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Dietary Supplements and Cardiovascular Disease Prevention

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In 2021, people in the United States spent an estimated $50 billion on dietary supplements.[1]

More than half of adults in the United States use dietary supplements, including more than 70% of adults aged 65 years and older.[2] Women and people with more education or higher socioeconomic status are more likely to take them.[2] Some reported reasons why individuals use dietary supplements include perceived efficacy, promotion of health over illness, prevention of cancer, prevention of vitamin deficiencies, and health maintenance and performance enhancement.[3]

Supplements contain one or more dietary ingredients (e.g., vitamins, minerals, amino acids, proteins, fatty acids, botanicals, herbs) and may be taken by mouth as pills, liquids, or energy bars, or applied as patches on the skin.

Although many vitamins and minerals may have antioxidative and anti-inflammatory properties that could decrease the prevalence of certain diseases, dietary supplements are not considered medicines and are not intended to prevent, diagnose, treat, or cure any disease. Their safety and efficacy are often unknown, and their use has resulted in 23,000 emergency department visits and 2,000 hospitalizations per year.[4]

Regulation of Dietary Supplements in the United States

The Dietary Supplement Health and Education Act of 1994 (DSHEA) defined dietary supplements and established rules for what product labels should contain.[5] DSHEA also created the Office of Dietary Supplementation (ODS), a branch of the National Institutes of Health (NIH) and the leading federal agency promoting the scientific study of supplements. DSHEA requires manufacturers to follow good manufacturing practices, which help assure the composition, purity, and strength of ingredients in products. Manufacturers are responsible for the safety of their products, yet there is no requirement for products to be proven effective for any advertised health benefits.

The Food and Drug Administration (FDA) oversees both dietary supplements and medications, yet the regulations for supplements differ from regulations for prescription and over-the-counter medications. Dietary supplements are regulated more like foods than drugs. Manufacturers do not need to register or obtain approval prior to marketing products, and there is no requirement for proof of efficacy or safety for products.

Dietary supplements are packaged with labels that list active ingredients, as well as fillers and binders. Labels are required to be truthful, not misleading, and indicate a suggested dose or serving size. The FDA may ban or remove products from the market, but only after it proves a product poses "a significant or unreasonable risk of illness or injury."[5]

Recommendations for Cardiovascular Disease

The United States Preventive Services Task Force (USPSTF) does not recommend the use of beta-carotene, calcium, vitamin A, vitamin D, or vitamin E for the prevention of cardiovascular disease (CVD).[6]

In addition, the Dietary Guidelines for Americans 2020-2025 from the United States Department of Agriculture (USDA) does not recommend vitamin and mineral dietary supplements.[7] Rather, the guidelines recommend that people obtain the necessary vitamins from a healthy diet rich in fruits and vegetables associated with decreased CVD and cancer.

Commonly Used Supplements

The following pages list supplements commonly used by patients with diabetes, hypertension, and hyperlipidemia. There is little, if any, evidence supporting their use. Patients should talk to their health care team before starting any supplements. The tables are not comprehensive, as patients may use many other supplements for these conditions, and the following considerations apply:

- Some supplements are used for more than one condition and have multiple proposed mechanisms of action.
- Studies on the use of these supplements by pregnant people and children are lacking, so even if not exclusively stated, those populations should not use these supplements.
- Some supplements have undesirable effects on certain conditions and should be avoided. For example:
  - Vitamin E increases mortality rates in hemorrhagic strokes, and beta carotene has been associated with a moderate increase of CVD.[6]
  - Bitter orange, ephedra, ginseng, and licorice root raise blood pressure.[8]
  - Biotin is commonly used to promote hair and nail growth, as well as to treat diabetes, lipids, and multiple sclerosis, but it has been shown to interfere with lab results (including hormonal assays [especially thyroid-stimulating hormone], brain natriuretic peptide, troponin, tumor markers, B12, folate, and ferritin) that can lead to misdiagnosis and inappropriate treatment. Patients should stop using biotin for 72 hours prior to completing labs.[9]

Additional information on supplements of interest is available at the National Center for Complementary and Integrative Health website.

Table 1. Commonly Used Supplements for Type 2 Diabetes

Supplement	Unproven Benefits	Side Effects	Contraindications	Medication Interactions
Alpha Lipoic Acid[10,11]	▪ Increases insulin sensitivity ▪ Increases glucose transport ▪ Antioxidant to reduce neuropathy pain	▪ GI problems ▪ Vertigo ▪ Skin allergies ▪ Decrease triiodothyronine levels	▪ Thiamin deficiency	▪ Insulin/insulin secretagogues ▪ Antacids ▪ Levothyroxine ▪ Chemotherapy
Berberine[12-14]	▪ Increases glucose uptake in muscles ▪ Increases insulin receptor expression	▪ GI upset ▪ Hypoglycemia	▪ Pregnancy ▪ Transplant recipients	▪ Cyclosporine ▪ Anticoagulants ▪ Insulin/insulin secretagogues ▪ Antihypertensives ▪ Midazolam ▪ Tacrolimus ▪ Dextromethorphan
Bitter Melon[10]	▪ Increases tissue glucose uptake ▪ Synthesizes glycogen ▪ Inhibits enzymes in glucose production ▪ Enhances oxidation of G6PDH	▪ GI discomfort ▪ Hypoglycemic coma ▪ Favism	▪ G6PDH deficiency ▪ Pregnancy ▪ Children	▪ Insulin/insulin secretagogues
Chromium[10,15]	▪ Sensitizes insulin ▪ Enhances beta cell function	▪ Abdominal pain ▪ Kidney damage ▪ Muscle problems ▪ Skin damage	▪ Dermatologic reactions ▪ Kidney impairment ▪ Hepatic dysfunction ▪ Mood disturbance	▪ Steroids ▪ Famotidine ▪ Omeprazole ▪ Zinc ▪ NSAIDs ▪ Insulin/insulin secretagogues ▪ Vitamin C
Cinnamon[10,16]	▪ Increases insulin sensitivity ▪ Promotes glucose uptake ▪ Promotes glycogen synthesis	▪ Skin irritation ▪ Acid reflux	▪ Allergic	▪ Insulin/insulin secretagogues
Fenugreek[10,17]	▪ Delays gastric emptying ▪ Increases red blood cell insulin receptors ▪ Increases direct insulin secretion	▪ Diarrhea ▪ Flatulence ▪ Hypersensitivity	▪ Peanut allergy	▪ Warfarin ▪ Insulin/insulin secretagogues
Magnesium[18]	▪ Act as a cofactor for enzymes in glucose metabolism pathways	▪ Diarrhea at high doses	▪ Renal failure	▪ More than 5,000 mg is deadly

NSAID = non-steroidal anti-inflammatory drug; GI = gastrointestinal; G6PDH = glucose-6-phosphate dehydrogenase

Table 2. Commonly Used Supplements for Hypertension

Supplement	Unproven Benefits	Side Effects	Contraindications	Medication Interactions
Cocoa[19]	▪ Flavanols lead to increased nitric oxide production ▪ Vasodilation	▪ Increased urination ▪ Sleeplessness ▪ Palpitations ▪ GI symptoms	▪ Allergic	▪ Stimulants
Fish Oil[10a]	▪ Acts as an anti-inflammatory ▪ Acts as an anti-thrombotic	▪ Unpleasant taste ▪ Halitosis ▪ Bad smelling sweat ▪ Headache ▪ GI symptoms	▪ Mercury	▪ OCP ▪ Secretagogues ▪ Antiplatelet agents
Flaxseed/ Flaxseed Oil[20,21]	▪ Acts as an anti-inflammatory	▪ Bowel changes ▪ Hormonal effects ▪ Raw/unripe seeds toxic	▪ Pregnancy	▪ Estrogen
Garlic[22]	▪ Produces nitric oxide ▪ Blocks angiotensin II	▪ Halitosis ▪ Body odor ▪ Heartburn ▪ Upset stomach	▪ Blood thinners ▪ Allergic	▪ Blood thinners ▪ Saquinavir
Probiotics[23]	▪ Microorganism in fermented dairy acts as an ACE-inhibitor	▪ GI symptoms	▪ Weakened immune system ▪ Recent surgery ▪ Critical illness	▪ Prednisone

GI = gastrointestinal; OCP = oral contraceptive pill; ACE = angiotensin-converting enzyme
[a]Fish oil is also used commonly by patients for high cholesterol, especially high triglycerides, as well as hypertension. Pharmaceutical-grade omega-3 preparations are preferred to the over-the-counter supplements.

Table 3. Commonly Used Supplements for Hyperlipidemia

Supplement	Unproven Benefits	Side Effects	Contraindications	Medication Interactions
Coenzyme Q10[10]	▪ Acts as an antioxidant ▪ Stabilizes cell membrane ▪ Increases tolerability of statins	▪ GI upset	▪ Pregnancy ▪ Children	▪ Warfarin ▪ Insulin/insulin secretagogues ▪ Antihypertensives
Red Yeast Rice[24]	▪ Monacolin K acts as an HMG-CoA reductase inhibitor	▪ Myopathy ▪ Rhabdomyolysis ▪ Liver toxicity	▪ Pregnancy ▪ Allergy	▪ Statins ▪ Fibrates ▪ Nefazodone ▪ Antifungal agents ▪ HIV medications
Soy[25]	▪ Lowers LDL	▪ GI upset ▪ Effects thyroid function in iodine deficiency	▪ Allergies	▪ Estrogens ▪ Warfarin ▪ Antihypertensives

HMG-CoA = 3-hydroxy-3-methylglutaryl coenzymeA; HIV = human immunodeficiency virus; GI = gastrointestinal; LDL = low-density lipoprotein

Guidance for Supplement Usage

Providers should have individual conversations with patients about the safety and efficacy of dietary supplements compared to alternative methods of management, such as lifestyle or medication therapy. Shared clinical decisions should include evidence-based resources to ensure accurate advice for dietary supplementation.

If a patient decides to move forward with supplement usage, the provider should ensure the patient is able to secure the supplement from verified sources. One way to do this is through United States Pharmacopeia (USP) certification. USP certifies that a supplement contains the ingredients listed on the label in the correct potency and amounts. It also ensures that the supplement does not contain harmful levels of certain contaminants and has been manufactured in a safe, well-documented, and well-controlled process.[26] USP does not ensure that the product is safe or efficacious. Manufacturers can voluntarily submit the product label and product to be verified by USP.

Reliable Information Sources for Shared Decision Making

Given the myriad of products available, with varying reports of efficacy and potential for risk and harm, it is essential for health care providers to navigate reliable information sources with their patients and to pursue effectively communicated, shared clinical decisions. The following resources can help providers and patients quickly find reliable information as they evaluate products.

- **National Institutes of Health Dietary Supplement Fact Sheets**
  ods.od.nih.gov/factsheets/list-all/
- **U.S. Food and Drug Administration Information for Consumers on Using Dietary Supplements**
  fda.gov/food/dietary-supplements/information-consumers-using-dietary-supplements
- **U.S. Food and Drug Administration Questions and Answers on Dietary Supplements**
  fda.gov/food/information-consumers-using-dietary-supplements/questions-and-answers-dietary-supplements

Assessing Supplement Use During the Medical Visit

Patients may not view supplements as potentially harmful and, as a result, may not mention them during medical appointments. As part of medication reconciliation, the patient should be asked to bring all their prescribed medications and to list any supplements they take.[27] Open-ended questions can help providers gather an accurate representation of how and why the patient is taking each medication, vitamin, and supplement.

Using both objective information (e.g., medication bottles, records of pharmacy filled prescriptions) and subjective information (e.g., patient interview), providers can more accurately assess concerns regarding supplement usage. Discussion techniques, such as motivational interviewing and "Ask, Tell, Ask," can help patients better comprehend dietary topics and identify their motivation for using supplements.[28]

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