthful benefits have always been a controversial feature of dietary supplements. Manufacturers often rely on them to sell their products, but consumers often wonder whether they can trust them. Under the DSHEA and previous food labeling laws, supplement manufacturers are allowed to use, when appropriate, three types of claims: nutrient-content claims, disease claims, and nutrition support claims, which include “structure-function claims.”

Nutrient-content claims describe the level of a nutrient in a food or dietary supplement. For example, a supplement containing at least 200 milligrams of calcium per serving could carry the claim “high in calcium.” A supplement with at least 12 mg per serving of vitamin C could state on its label, “Excellent source of vitamin C.”

Disease claims show a link between a food or substance and a disease or health-related condition. The FDA authorizes these claims based on a review of the scientific evidence. Or, after the agency is notified, the claims may be based on an authoritative statement from certain scientific bodies, such as the National Academy of Sciences, that shows or describes a well-established diet-to-health link. As of this writing, certain dietary supplements may be eligible to carry disease claims, such as claims that show a link between the following:

1. The vitamin folic acid and a decreased risk of neural tube defect-affected pregnancy, if the supplement contains sufficient amounts of folic acid
2. Calcium and a lower risk of osteoporosis, if the supplement contains sufficient amounts of calcium
3. Psyllium seed husk (as part of a diet low in cholesterol and saturated fat) and coronary heart disease, if the supplement contains sufficient amounts of psyllium seed husk

Nutrition support claims can describe a link between a nutrient and the deficiency disease that can result if the nutrient is lacking in the diet. For example, the label of a vitamin C supplement could state that vitamin C prevents scurvy. When these types of claims are used, the label must mention the prevalence of the nutrient—deficiency disease in the United States.

These claims also can refer to the supplement's effect on the body's structure or function, including its overall effect on a person's well-being. These are known as structure—function claims.

The following are examples of structure-function claims:

1. Calcium builds strong bones.
2. Antioxidants maintain cell integrity.
3. Fiber maintains bowel regularity.

Manufacturers can use structure-function claims without FDA authorization. They base their claims on their review and interpretation of the scientific literature. Like all label claims, structure-function claims must be true and not misleading. Structure-function claims are easy to spot because, on the label, they must be accompanied with the disclaimer “This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.”

Manufacturers who plan to use a structure-function claim on a particular product must inform the FDA of the use of the claim no later than 30 days after the product is first marketed. While the manufacturer must be able to substantiate its claim, it does not have to share the substantiation with the FDA or make it publicly available. If the submitted claims promote the products as drugs instead of supplements, the FDA can advise the manufacturer to change or delete the claim.

Because there often is a fine line between disease claims and structure-function claims, the FDA has established criteria under which a label claim would or would not qualify as a disease claim. Among label factors are these:

1. The naming of a specific disease or class of diseases
2. The use of scientific or lay terminology to describe the product's effect on one or more signs or symptoms recognized by healthcare professionals and consumers as characteristic of a specific disease or a number of different specific diseases
3. Product name
4. Statements about product formulation
5. Citations or references that refer to disease
6. Use of the words *disease* or *diseased*
7. Art, such as symbols and pictures
8. Statements that the product can substitute for an approved therapy (for example, a drug)

If shoppers find dietary supplements whose labels state or imply that the product can help diagnose, treat, cure, or prevent a disease (for example, “cures cancer” or “treats arthritis”), they should realize that the product is being marketed illegally as a drug and as such has not been evaluated for safety or effectiveness.

The FTC regulates claims made in the advertising of dietary supplements, and in recent years, that agency has taken a number of enforcement actions against companies whose advertisements contained false and misleading information. The actions targeted, for example, erroneous claims that chromium picolinate was a treatment for weight loss and high blood cholesterol. An action in 1997 targeted ads for an ephedrine alkaloid supplement because they understated the degree of the product's risk and featured a man falsely described as a doctor.

## PROGRESS CHECK ON ACTIVITY 1

### FILL-IN

1. The label of a dietary supplement should include:
  - a. \_\_\_\_\_
  - b. \_\_\_\_\_
  - c. \_\_\_\_\_
  - d. \_\_\_\_\_
  - e. \_\_\_\_\_
  - f. \_\_\_\_\_
2. Under the DSHEA and previous food labeling laws, supplement manufacturers are allowed to use, when appropriate, which three types of claims:
  - a. \_\_\_\_\_
  - b. \_\_\_\_\_
  - c. \_\_\_\_\_
3. Labels of dietary supplement include two portions:
  - a. \_\_\_\_\_
  - b. \_\_\_\_\_

### MULTIPLE CHOICE

Circle the letter of the correct answer.

4. An official compendium applicable to dietary supplements can be which of the following:
  - a. U.S. Pharmacopeia
  - b. Homeopathic Pharmacopeia of the United States
  - c. National Formulary
  - d. All of the above
5. A supplement that carries the claim “high in calcium” should have, per serving, at least:
  - a. 100 milligrams of calcium
  - b. 200 milligrams of calcium
  - c. 400 milligrams of calcium

### TRUE/FALSE

Circle T for True and F for False.

6. T F The FDA is authorized to test dietary supplements.
7. T F Under the DSHEA, firms cannot make statements about classical nutrient deficiency diseases—even though these statements disclose the prevalence of the disease in the United States.

8. T F Manufacturers using health claims must have substantiation that the statements are truthful and not misleading and the product label must bear the statement “This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.”
9. T F Ingredient and nutrition information labeling of dietary supplements are strictly regulated.
10. T F Ingredients listed in the nutrition label of a dietary supplement must also appear in the ingredient label.
11. T F Supplement suppliers have the burden to show that new ingredients in their dietary supplements are reasonably safe.
12. T F The Federal Trade Commission regulates the advertising of dietary supplements.
13. T F FDA review and approval of supplement ingredients and products is not required before marketing.
14. T F Food additives not generally recognized as safe must undergo the FDA’s premarket approval process for new food ingredients.
15. T F Under the DSHEA, once a dietary supplement is marketed, the FDA has the responsibility for showing that a dietary supplement is unsafe before it can take action to restrict the product’s use.
16. T F Calcium can be claimed to have a link with a lower risk of osteoporosis, if the supplement contains sufficient amounts of calcium.
17. T F Nutrient-content claims describe the level of a nutrient in a food or dietary supplement.
18. T F When nutrition support claims are used, the label must mention the prevalence of the nutrient-deficiency disease in the United States.
19. T F Structure-function claims refers to the supplement’s effect on the body’s structure or function, including its overall effect on a person’s well-being.

## ACTIVITY 2:

### Folate or Folic Acid

For basic information on this vitamin, consult Chapter 5. The information in this activity has been modified from fact sheets distributed by the Office of Dietary Supplements, National Institutes of Health.

Folate and folic acid are forms of a water-soluble B vitamin. Folate occurs naturally in food. Folic acid is the synthetic form of this vitamin that is found in supplements and fortified foods. Folate gets its name from the Latin word *folium* for *leaf*. A key observation of researcher Lucy Wills nearly 70 years ago led to the iden-

tification of folate as the nutrient needed to prevent the anemia of pregnancy. Dr. Wills demonstrated that the anemia could be corrected by a yeast extract. Folate was identified as the corrective substance in yeast extract in the late 1930s and was extracted from spinach leaves in 1941. Folate is necessary for the production and maintenance of new cells. This effect is especially important during periods of rapid cell division and growth such as infancy and pregnancy. Folate is needed to make DNA and RNA, the building blocks of cells. It also helps prevent changes to DNA that may lead to cancer.

Both adults and children need folate to make normal red blood cells and prevent anemia. Leafy greens such as spinach and turnip greens, dry beans and peas, fortified cereals and grain products, and some fruits and vegetables are rich food sources of folate. Some breakfast cereals (ready-to-eat and others) are fortified with 25% or 100% of the Daily Value (DV) for folic acid.

### NEED FOR EXTRA FOLIC ACID

Women of childbearing age, people who abuse alcohol, anyone taking anticonvulsants or other medications that interfere with the action of folate, individuals diagnosed with anemia from folate deficiency, and individuals with malabsorption, liver disease, or who are receiving kidney dialysis treatment may benefit from a folic acid supplement. Folic acid is very important for all women who may become pregnant. Adequate folate intake during the periconceptual period, the time just before and just after a woman becomes pregnant, protects against a number of congenital malformations including neural tube defects. Neural tube defects result in malformations of the spine (spina bifida), skull, and brain (anencephaly). The risk of neural tube defects is significantly reduced when supplemental folic acid is consumed in addition to a healthful diet prior to and during the first month following conception. Women who could become pregnant are advised to eat foods fortified with folic acid or take supplements in addition to eating folate-rich foods to reduce the risk of some serious birth defects. Taking 400 micrograms of synthetic folic acid daily from fortified foods and/or supplements has been suggested.

### VITAMIN B<sub>12</sub> AND FOLIC ACID

Folic acid supplements can correct the anemia associated with vitamin B<sub>12</sub> deficiency. Unfortunately, folic acid will not correct changes in the nervous system that result from vitamin B<sub>12</sub> deficiency. Permanent nerve damage can occur if vitamin B<sub>12</sub> deficiency is not treated. Intake of supplemental folic acid should not exceed 1000 micrograms (mcg) per day to prevent folic acid from masking symptoms of vitamin B<sub>12</sub> deficiency. It is very important for older adults to be aware of the relationship between

folic acid and vitamin B<sub>12</sub> because they are at greater risk of having a vitamin B<sub>12</sub> deficiency. Persons 50 years of age or older should ask their physicians to check B<sub>12</sub> status before taking a supplement that contains folic acid.

## FOLIC ACID, HEART DISEASE, AND CANCER

A deficiency of folate, vitamin B<sub>12</sub>, or vitamin B<sub>6</sub> may increase the level of homocysteine, an amino acid normally found in your blood. There is evidence that an elevated homocysteine level is an independent risk factor for heart disease and stroke. The evidence suggests that high levels of homocysteine may damage coronary arteries or make it easier for blood clotting cells called platelets to clump together and form a clot. However, there is currently no evidence available to suggest that lowering homocysteine with vitamins will reduce the risk of heart disease. Clinical intervention trials are needed to determine whether supplementation with folic acid, vitamin B<sub>12</sub>, or vitamin B<sub>6</sub> can lower the risk of developing coronary heart disease.

Some evidence associates low blood levels of folate with a greater risk of cancer. Folate is involved in the synthesis, repair, and functioning of DNA, our genetic map, and a deficiency of folate may result in damage to DNA that may lead to cancer. Several studies have associated diets low in folate with increased risk of breast, pancreatic, and colon cancer. Findings from a study of over 121,000 nurses suggested that long-term folic acid supplementation (for 15 years) was associated with a decreased risk of colon cancer in women aged 55 to 69 years of age. However, associations between diet and disease do not indicate a direct cause. Researchers are continuing to investigate whether enhanced folate intake from foods or folic acid supplements may reduce the risk of cancer. Until results from such clinical trials are available, folic acid supplements should not be recommended to reduce the risk of cancer.

## FOLIC ACID AND METHOTREXATE FOR CANCER

Folate is important for cells and tissues that rapidly divide. Cancer cells divide rapidly, and drugs that interfere with folate metabolism are used to treat cancer. Methotrexate is a drug often used to treat cancer because it limits the activity of enzymes that need folate. Unfortunately, methotrexate can be toxic, producing side effects such as inflammation in the digestive tract that make it difficult to eat normally. Leucovorin is a form of folate that can help “rescue” or reverse the toxic effects of methotrexate. It is not known whether folic acid supplements can help control the side effects of methotrexate without decreasing its effectiveness in chemotherapy. It is important for anyone receiving methotrexate to follow a medical doctor’s advice on the use of folic acid supplements.

## FOLIC ACID AND METHOTREXATE FOR NONCANCEROUS DISEASES

Low-dose methotrexate is used to treat a wide variety of noncancerous diseases such as rheumatoid arthritis, lupus, psoriasis, asthma, sarcoidosis, primary biliary cirrhosis, and inflammatory bowel disease. Low doses of methotrexate can deplete folate stores and cause side effects that are similar to folate deficiency. Both high-folate diets and supplemental folic acid may help reduce the toxic side effects of low-dose methotrexate without decreasing its effectiveness. Anyone taking low-dose methotrexate for the health problems listed here should consult with a physician about the need for a folic acid supplement.

## HEALTH RISK

The risk of toxicity from folic acid is low. The Institute of Medicine has established a tolerable upper intake level (UL) for folate of 1000 mcg for adult men and women, and a UL of 800 mcg for pregnant and lactating (breast-feeding) women less than 18 years of age. Supplemental folic acid should not exceed the UL to prevent folic acid from masking symptoms of vitamin B<sub>12</sub> deficiency.

## PROGRESS CHECK ON ACTIVITY 2

### TRUE/FALSE

1. T F Folate and folic acid are forms of a fat-soluble B vitamin.
2. T F Folate does not occur naturally in food.
3. T F Folate was identified as the corrective substance in yeast extract in the late 1930s and was extracted from spinach leaves in 1941.
4. T F Folate is not needed to make DNA and RNA, the building blocks of cells, but it helps prevent changes to DNA that may lead to cancer.
5. T F Breakfast cereals (ready-to-eat and others) are required to be fortified with folic acid.
6. T F Folic acid is only important for all women who may become pregnant.
7. T F The risk of neural tube defects is significantly reduced when supplemental folic acid is consumed in addition to a healthful diet prior to and during the first month following conception.
8. T F Folic acid supplements can correct the anemia associated with vitamin B<sub>12</sub> deficiency but not correct changes in the nervous system that result from vitamin B<sub>12</sub> deficiency.
9. T F Intake of supplemental folic acid should not exceed 1000 micrograms (mcg) per day to prevent folic acid from masking symptoms of vitamin B<sub>12</sub> deficiency.



10. T F There is evidence that an elevated homocysteine level is a dependent risk factor for heart disease and stroke.
11. T F Folic acid supplements can help control the side effects of methotrexate without decreasing its effectiveness in chemotherapy.
12. T F Low doses of methotrexate can deplete folate stores and cause side effects that are similar to folate deficiency.
13. T F A megadose of folic acid may be toxic.

#### FILL-IN

14. List seven groups of people who may benefit from folic acid supplementation.
  - a. \_\_\_\_\_
  - b. \_\_\_\_\_
  - c. \_\_\_\_\_
  - d. \_\_\_\_\_
  - e. \_\_\_\_\_
  - f. \_\_\_\_\_
  - g. \_\_\_\_\_
15. Neural tube defects caused by folate deficiency result in malformations of the:
  - a. \_\_\_\_\_
  - b. \_\_\_\_\_
  - c. \_\_\_\_\_
16. The recommended daily intake of folic acid either from fortified foods and/or supplemented (synthetic) folic acid is \_\_\_\_\_.

### ACTIVITY 3:

#### Kava Kava, *Ginkgo Biloba*, Goldenseal, Echinacea, Comfrey, and Pulegone

Currently, there are thousands of botanicals being sold as dietary supplements. This chapter is not the proper forum to discuss all of them. Rather, six popular ones are discussed here. To make sure that the information is based on science and not testimony, the data have been derived from the following government documents:

1. National Institutes of Health, Office of Dietary Supplements
2. National Institutes of Health, National Toxicology Program
3. National Institutes of Health, National Institute of Aging

The six commercial dietary supplements discussed in this activity are kava kava, *Ginkgo biloba*, goldenseal, echinacea, comfrey, and pulegone.

#### KAVA KAVA

On March 25, 2002, the Food and Drug Administration (FDA) issued the following warning:

The FDA is advising consumers of the potential risk of severe liver injury associated with the use of kava-containing dietary supplements. Kava *Piper methysticum* is a plant indigenous to the islands in the South Pacific where it is commonly used to prepare a traditional beverage. Supplements containing the herbal ingredient kava are promoted for relaxation (e.g., to relieve stress, anxiety, and tension), sleeplessness, menopausal symptoms, and other uses. The FDA has not made a determination about the ability of kava dietary supplements to provide such benefits.

Liver-related risks associated with the use of kava have prompted regulatory agencies in other countries, including those in Germany, Switzerland, France, Canada, and the United Kingdom, to take action ranging from warning consumers about the potential risks of kava use to removing kava-containing products from the marketplace. Although liver damage appears to be rare, the FDA believes consumers should be informed of this potential risk.

Kava-containing products have been associated with liver-related injuries—including hepatitis, cirrhosis, and liver failure—in over 25 reports of adverse events in other countries. Four patients required liver transplants. In the United States, the FDA has received a report of a previously healthy young female who required liver transplantation, as well as several reports of liver-related injuries.

Given these reports, people who have liver disease or liver problems, or people who are taking drug products that can affect the liver, should consult a physician before using kava-containing supplements.

Consumers who use a kava-containing dietary supplement and who experience signs of illness associated with liver disease should also consult their physician. Symptoms of serious liver disease include jaundice (yellowing of the skin or whites of the eyes) and brown urine. Nonspecific symptoms of liver disease can include nausea, vomiting, light-colored stools, unusual tiredness, weakness, stomach or abdominal pain, and loss of appetite.

The FDA urges consumers and their healthcare professionals to report any cases of liver and other injuries that may be related to the use of kava-containing dietary supplements. Adverse events associated with the use of dietary supplements should be reported as soon as possible.

The presence of kava in a supplement should be identified on the product label in the Supplement Facts box. The following are commonly used names for kava:

ava  
 ava pepper  
 awa  
 intoxicating pepper  
 kava  
 kava kava  
 kava pepper  
 kava root  
 kava-kava  
 kawa  
 kawa kawa  
 kawa-kawa  
 kew  
*Piper methysticum*  
*Piper methysticum* Forst.f.  
*Piper methysticum* G. Forst.  
 rauschpfeffer  
 sakau  
 tonga  
 wurzelstock  
 yangona

The FDA will continue to investigate the relationship, if any, between the use of dietary supplements containing kava and liver injury. The agency's investigation includes attempting to determine a biological explanation for the relationship and to identify the different sources of kava in the United States and Europe. The agency will alert consumers, and if warranted, take additional action as more information becomes available.

## GINKGO BILOBA

### Introduction

*Ginkgo biloba*, a readily available natural product, has been the focus of recent media reports as a potential treatment for Alzheimer's disease. Although a 1997 study in the United States suggests that a ginkgo extract may be of some help in treating the symptoms of Alzheimer's disease and vascular dementia, there is no evidence that *Ginkgo biloba* will cure or prevent Alzheimer's disease.

In addition, some recent case studies imply that daily use of *Ginkgo biloba* extracts may cause side effects, such as excessive bleeding, especially when combined with daily use of aspirin. Much more research is needed before scientists will know whether and how *Ginkgo biloba* extracts benefit people.

### Research Outside of the United States

For centuries, extracts from the leaves of the ginkgo tree have been used as Chinese herbal medicine to treat a va-

riety of medical conditions. In Europe and some Asian countries, standardized extracts from ginkgo leaves are taken to treat a wide range of symptoms, including dizziness, memory impairment, inflammation, and reduced blood flow to the brain and other areas of impaired circulation. Because *Ginkgo biloba* is an antioxidant, some claims have been made that it can be used to prevent damage caused by free radicals (harmful oxygen molecules). Although Germany recently approved ginkgo extracts (240 mg a day) to treat Alzheimer's disease, there is not enough information to recommend its broad use.

### Research in the United States

Researchers at the New York Institute for Medical Research in Tarrytown, New York, conducted the first clinical study of *Ginkgo biloba* and dementia in the United States. Their findings were published in the *Journal of the American Medical Association* (October 22/29, 1997). These scientists examined how taking 120 mg a day of a *Ginkgo biloba* extract affected the rate of cognitive decline in people with mild to moderately severe dementia caused by Alzheimer's disease and vascular dementia. At the end of the study, they reported a small treatment difference in people given the *Ginkgo biloba* extract.

Three tests were used to measure changes in the condition of participants. First, participants showed a slight improvement on a test that measured their cognitive function (mental processes of knowing, thinking, and learning). Second, participants showed a slight improvement on a test that measured social behavior and mood changes that were observed by their caregivers. Third, participants showed no improvement on a doctor's assessment of change test.

Because 60% of the people did not complete the study, findings are difficult to interpret and may even be distorted. In addition, this study did not address the effect of *Ginkgo biloba* on delaying or preventing the onset of Alzheimer's disease or vascular dementia. The researchers recommend more investigation to accomplish the following: determine if these findings are valid, understand how *Ginkgo biloba* works on brain cells, and identify an effective dosage and potential side effects.

The extract of the ginkgo leaf contains a balance of flavone glycosides (including one suspected high-dose carcinogen, quercetin) and terpene lactones. Other claims are as follows: Ginkgo acts as a blood thinner; it improves circulation and is therefore used to treat migraine headaches, depression, and a range of lung and heart problems.

People should consult with their family doctors before using *Ginkgo biloba* extracts. This recommendation is especially true for those with disorders in blood circulation or blood clotting and those taking anticoagulants such as aspirin. Many different preparations of *Ginkgo*

*biloba* extract are available over the counter. They vary in content and active ingredients. Because not enough research has been done, no specific daily amount of a *Ginkgo biloba* extract can be recommended as safe or effective at this time.

## GOLDENSEAL

The root of the goldenseal plant is traditionally used to treat wounds, ulcers, digestive problems, and eye and ear infections. Today, the herb is also used as a laxative, tonic, and diuretic. Goldenseal is used in feminine products such as vaginal douches and is claimed to help with menstrual disorders such as irregular cycle and excessive bleeding. Berberine, one of the chief active components in goldenseal, has antimicrobial and vasodilatory properties and may also be effective in preventing the growth of cancer cells. The other major component of goldenseal, hydrastine (which can be made from berberine), has abortifacient effects and has been shown to induce labor in pregnant women when taken orally. Large internal doses of goldenseal may cause convulsions and irritation of the mouth, throat, and stomach, tingling of the skin, paralysis, respiratory failure, and possibly death at very high doses. Chronic use may inhibit vitamin B absorption.

At present goldenseal is being studied by the federal health authorities and clinical experts to determine its effectiveness, safety, and toxicology.

## ECHINACEA

This member of the daisy family is one of the top medicinal herb sellers in the United States. Although once used for everything from snakebites to typhoid, echinacea as a dietary supplement is most commonly used today as an immunostimulant to treat the common cold, sore throat, and flu. Echinacea is not known to have any serious adverse side effects, although there have been reports of skin rash and insomnia among users. The herb is available in many forms—dried root or leaf, liquid extract, powder, capsules, tablets, creams, gels, and injections (outside of North America). It has yet to be determined how echinacea is best administered or exactly how—or if—the plant's complex mixture of polysaccharides, flavonoids, essential oils, and other compounds actually produces beneficial effects. Again, this dietary supplement is being studied for its clinical effect and safety.

## COMFREY

Certain dietary supplements contain the herbal ingredient comfrey *Symphytum officinale* (common comfrey), *S. asperum* (prickly comfrey), and *S. x uplandicum* (Russian comfrey). Claims have been made about comfrey.

Applied externally, comfrey acts as an anti-inflammatory to promote healing of bruises, sprains, and open wounds. The roots and leaves of the plant contain the protein allantoin, which stimulates cell proliferation. Comfrey is said to help wounds to heal and broken bones to knit. It is also taken internally as an herbal tea to treat gastric ulcers, rheumatic pain, arthritis, bronchitis, and colitis. This ingestion is a matter of some concern because comfrey contains several pyrrolizidine alkaloids, primarily symphytine, which have been linked to liver and lung cancer in rats. The hepatotoxic effects of pyrrolizidine alkaloids are well established in both animals and humans.

The use of comfrey in dietary supplements is a serious concern to the FDA. These plants contain pyrrolizidine alkaloids, substances that are firmly established to be hepatotoxins in animals. Reports in the scientific literature clearly associate oral exposure of comfrey and pyrrolizidine alkaloids with the occurrence of veno-occlusive disease (VOD) in animals. Moreover, outbreaks of hepatic VOD have been reported in other countries over the years, and the toxicity of these substances in humans is generally accepted. The use of products containing comfrey has also been implicated in serious adverse incidents over the years in the United States and elsewhere. However, while information is generally lacking to establish a cause-effect relationship between comfrey ingestion and observed adverse effects humans, the adverse effects that have been seen are entirely consistent with the known effects of comfrey ingestion that have been described in the scientific literature. The pyrrolizidine alkaloids that are present in comfrey, in addition to being potent hepatotoxins, have also been shown to be toxic to other tissues as well. There is also evidence that implicates these substances as carcinogens. Taken together, the clear evidence of an association between oral exposure to pyrrolizidine alkaloids and serious adverse health effects and the lack of any valid scientific data that would enable the agency to determine whether there is an exposure, if any, that would present no harm to consumers, indicates that this substance should not be used as an ingredient in dietary supplements.

Since 2000, the position of the FDA is as follows:

1. The FDA believes that the available scientific information is sufficient to firmly establish that dietary supplements that contain comfrey or any other source of pyrrolizidine alkaloids are adulterated under the act.
2. The FDA strongly recommends that firms marketing a product containing comfrey or another source of pyrrolizidine alkaloids remove the product from the market and alert its customers to immediately stop using the product.
3. The FDA is prepared to use its authority and resources to remove products from the market that appear to violate the act.

4. The FDA believes that manufacturers need to take adequate steps to identify and report adverse events, especially adverse events that may include liver disorders, associated with any product that has an ingredient that may contain pyrrolizidine alkaloids.

Further, since 2000, the Federal Trade Commission (FTC) has also taken action against unsafe products containing comfrey. The FTC is against the marketing of any comfrey-containing product intended for internal use or use on open wounds and requires a warning on comfrey products marketed for external uses.

## PULEGONE

Pulegone is the active ingredient in pennyroyal and is also found in several other species of mint. Pennyroyal is traditionally used as a carminative, insect repellent, emmenagogue, and abortifacient. Prior studies have demonstrated hepatic, renal, and pulmonary toxicity in humans, as well as central nervous system toxicity resulting in seizure, coma, and death. Pulegone is toxic to the developing fetus.

### PROGRESS CHECK ON ACTIVITY 3

#### FILL-IN

- Name five commercial dietary supplements:
  - \_\_\_\_\_
  - \_\_\_\_\_
  - \_\_\_\_\_
  - \_\_\_\_\_
  - \_\_\_\_\_
- Name five commonly used names for *Piper methylicum*:
  - \_\_\_\_\_
  - \_\_\_\_\_
  - \_\_\_\_\_
  - \_\_\_\_\_
  - \_\_\_\_\_

#### TRUE/FALSE

Circle T for True and F for False.

- T F Kava has been used by Pacific islanders for centuries. Therefore kava-containing supplements have no side effects.
- T F Supplements containing kava are effective for relaxation, sleeplessness, and menopausal symptoms.

- T F Dietary supplements are considered as safe by manufacturers. Therefore, consumers do not need to consult a physician before using them.
- T F *Ginkgo biloba* is effective in preventing Alzheimer's disease.
- T F Daily use of *Ginkgo biloba* extracts is safe when used with other medications.
- T F *Ginkgo biloba* is an antioxidant, and can prevent damage caused by free radicals.
- T F Taking 120 mg a day of a *Ginkgo biloba* extract may affect the rate of cognitive decline in people with mild to moderately severe dementia caused by Alzheimer's disease and vascular dementia.
- T F Goldenseal root should not be taken by pregnant women.
- T F Goldenseal root has antimicrobial properties and is therefore useful in treating eye and ear infections.
- T F Echinacea as a dietary supplement is most commonly used today as an immunostimulant to treat the common cold, sore throat, and flu.
- T F Comfrey is safe when it is used for external treatment of wounds.
- T F The main pyrrolizidine alkaloid in comfrey, symphytine, is hepatotoxic and carcinogenic.
- T F Ingestion of pennyroyal can be fatal as it affects the central nervous system resulting in seizure and coma.
- T F Pennyroyal should not be taken by pregnant women as it is toxic to a developing fetus.

## ACTIVITY 4:

### An Example of Side Effects from Medications for Hyperactivity

In the March-April 2002 issue of the *FDA Consumer* magazine, the FDA published an article titled "Tips for the savvy supplement user: Making informed decisions." A slightly modified version is presented here.

The choice to use a dietary supplement can be a wise decision that provides health benefits. However, under certain circumstances, these products may be unnecessary for good health, or they may even create unexpected risks.

Clearly, people choosing to supplement their diets with herbals, vitamins, minerals, or other substances want to know more about the products they choose so that they can make informed decisions about them. Given the abundance and conflicting nature of information now available about dietary supplements, you may need help to sort the reliable information from the questionable. The FDA has prepared these tips and resources to help you become a savvy dietary supplement user. The principles underlying these tips are similar to those principles a savvy consumer would use for any product.



Do I need to think about my total diet?

Yes. Dietary supplements are intended to supplement the diets of some people but not to replace the balance of the variety of foods important to a healthy diet. While you need enough nutrients, too much of some nutrients can cause problems. You can find information on the functions and potential benefits of vitamins and minerals, as well as upper safe limits for nutrients from many nonprofit organizations such as government agencies (e.g., the FDA), university extension offices, American Dietetic Association, and so on, including Chapters 3 to 7 in this book.

Should I check with my doctor or healthcare provider before using a supplement?

This is a good idea, especially for certain population groups. Dietary supplements may not be risk-free under certain circumstances:

- If you are pregnant, nursing a baby, or have a chronic medical condition, such as diabetes, hypertension or heart disease, be sure to consult your doctor or pharmacist before purchasing or taking any supplement.
- While vitamin and mineral supplements are widely used and generally considered safe for children, you may wish to check with your doctor or pharmacist before giving these or any other dietary supplements to your child.
- If you plan to use a dietary supplement in place of drugs or in combination with any drug, tell your healthcare provider first. Many supplements contain active ingredients that have strong biological effects, and their safety is not always assured in all users.
- If you have certain health conditions and take these products, you may be placing yourself at risk.
- Some supplements may interact with prescription and over-the-counter (OTC) medicines. Taking a combination of supplements or using these products together with medications (whether prescription or OTC drugs) could, under certain circumstances, produce adverse effects, some of which could be life threatening.

Be alert to advisories about these products, whether taken alone or in combination. For example, Coumadin (a prescription medicine), *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. Combining St.-John's-wort with certain HIV drugs significantly reduces their effectiveness. St.-John's-wort may also reduce the effectiveness of prescription drugs for heart disease, depression, seizures, certain cancers, or oral contraceptives.

Some supplements can have unwanted effects during surgery. It is important to fully inform your doctor about the vitamins, minerals, herbals, or any other supplements you are taking, especially before elective surgery. You may be asked to stop taking these products at least 2 to

3 weeks ahead of the procedure to avoid potentially dangerous supplement/drug interactions—such as changes in heart rate and blood pressure or increased bleeding—that could adversely affect the outcome of your surgery.

Who is responsible for ensuring the safety and efficacy of dietary supplements?

Under the law, manufacturers of dietary supplements are responsible for making sure their products are safe before they go to market. Manufacturers are also responsible for determining that the claims on their labels are accurate and truthful. Dietary supplement products are not reviewed by the government before they are marketed, but the FDA can take action against any unsafe dietary supplement product that reaches the market. If the FDA can prove that claims on marketed dietary supplement products are false and misleading, the agency may take action against these products.

When searching the Web for information about dietary supplements, try using directory sites of respected organizations, rather than doing blind searches with a search engine. Ask yourself the following questions:

- Who operates the site?
- Is the site run by the government, a university, or a reputable medical or health-related association (such as the American Medical Association, American Diabetes Association, American Heart Association, American Dietetic Association, National Institutes of Health, National Academy of Sciences, or the FDA)?
- Is the information written or reviewed by qualified health professionals, experts in the field, academia, government, or the medical community?
- What is the purpose of the site?
- Is the purpose of the site to objectively educate the public or just to sell a product?

Be aware of practitioners or organizations whose main interest is in marketing products, either directly or through sites with which they are linked. Commercial sites should clearly distinguish scientific information from advertisements. Most nonprofit and government sites contain no advertising, and access to the site and materials offered are usually free.

- What is the source of the information and does it have any references?
- Has the study been reviewed by recognized scientific experts and published in reputable peer-reviewed scientific journals, such as the *New England Journal of Medicine*?
- Does the information say “some studies show . . .” or does it state where the study is listed so that you can check the authenticity of the references? For example, can the study be found in the National Library of Medicine’s database of literature citations?
- Is the information current? Check the date when the material was posted or updated. Often new research or

other findings are not reflected in old material, for example, side effects or interactions with other products or new evidence that might have changed earlier thinking. Ideally, health and medical sites should be updated frequently.

- How reliable are the Internet and e-mail solicitations? While the Internet is a rich source of health information, it is also an easy vehicle for spreading myths, hoaxes, and rumors about alleged news, studies, products, or findings. To avoid falling prey to such hoaxes, be skeptical and watch out for overly emphatic language with UPPERCASE LETTERS and lots of exclamation points!!!! Beware of such phrases such as: “This is not a hoax” or “Send this to everyone you know.”

## MORE TIPS AND TO-DO'S

Ask yourself:

- Does it sound too good to be true?
- Do the claims for the product seem exaggerated or unrealistic?
- Are there simplistic conclusions being drawn from a complex study to sell a product?

While the Web can be a valuable source of accurate, reliable information, it also has a wealth of misinformation that may not be obvious. Learn to distinguish hype from evidence-based science. Nonsensical lingo can sound very convincing. Also, be skeptical about anecdotal information from people who have no formal training in nutrition or botanicals, or personal testimonials (from store employees, friends, or online chat rooms and message boards) about incredible benefits or results obtained from using a product. Question these people on their training and knowledge in nutrition or medicine.

Think twice about chasing the latest headline. Sound health advice is generally based on a body of research, not a single study. Be wary of results claiming a “quick fix” that depart from previous research and scientific beliefs. Keep in mind science does not proceed by dramatic breakthroughs, but by taking many small steps, slowly building towards a consensus. Furthermore, news stories about the latest scientific study, especially those on TV or radio, are often too brief to include important details that may apply to you or allow you to make an informed decision.

Check your assumptions about the following:

Questionable Assumption 1: “Even if a product may not help me, at least it won’t hurt me.” It’s best not to assume that this will always be true. When consumed in high enough amounts, for a long enough time, or in combination with certain other substances, all chemicals can be toxic, including nutrients, plant components, and other biologically active ingredients.

Questionable Assumption 2: “When I see the term ‘natural,’ it means that a product is healthful and

safe.” Consumers can be misled if they assume this term assures wholesomeness, or that these foodlike substances necessarily have milder effects, which makes them safer to use than drugs. The term *natural* on labels is not well defined and is sometimes used ambiguously to imply unsubstantiated benefits or safety. For example, many weight-loss products claim to be “natural” or “herbal,” but this doesn’t necessarily make them safe. Their ingredients may interact with drugs or may be dangerous for people with certain medical conditions.

Questionable Assumption 3: “A product is safe when there is no cautionary information on the product label.” Dietary supplement manufacturers may not necessarily include warnings about potential adverse effects on the labels of their products. If consumers want to know about the safety of a specific dietary supplement, they should contact the manufacturer of that brand directly. It is the manufacturer’s responsibility to determine that the supplement it produces or distributes is safe and that there is substantiated evidence that the label claims are truthful and not misleading.

Questionable Assumption 4: “A recall of a harmful product guarantees that all such harmful products will be immediately and completely removed from the marketplace.” A product recall of a dietary supplement is voluntary, and, while many manufacturers do their best, a recall does not necessarily remove all harmful products from the marketplace. Contact the manufacturer for more information about the specific product that you are purchasing. If you cannot tell whether the product you are purchasing meets the same standards as those used in the research studies you read about, check with the manufacturer or distributor. Ask to speak to someone who can address your questions, some of which may include: What information does the firm have to substantiate the claims made for the product? Be aware that sometimes firms supply so-called proof of their claims by citing undocumented reports from satisfied consumers, or “internal” graphs and charts that could be mistaken for evidence-based research. Does the firm have information to share about tests it has conducted on the safety or efficacy of the ingredients in the product? Does the firm have a quality control system in place to determine if the product actually contains what is stated on the label and is free of contaminants? Has the firm received any adverse event reports from consumers using their products?

## NURSING IMPLICATIONS

When a nurse is caring for a patient who is involved with dietary supplements (using them, intending to use them,

or asking questions about them), the major nursing implication is mainly patient education.

1. Be prepared to teach clients how to do the following:
  - a. Detect fraudulent products and deceptive advertising.
  - b. Purchase quality products if they intend to use supplements.
  - c. Read product labels.
  - d. File a report if side effects are experienced.
  - e. Recognize that dietary supplements can cause harm, the reasons they can be harmful, and the types of reactions that may occur.
  - f. Reduce the chances of suffering adverse effects from supplement use.
2. Counsel patients to seek expert advice from their physicians before beginning any supplement regime.

The following information will assist you in preparing a teaching plan.

### Fraudulent Products

Consumers need to be on the lookout for fraudulent products. These are products that don't do what they say they can or don't contain what they say they contain. At the very least, they waste consumers' money, and they may cause physical harm.

Fraudulent products often can be identified by the types of claims made in their labeling, advertising, and promotional literature. Some possible indicators of fraud, according to the National Council Against Health Fraud, are the following:

1. Claims that the product is a secret cure and use of such terms as *breakthrough*, *magical*, *miracle cure*, and *new discovery*. If the product were a cure for a serious disease, it would be widely reported in the media and used by healthcare professionals.
2. "Pseudomedical" jargon, such as *detoxify*, *purify*, and *energize* to describe a product's effects. These claims are vague and hard to measure, and so they make it easier for success to be claimed.
3. Claims that the product can cure a wide range of unrelated diseases. No product can do that.
4. Claims that a product is backed by scientific studies but with no list of references or references that are inadequate. For instance, if a list of references is provided, the citations cannot be traced, or if they are traceable, the studies are out-of-date, irrelevant, or poorly designed.
5. Claims that the supplement has only benefits-and no side effects. A product "potent enough to help people will be potent enough to cause side effects."
6. Accusations that the medical profession, drug companies, and the government are suppressing information about a particular treatment. It would be illogical for large numbers of people to withhold information

about potential medical therapies when they or their families and friends might one day benefit from them.

Though often more difficult to do, consumers also can protect themselves from economic fraud, a practice in which the manufacturer substitutes part or all of a product with an inferior, cheaper ingredient and then passes off the fake product as the real thing but at a lower cost. Avoid products sold for considerably less money than competing brands.

### Quality Products

Poor manufacturing practices are not unique to dietary supplements, but the growing market for supplements in a less restrictive regulatory environment creates the potential for supplements to be prone to quality-control problems. For example, the FDA has identified several problems where some manufacturers were buying herbs, plants, and other ingredients without first adequately testing them to determine whether the product they ordered was actually what they received or whether the ingredients were free from contaminants.

To help protect themselves, consumers should do the following:

1. Look for ingredients in products with the U.S.P. notation, which indicates the manufacturer followed standards established by the U.S. Pharmacopoeia.
2. Realize that the label term *natural* doesn't guarantee that a product is safe. Think of poisonous mushrooms—they are natural.
3. Consider the name of the manufacturer or distributor. Supplements made by a nationally known food and drug manufacturer, for example, have likely been made under tight controls because these companies already have in place manufacturing standards for their other products.
4. Write to the supplement manufacturer for more information. Ask the company about the conditions under which its products were made.

### Reading and Reporting

Consumers who use dietary supplements should always read product labels, follow directions, and heed all warnings.

Supplement users who suffer a serious harmful effect or illness that they think is related to supplement use should call a doctor or other healthcare provider. He or she in turn can report it to the FDA. To file a report, consumers will be asked to provide:

1. Name, address, and telephone number of the person who became ill
2. Name and address of the doctor or hospital providing medical treatment
3. Description of the problem
4. Name of the product and store where it was bought

Consumers also should report the problem to the manufacturer or distributor listed on the product's label and to the store where the product was bought.

### Expert Advice

Before starting a dietary supplement, it is always wise to check with a medical doctor. It is especially important for people who have the following characteristics:

1. Pregnant or breastfeeding
2. Chronically ill
3. Elderly
4. Under 18
5. Taking prescription or over-the-counter medicines. Certain supplements can boost blood levels of certain drugs to dangerous levels.

### Harm

Can dietary supplements be harmful? Under some circumstances, anything we ingest can be harmful, even ordinary food, and the same applies to dietary supplements. A dietary supplement (DS), especially one with multiple ingredients, can be harmful under one of the following circumstances (REASONS), assuming it is not a poison and it has been used by at least some individuals without adverse effects. Each circumstance has been substantiated by actual events of poisoning from dietary supplements in some individuals:

- R Raw impurities: The DS is not pure. It is mixed with some known or unknown ingredient or ingredients that are harmful at least to some individuals.
- E Excess levels of ingredients used: Intentionally or unintentionally the manufacturer has included an excess level of some of the ingredients. The excess substances have proved harmful to some consumers.
- A Allergic reactions to some ingredients in the dietary supplement for some individuals: The occurrence of this type of adverse effects is probably one of the most common observations among the consumers.
- S Systemic poisoning: This means the ingredients in the dietary supplement are distributed via the blood stream to various parts of the body and produce general poisonous effects in the body of some users. Most of the time, the cause of such poisoning is difficult to assess. One possibility is the interaction of ingredients in the body to a harmful by-product. Or, the ingredients interact with body organs or fluid to produce general by-products that interact among themselves to produce another by-product that is harmful.
- O Overdosing oneself: This is another common situation when adverse effects occur. Many users do

not comply with the written instructions on the label. Instead of one tablet a day, three may be taken. Instead of swallowing a capsule, some open it and chew on the powder.

- N Negative reactions in some individuals because of a specific sensitivity: The substance is harmless for the average adult but may be harmful to infants, small children, and some elderly. The substance is not harmless under normal circumstances but may be harmful to individuals with certain clinical conditions, such as pregnancy, high blood pressure, and kidney diseases.
- S Safety of the product has not been carefully evaluated: In spite of legal requirements, many manufacturers have failed to conduct safety testing of their products.

Any consumer who enjoys using dietary supplements for whatever reasons, for example, nutritional benefits, clinical therapy, reversal of aging, is advised to perform a minimum amount of "homework" so that the chances of suffering adverse effects can be reduced. The following HOPES criteria serve as a good start:

- H Health status is an important clue. Are you sick? Do you have a terminal illness? Are you pregnant? You must be careful with the potential effect of any dietary supplement. The precaution applies even if you are taking the dietary supplement with an intention that it may cure your illness.
- O Overacting is a human weakness. When it comes to a dietary supplement, avoid it if you can. Even if it works and makes you feel better, there is no need to be excited. It may be a chance occurrence. Most important of all, do not overdose immediately because it "works." That is, if the label recommends 2 tablets a day, do not take 4 or 5.
- P Product description is your major weapon for self-protection. Read the label several times. Ask yourself the following questions: Is there a name for the product? Are the ingredients listed? Is there a recommended daily dosage? Are there precaution statements? Is there a name and address for the manufacturer? It is not a good idea to put something in your mouth if there is no name and address for the manufacturer. Why? Because, if there is something wrong, no one can trace it to the manufacturer. The store where you buy it may have obtained it from a distributor. Without the manufacturer, no one knows what is inside, and your doctor cannot treat you if you show harmful effects.
- E Education is invariably a part of any health program. If you are serious about taking dietary supplements and willing to spend money on one or more such products, then you have the responsibility of educating yourself about dietary supplements. Talk to your friends with similar interest. Read up



on products, claims, and effects. Use the toll-free numbers for the FDA, FTC, and state consumer protection agencies to find out about any dietary supplement you are taking.

- S Symptoms from taking a dietary supplement are of course valuable indications that there is something wrong with the product. If you detect a slight sign of unwelcome symptoms in your body, stop the supplement immediately and seek medical attention.

Your HOPES of a minimum protection from adverse effects of any dietary supplement is to implement these five simple steps.

## FDA ENFORCEMENT

The FDA uses many tools to enforcement laws and regulations and some are described below:

1. **Warning letters:** The FDA sends a warning letter to inform a manufacture that one or more of its products is illegal or needs correction. Responses are then processed between the FDA and the manufacturers.
2. **Recalls:** Recalls are actions taken by a firm to remove a product from the market. Recalls may be conducted on a firm's own initiative, by FDA request, or by FDA order under statutory authority. There are three classes of recalls:
  - **Class I recall**—A situation in which there is a reasonable probability that the use of or exposure to a violative product will cause serious adverse health consequences or death
  - **Class II recall**—A situation in which use of or exposure to a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote
  - **Class III recall**—A situation in which use of or exposure to a violative product is not likely to cause adverse health consequences
3. **Seizures:** When the FDA decides that a product may pose danger to the public and recall is not implemented, it will work with the appropriate law enforcement agency to seize the product and remove it from the market.

Each of the above enforcement approach has been applied to manufacturers whose dietary supplements have raised the issues of safety or illegal claims. Some examples follow.

### Warning Letters

In April 2007, the FDA sent a warning letter to the manufacturer of a dietary supplement affecting public safety and illegal claims. The company sells a dietary supple-

mented called “Cocaine.” Its Web site use the following descriptions or claims:

- “The Legal Alternative”
- The product name is “Cocaine,” and the letters in the product name appear to be spelled out in a white granular substance that resembles cocaine powder.
- “Speed in a Can”
- “Liquid Cocaine”
- “Cocaine - Instant Rush”
- “The question you have to ask yourself is: ‘Can I handle the rush?’”
- “This beverage should be consumed by responsible adults. Failure to adhere to this warning may result in excess excitement, stamina, . . . and possible feeling of euphoria.”
- Certain ingredients intended “to prevent, treat, or cure disease conditions.” “Inositol . . . reduces cholesterol in the blood; it helps prevent hardening of the arteries, and may protect nerve fibers from excess glucose damage. Inositol has a natural calming effect and may be used in the treatment of anxiety, depression, and obsessive-compulsive disorder without the side effects of prescription medications.”

According to the FDA, dietary supplements are products that are intended to supplement the diet. Street drug alternatives, meaning products that claim to mimic the effects of recreational drugs, are not intended to supplement the diet and, as a result, cannot lawfully be marketed as dietary supplements. Also, a dietary supplement may not bear claims that it prevents or treats a disease, except for authorized health claims about reducing the risk of a disease.

Since the outcome of each varies with conditions such as responses, remedies, legal actions, and so on, an interested party may access the FDA Web site to find more details about accessing the FDA's archive of warning letters.

### Recalls

Some examples of class I recalls are listed in Table 11-1.

### Seizures

On October 12, 2007, the FDA distributed this news release:

At the request of the FDA, U.S. Marshals seized ~\$71,000 of products from FullLife Natural Options, Inc., of Boca Raton, Florida, which marketed and distributed Charantea Ampalaya Capsules and Charantea Ampalaya Tea.

Although these products are labeled as dietary supplements, they are being promoted by FullLife for use in treating serious conditions, such as diabetes, anemia, and hypertension, both in printed

**TABLE 11-1** Recalled Dietary Supplements

Dietary Supplements Recalled	Reason	Recall Company	Manufacturer
LIVIRO3 Natural Energy Enhancer Nutritional Supplement Recall: May 2007	Containing the legal prescription drug ingredient Tadalafil (treating erectile dysfunction)	Ebek, Inc, Los Angeles, CA	West Coast Laboratories Inc, Gardena, CA
Avian-Rx tablets labeled to contain herbal ingredients to bulletproof your immune system. The primary ingredients on the label: star anise extract, shikimic acid, and <i>Hypericum perforatum</i> . Recall: July 2007	Unapproved drug claim that it can prevent "Bird Flu"	Hi-Tech Pharmaceuticals, Inc., Norcross, GA	Hi-Tech Pharmaceuticals, Inc., Norcross, GA
Metaboslim All Natural Fat Eater Apple Cider Vinegar Recall: October 2007	Containing undeclared sibutramine, an active legal pharmaceutical ingredient used for weight loss in treatment of obesity	Confidence Inc., Port Washington, NY	Island Vitamins Inc., Farmingdale, NY
V.MAX Herbal Stamina Enhancer for Men Dietary Supplement, Cordyceps Militaries, L-Arginine, Psyllium Husk Powder, Licorice Root, Astragalus Membranaceus, Steamed Panax Ginseng Recall: November 2007	Containing aminotadalafil, an analogue of tadalafil, a legal drug used to treat erectile dysfunction	Barodon S.F., Inc., Los Angeles, CA	MegaCare Inc., Las Vegas, NV
True Man Sexual Energy Nutriment, Men's formula, Natural Herbs Energy Max Energy Supplement Men's formula Natural Herbs Recall: December 2007	Containing various analogues of legal drug ingredients approved for treating erectile dysfunction (ED)	America True Man Health, Inc., West Covina, CA	H & L Industries, Inc., dba Natural Source Int'l, Inc., LaVerne, CA
Gripe Water All Natural Apple Flavor. An herbal supplement used to ease the gas and stomach discomfort often associated with colic, hiccups, and teething Recall: January 2008	Containing cryptosporidium, confirmed after investigating the illness of a 6-week-old infant in Minnesota who consumed the product. Cryptosporidium is a parasite that can cause intestinal infections.	MOM Enterprises, Inc., San Rafael, CA	Botanical Laboratories Inc., Ferndale, WA

and electronic (Web site) media distributed by the company.

FDA considers these products to be unapproved new drugs because they make claims related to the prevention or treatment of diseases in the products' labeling. Such seizures protect consumers who may rely on unapproved products and unsubstantiated claims associated with these products when making important decisions about their health.

Following an investigation of the firm's marketing practices, FDA officials advised FullLife that the claims related to prevention or treatment of diseases made these products subject to regulation as

drugs. Despite FDA's warnings, the firm failed to bring its marketing into compliance with the law. During subsequent inspections, FDA inspectors found that the offending claims were still being made.

On August 23, 2007, at the request of FDA, U.S. Marshals in the Northern District of Florida seized an estimated \$41,000 worth of inventory of Glucobetic, Neuro-betic, Ocu-Comp, Atri-Oxi, Super-Flex, MSM-1000, and Atri-E-400 capsules being promoted and distributed by Charron Nutrition of Tallahassee, Florida, for use in treating diabetes, arthritis, and other serious health conditions.

### PROGRESS CHECK ON ACTIVITY 4

#### TRUE/FALSE

Circle T for True and F for False.

1. T F I do not need to think about my total diet if I am taking dietary supplements.
2. T F Essential nutrients are safe, even when they are consumed in large doses.
3. T F I don't need to check with my doctor or health-care provider before using supplements if I have read the labels on these supplements.
4. T F All dietary supplements are risk free because they are sold over the counter.
5. T F Because vitamin and mineral supplements are widely used and generally considered safe, you may safely give them to your children.
6. T F If one plans to use a dietary supplement in place of drugs or in combination with any drug, one should tell one's healthcare provider first.
7. T F Dietary supplements, generally considered as safe, should not interact with prescription and over-the-counter (OTC) medicines.
8. T F When taking medication(s) or dietary supplement(s), advisories about these products should not be taken too seriously.
9. T F It is important to fully inform your doctor about the vitamins, minerals, herbals, or any other supplements you are taking before elective surgery.
10. T F Under the law, manufacturers of dietary supplements are not responsible for making sure their products are safe before they go to market.
11. T F Manufacturers of dietary supplements are responsible for determining that the claims on their labels are accurate and truthful.
12. T F If the FDA can prove that claims on marketed dietary supplement products are false and misleading, the agency may take action against products with such claims.
13. T F When searching on the Web, the directory sites of organizations included in all search engines are reliable.
14. T F Most nonprofit and government sites contain no advertising, and access to the site and materials offered are usually free.
15. T F While the Web can be a valuable source of accurate, reliable information, it also has a wealth of misinformation that may not be obvious.
16. T F Information from trained people is usually more much more reliable than that from lay people.
17. T F Even if a product may not help me, at least it won't hurt me.
18. T F When I see the term *natural*, it means that a product is healthful and safe.
19. T F A recall of a harmful product guarantees that all such harmful products will be immediately and completely removed from the marketplace.
20. T F It is appropriate to contact the manufacturer for more information about the specific product that one is purchasing.
21. T F When a nurse is caring for a patient who is involved with dietary supplements (using them, intending to use them, or asking questions about them), he or she should assist the patient in making appropriate choices through educating the patient and family regarding their use.
22. T F Fraudulent products often can be identified by the types of claims made in their labeling, advertising, and promotional literature.
23. T F According to the National Council Against Health Fraud, a product may be fraudulent if it contains claims such as *breakthrough*, *magical*, *miracle cure*, *new discovery*, *detoxify*, *purify*, *energize*, *cure a wide range of unrelated diseases*, and *only benefits but no side effects*.
24. T F Quality dietary supplements have no reason to carry the U.S.P. notation for their ingredients.
25. T F Nationally known food and drug manufacturers usually have tighter controls in their manufacturing methods for their products.
26. T F When a consumer starts to take a dietary supplement, he or she must check with a medical doctor.
27. T F Dietary supplements often contain plant products that may also be used in prescription medicine.

#### FILL-IN

28. Before starting a dietary supplement, it is always wise to check with a medical doctor. It is especially important for people who have the following characteristics:
  - a. \_\_\_\_\_
  - b. \_\_\_\_\_
  - c. \_\_\_\_\_
  - d. \_\_\_\_\_
  - e. \_\_\_\_\_
29. The following minimal criteria should be followed when a person starts to take dietary supplements:
  - H. \_\_\_\_\_
  - O. \_\_\_\_\_

- P. \_\_\_\_\_  
 E. \_\_\_\_\_  
 S. \_\_\_\_\_

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