



Drug Interactions With Dietary Supplements

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- Upon successful completion of this article, pharmacists should be able to:
1. Describe the common uses and proposed mechanisms of action of 19 dietary supplements.
 2. Describe adverse effects associated with the use of dietary supplements.
 3. Describe the mechanisms of drug interactions involving a given dietary supplement.
 4. Evaluate resources for pharmacists, physicians, and consumers for dietary supplements.

Pharmacy Technician CE Objectives

1. Describe the common uses of 19 herbal therapies.
2. Describe adverse effects associated with the use of dietary supplements.
3. List prescription drugs that interact with dietary supplements.

INTRODUCTION

Patients understand that interactions between two prescription medications, or “drug-drug interactions,” can be very dangerous. Pharmacists can easily scan for these possible interactions using drug information software available at most pharmacies and hospitals. With a complete list of a patient’s medications, the pharmacist can prevent many drug-drug interactions from occurring. But what about the list of over-the-counter products that patients are taking that they don’t consider to be medications or drugs? Dietary supplements (see Table 1) and vitamins have just as much potential to cause drug interactions as prescription medications. Throughout

this CE presentation, there will be a review of the most commonly used dietary supplements including an explanation of the therapeutic uses as well as the potential adverse effects of each. Also, each section will address possible drug interactions related to the supplement. After completing this presentation, the reader will be adept at reviewing a patient’s complete supplement and medication list and identifying potential drug-supplement interactions.

ANTACIDS

Antacids are one of the most common drugs that are purchased over the counter. Most people do not consider them to be medications and therefore do not list them as such. This can be an issue when new medications are prescribed as drug-drug interactions can occur with antacids. There are three main types of antacids: aluminum, calcium, and magnesium based. All three types can interact with medications in different ways.

Aluminum-based antacids release a free aluminum ion when they react with hydrochloride in the stomach. The aluminum ion is then available for intraluminal binding and adsorption to drugs. Aluminum-based antacids also decrease gastrointestinal motility, which can affect drugs in several ways. Decreased motility prolongs the exposure of acid-labile drugs to the hydrochloric acid of the stomach, which can lead to degradation and decreased total absorption. Also, the delay in gastric emptying can

Useful Websites

■ www.mskcc.org/mskcc/html/44.cfm
Memorial Sloan-Kettering Cancer Center
Contains an entire database of dietary supplement medicines. Of note on this site is that chemotherapy drug interactions are included with all other drug interactions.

■ www.altnature.com/gallery/index.html
Alternative Nature Enterprises
Contains information about the most commonly used herbs. It includes pictures of the natural source, as well as information about its use and adverse effects.

affect drugs stable in an acidic environment by leading to increased serum concentrations and resulting in toxicity.

Calcium carbonate antacids release carbonate when they react with hydrochloride, which can alkalize the urine and decrease excretion. This interaction is commonly seen when antacids are given concomitantly with digoxin, resulting in digoxin toxicity from decreased excretion.

Magnesium-based antacids increase gastrointestinal motility, which can decrease the absorption of drugs from the gastrointestinal tract. This is particularly true for medications that require prolonged intestinal contact for absorption.

Antacids have been shown to interact with numerous medications. Drug interactions are a result of either increased gastric pH or presence of a cation. Common interactions are found with thyroid replacement (cation), antibiotics (cation), iron supplementation (gastric pH), and enteric coated products (gastric pH). Changes in absorption may also be observed due to changes in gastrointestinal motility. Calcium slows GI motility while aluminum and magnesium both speed motility. The rest of this section will give a brief overview of these specific groups.

The three major cardiovascular drugs interactions that have been studied extensively are the quinidine anti-arrhythmics, beta blockers, and angiotensin converting enzyme (ACE) inhibitors. Quinidine excretion is extensively decreased due to the alkalinization of urine, resulting in toxicity and prolongation of the QT interval. Beta blockers are rendered nearly ineffective due to decreased absorption as a result of both a change in the gastric emptying and an increase in the gastric pH. ACE inhibitors also experience decreased absorption due to changes in gastric emptying. Antacids may reduce serum levels of cardiovascular medications therefore concomitant administration of antacids and cardiovascular medications should be avoided.

Interactions between antimicrobials and antacids can be traced as far back as the early to mid-1980s. When given concomitantly, fluoroquinolones, macrolides, and tetracyclines bioavailability is significantly reduced, possibly leading to treatment failure. It is believed that one of the functional groups on these drug molecule chelates the metallic cations. The chelation leads to decreased bioavailability and absorption. Interaction with antifungals, most notably itraconazole, occurs due to the increase in gastric pH, leading to decreased dissolution of the drugs and thus decreased absorption. Concomitant adminis-

tration of antacids and certain antimicrobials should be avoided.

The last group of interactions involves anti-inflammatory agents, specifically nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids. Changes in gastric emptying due to antacids decrease the bioavailability of anti-inflammatory agents resulting in a decrease in absorption. Also, an increase in the gastric pH results in decreased drug dissolution, resulting in a decrease in bioavailability. Concomitant administration of antacids and anti-inflammatory agents should be avoided.

BLACK COHOSH

Black cohosh is a rhizome of *Cimicifuga racemosa* or *Actaea racemosa*. It contains phytoestrogens that mimic the effects of estrogen, and is used to treat the symptoms of menopause and dysmenorrhea. Clinical studies are conflicting whether black cohosh possesses estrogenic activity. Currently marketed products claim to work with the body to reduce night sweats, vaginal dryness, and hot flashes.

Adverse effects associated with the use of black cohosh include nausea, headache, rash, and dizziness. Due to case reports of autoimmune hepatitis and liver failure associated with the use of black cohosh, liver function tests should be monitored frequently. Black cohosh has been reported to stimulate uterine contractions, so its use should be avoided in pregnancy. Use of black cohosh is not recommended in women with a history of breast cancer and other estrogen-dependent tumors or endometrial cancer.

Black cohosh has the potential to interact with medications used for the treatment of menopausal symptoms, and may potentiate the effects of hepatotoxic agents. Metabolism of drugs that are eliminated through cytochrome P450 (CYP) 2D6 enzyme may be inhibited with the coadministration of black cohosh, resulting in increased levels of these medications. Caution should be taken if patients are prescribed agents metabolized via this pathway. (See Table 2 for CYP-related information.)

CHAMOMILE

Chamomile may be the herb with the earliest recorded history. Its use can be dated back to 90 BC when Pliny the Elder, a Roman naturalist and philosopher, extensively wrote of its use in healing. Ancient Egyptians used it cure the “ague” also known as acute fever. It is used for anything from hay fever and muscle spasms, to menstrual disorders and insomnia.

There are several varieties of chamomile. Roman and German are the two most commonly used and chamomile is most frequently consumed as a drinking tea. Chamomile is metabolized into about 120 different metabolites including 28 terpenoids and 36 flavonoids. The terpenoids and flavonoids are thought to be responsible for chamomile’s medicinal properties.

Traditionally chamomile has been used as an anti-inflammatory, anti-oxidant, and a mild astringent. Chamomile can be applied topically to sites of eczema to relieve the itching and dry skin. Chamomile has been shown to be about 60 percent as effective as hydrocortisone cream when used for eczema. Finally when used as an aromatherapy it may help reduce anxiety and insomnia. The smell has been shown to have soothing effects.

There have been numerous studies evaluating the possible effects of chamomile to treat side effects of chemotherapy. Studies have shown that while chamomile does not increase the efficacy of chemotherapy or affect the mortality of the patient, it did improve morbidity and quality of life. Patients who used chamomile had less anxiety, depression, and gastrointestinal discomfort.

Chamomile is generally well tolerated with limited adverse effects. Skin irritation and contact dermatitis were the most common side effects experienced with topical or inhaled forms. Gastrointestinal upset was the most common side effect experienced with tea.

Chamomile has been shown to interact with benzodiazepines and central nervous system depressants. When given concomitantly, there is an increase in the sedative properties. Chamomile has also been shown to inhibit CYP 1A2 and 3A4 enzymes. When chamomile is given with a drug

that is metabolized by these enzymes, there is an increase in serum concentrations of the concomitant drug that can lead to toxicity. Chamomile interacts with warfarin (Coumadin®), leading to bleeding events. The exact mechanism of this interaction is not fully understood.

CO-ENZYME Q10

Co-enzyme Q10 (Co-Q10) is a substance that has been used for a variety of disorders associated with oxidative stress. Co-Q10 is a fat-soluble molecule with a structure similar to quinones and is commonly known as ubiquinone. Studies on beef cattle conducted in 1957 discovered that Co-Q10 was found in high quantities in areas of high cellular turnover. Specifically the heart, kidney, liver, pancreas, and brain contained the highest quantities. Co-Q10 is essential for the transfer of electrons needed for the production of adenosine triphosphate. It has also been shown to act as an antioxidant scavenger and indirectly to stabilize calcium channels within a cell.

The majority of research on Co-Q10 has been on its use in neurologic disorders. When used in Parkinson’s disease and Huntingdon’s disease it has been shown to reduce neurological decline in 44 percent of patients. Studies investigating its use in diminishing the motor symptoms of patients with Parkinson’s have been inconclusive. Most studies have shown little improvement in the motor ticks, none of which were statistically significant.

There have been numerous randomized, controlled trials studying Co-Q10 use in congestive heart failure (CHF). Most of the studies proved that Co-Q10 is effective in reducing the frequency of hospitalizations associated with acute attacks. It has also been shown to reduce edema and dyspnea, increase ejection fraction, and improve the patient’s quality of life. Currently the American Heart Association is testing Co-Q10’s usefulness in treating CHF.

Co-Q10 has been studied in the prevention of anthracycline-associated toxicity. Anthracyclines, such as doxorubicin, daunorubicin, and idarubicin are used as antineoplastic agents in the treatment of numerous cancers. One of the major side effects associated with anthracyclines is cardiotoxicity. The proposed mechanism is irreversible damage to the myocardial mitochondria. Concomitant administration with Co-Q10 has been shown to prevent this irreversible damage without compromising the antineoplastic activity of the anthracyclines.

Co-Q10 is generally well tolerated with gastrointestinal discomfort being the most frequent complaint, and can be

minimized by using two divided doses. The most common symptoms are upset stomach, loss of appetite, nausea, and vomiting. Co-Q10 should be avoided during invasive procedures or surgery. It has been shown to interfere with blood pressure control as well as bleeding, and should be stopped two weeks prior to any scheduled invasive procedure or surgery.

Co-Q10 has been shown to interact significantly with warfarin. It is structurally similar to vitamin K and possesses some pro-coagulant activity. Coadministration with warfarin can result in subtherapeutic international normalized ratios (INR) therefore should be avoided.

CYANOCOBALAMIN (VITAMIN B12)

Vitamin B12 is a naturally occurring B complex vitamin that is formed by bacteria. It is essential for normal nerve function, DNA synthesis, hematopoiesis, fatty acid metabolism, and amino acid synthesis in the mitochondria. It also plays an important role in the metabolism of homocysteine. There is some evidence that suggests elevated homocysteine levels might cause vascular endothelial cell damage, impaired endothelium-dependent vasodilation due to reduced nitric oxide activity, increased oxidation and arterial deposition of low-density lipoproteins (LDL), increased platelet adhesiveness, and activation of the clotting cascade.

Vitamin B12 can be found in meat, fish, shellfish, liver, and dairy products. A deficiency in vitamin B12 can result in hematologic, psychiatric, and neurologic disorders. Normal serum vitamin B12 levels range from 200 – 900 pg/ml. B12 toxicities include diarrhea, peripheral vascular thrombosis, polycythemia vera, pulmonary edema, generalized edema, and urticaria. Vitamin B12 requires an acidic environment in order to be absorbed in the terminal ileum. Therefore, drugs that reduce the gastric pH, such as antacids, may lead to decreased absorption. Coadministration with folic acid may mask the symptoms of vitamin B12 deficiency. Other reported drug interactions include chloramphenicol, potassium supplements, and prescription potassium, as well as vitamin C containing products. Utilizing these medications with vitamin B12 could result in decreased absorption of vitamin B12 from the gastrointestinal tract. Vitamin B12 is Pregnancy Category C, but it is an essential vitamin, when administered in recommended doses, vitamin B12 may be safe in pregnancy and lactating women.

ECHINACEA

Echinacea is a flowering plant native to North America.

There are three main species: *Echinacea angustifolia*, *Echinacea pallida*, and *Echinacea purpurea*. These species differ in the amounts of active constituents. There is little research comparing the three, although it is accepted that *Echinacea purpurea* is likely the most potent.

The roots and above-ground parts contain different substances thought to act on slightly different complaints, but are commonly combined. Its utilization began as a traditional remedy used by the Great Plains Indian tribes and was continued through the medicinal use of American settlers.

Echinacea is most commonly used to prevent or treat the common cold and other upper respiratory tract infections. Although its use fell out of favor in the United States due to antibiotic development, the interest and use of echinacea has resumed due to increasing development of antibiotic resistance and better understanding by the public that antibiotics are not effective against the influenza virus. Echinacea is considered possibly effective for reducing the duration of the common cold by 10–30 percent. It is most effective if started at the first sign or symptom of a cold or infection and continued for seven to 10 days. Echinacea is less effective when taken as daily prophylaxis and it is suggested to take a one week drug holiday for every eight weeks of treatment.

Echinacea also acts as an immunostimulant. It increases phagocytosis and lymphocyte activity. It may have anti-inflammatory activity since it has been shown to inhibit cyclooxygenase. Because echinacea's mechanism of action includes stimulating the immune system, there is moderate interaction with immunosuppressant drugs.

Echinacea affects CYP 1A2 and 3A4. Echinacea modestly inhibits CYP1A2 in vivo. Caffeine is cleared via CYP 1A2 leading to a moderate interaction between caffeine and echinacea. Echinacea can inhibit caffeine clearance by 27 percent, causing a 30 percent increase in plasma concentrations of caffeine. Echinacea may similarly increase plasma concentrations of other drugs metabolized by CYP 1A2. Echinacea induces hepatic CYP3A4, but inhibits intestinal CYP3A4,

leading to little or no change in drug levels.

Echinacea is possibly safe for children when used orally and short-term. Specifically, echinacea purpurea juice extract has been used for up to 10 days in children between the ages of 2 and 11. Echinacea may increase the risk of rash in some children. The rash may be attributed to an allergic reaction and occurs in about 7 percent of children.

EVENING PRIMROSE

Evening primrose is obtained from the plant *Oenothera biennis*. It contains high amounts of the omega-6 fatty acid gamma-linolenic acid (GLA), which is a precursor to prostaglandin. Evening primrose oil has been used to treat menopausal symptoms, eczema, and hyperactivity in children.

Having pharmacological effects similar to GLA, evening primrose oil has the potential to inhibit platelet aggregation. Concomitant use of evening primrose with anticoagulant and antiplatelet therapy can result in prolonged bleeding time, increasing the risk of bruising and bleeding. Case reports suggest the use of evening primrose may lower the seizure threshold. Its use should be avoided in patients with seizures or epilepsy. Adverse effects seen with the use of evening primrose include gastrointestinal upset, headache, and nausea. Evening primrose may increase pregnancy complications and therefore should not be used in pregnant women. Evening primrose has safely been used in children, but its routine use is not recommended due to conflicting data proving efficacy.

FISH OIL

Fish oil is high in the omega-3-fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The human body cannot produce omega-3-fatty acids on its own. These fatty acids have anti-inflammatory and antithrombotic properties. They compete with arachidonic acid to suppress cyclooxygenase-2 (COX-2) production, thereby reducing inflammation, and the synthesis of thromboxane A₂ which decreases platelet aggregation and vasoconstriction. Fish

oil also which leads to reduced triglyceride levels via decreased production of very-low density lipoproteins (VLDL). A FDA-approved prescription product based on omega-3 fatty acids available and indicated as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia. Therefore, it is reasonable to conclude that a high-quality fish oil product supports healthy lipids and reduces cardiovascular diseases.

Fish oil is not a substrate nor an inhibitor or inducer of CYP450 isoenzymes. The drug interactions caused by fish oil are related to its pharmacologic actions. Although not as potent as aspirin, fish oil reduces platelet aggregation and function. Concomitant use of fish oil with anticoagulant or antiplatelet drugs may potentially increase the risk of bleeding. However, the research has shown that this may not be seen clinically. Taking fish oil up to 6 grams per day did not significantly affect the INR of patients taking warfarin. Also, there is evidence that fish oil does not have an additive effect on platelets when combined with aspirin. Patients should be monitored for signs and symptoms of bleeding.

Fish oil can lower blood pressure by causing vasodilation. Combining fish oil with other antihypertensive drugs could cause an additive reduction in blood pressure. Caution should be used with this combination.

In children, the use of fish oil supplements is considered safe when used orally and appropriately in studied doses. Consuming large amounts of fish oil through dietary sources could potentially be unsafe for children. Fatty fish may contain toxins such as mercury that have been linked to learning disabilities, blindness, and seizures.

GARLIC

Garlic, *Allium sativum*, is a member of the onion family and has been used for thousands of years in cooking recipes. The garlic clove can be consumed raw or cooked. The cloves can also be dried into a powder for cooking or for making capsules.

Garlic is most commonly used as a dietary supplement to support healthy lipids, healthy blood pressure, and heart health. Many trials using garlic were conducted during the 1990s, showing modest benefit but with flaws. More recent evidence has shown that garlic does not cause a clinically significant reduction in cholesterol or triglycerides. In one trial, taking garlic orally reduced systolic blood pressure by about 8 per-

cent and diastolic blood pressure by about 7 percent in patients with hypertension.

Topically, garlic oil is used for fungal infections of the skin such as tinea pedis (athlete's foot), tinea corporis (ring worm), and tinea cruris (jock itch). Garlic gel applied twice daily for one week seems to be as effective as terbinafine (Lamisil®) cream.

The garlic clove, or bulb, is the part of the plant used for dietary supplements. The pharmacologic effects of garlic are attributed to allicin; therefore, the effectiveness of garlic preparations is determined by the product's ability to yield allicin. The production of allicin comes from crushing the bulb. Crushing allows alliin, an odorless amino acid, to come into contact with the alliinase enzyme to produce the odorous compound allicin. Fresh garlic contains about 1–3 percent alliin and every 1 milligram (mg) of alliin produces 0.458mg allicin.

To support healthy cholesterol, garlic may act as a HMG-CoA reductase inhibitor, by acting as an antioxidant to reduce oxidative stress and inhibit low-density lipoprotein (LDL) oxidation. Garlic is thought to activate the production of nitric oxide which in turn causes smooth muscle relaxation and vasodilation, thereby reducing blood pressure.

In support of a healthy heart, garlic powder and aged garlic preparations have been shown to have antiplatelet and antithrombotic properties. It has been found to increase fibrinolytic activity, decrease platelet aggregation and adhesion, and increase prothrombin time (PT). Garlic is likely to interact with anticoagulant and antiplatelet drugs causing an increased risk of bleeding.

Oral garlic preparations have the potential to inhibit CYP 2C9, 2C19, 2D6, and 3A4. Caution should be taken when combining garlic with drugs that are metabolized by these isoenzymes. Clinical evidence suggests that garlic, especially garlic oil, inhibits CYP 2E1 by up to 39 percent. There is conflicting evidence about garlic's effect on CYP 3A4. High doses may cause inhibition or induction of CYP 3A4. Until more definitive information is available, use caution with drugs that are metabolized by the CYP 3A4 or 2E1 enzymes.

There is a strong recommendation not to combine garlic and isoniazid (Nydrazid®). Animal models have shown the garlic reduces isoniazid levels by up to 65 percent. The exact mechanism is unknown, but is thought to be a reduction in isoniazid absorption across the intestinal mucosa. Garlic is considered safe for short-term oral use in small doses in children.

GINKGO

Ginkgo is one of the most popular dietary supplement medicines in the world. Ginkgo is often recommended to help slow age-related decline in mental functions, as well as vascular dementia and Alzheimer's disease. Studies examining the effectiveness of ginkgo for the above conditions are conflicting. Other effects include increased cerebral blood flow through arterial vasodilation.

Ginkgo has been reported to have antiplatelet and antithrombotic effects and therefore has a high potential to interact with anticoagulants such as warfarin, as well as aspirin and NSAIDs. Ginkgo has been shown to inhibit CYP 3A4, 1A2, and to a lesser extent other CYP isoenzymes. Coadministration of ginkgo with drugs that are metabolized through these pathways should be avoided. Adverse effects of ginkgo have been reported as headache, convulsions, dizziness, gastrointestinal upset, palpitations, seizures, and spontaneous bleeding. It is recommended to monitor PT, INR, and activated partial thromboplastin time (aPTT) in patients consuming ginkgo.

Ginkgo should also be avoided in pregnancy and breastfeeding. The safe use of ginkgo has been studied in children but should only be used for a short period of time.

GLUCOSAMINE-CHONDROITIN

Glucosamine is a naturally occurring chemical that can be found in the human body. It is most commonly found in the synovial fluid of joints. It can also be found in the shells of shellfish and is harvested by pulverizing the shells. Chondroitin is also a naturally occurring chemical that is found in the synovial fluid of joints. Chondroitin can also be found in bovine cartilage.

Glucosamine and chondroitin can be formulated in dietary supplements separately or combined. Glucosamine used alone has been studied for glaucoma and weight loss, although scientific studies proving its efficacy have been controversial. Chondroitin alone may support lowered risk of heart attacks as well as lower cholesterol. Chondroitin has also been used as

an eye drop for dry eyes and during cataract surgery to support healing corneas. Like with glucosamine, there have been limited studies proving chondroitin's efficacy, when used alone.

The most common use of glucosamine and chondroitin in combination is for joint health of patients with arthritis, specifically osteoarthritis. In the glucosamine/chondroitin arthritis intervention trial (GAIT), the combination was rigorously evaluated to determine efficacy in treating knee pain related to osteoarthritis. Though the results were not statistically significant, it did show relief of knee pain as well as improved patient quality of life.

Glucosamine and chondroitin are usually well tolerated. The most common adverse effects are mild stomach pain and nausea. It has been shown to cause constipation, swollen eyelids, leg swelling as well as an irregular heartbeat. Patients allergic to shellfish or shark should avoid it due to an increased risk of allergic reaction.

Glucosamine and chondroitin have also been shown to worsen the symptoms of asthma. When used concomitantly in an otherwise controlled asthma patient, it has been shown to increase the incidence and severity of symptoms. There have been numerous case studies proving this interaction. This interaction is most commonly seen after three to four weeks of coadministration. Therefore, patients with asthma avoid this dietary supplement or, if benefit outweighs risk, patients should monitor their peak flow readings and symptoms.

There is a significant drug interaction between warfarin and glucosamine and chondroitin, alone or in combination. The exact mechanism is unknown. Numerous studies have shown that when taken concomitantly, warfarin's effects are increased, resulting in increased bleeding and warfarin levels. This interaction was seen within a few days of the initiation of glucosamine and chondroitin.

Glucosamine has another significant interaction with antineoplastic drugs. Glucosamine has been shown to increase the frequency at which cancer cells replicate. Concomitant administration may lead to decreased efficacy of the antineoplastic agents. It is theorized that the risk

Table 1. Dietary Supplements and Indications

Score	Medications
Anxiety Valerian, lemon balm, glutamine, kava, and teas: passion flower, hops, and chamomile	Inflammation Fish oil and willow bark
Cancer Beta carotene, fish oil, black or green teas, garlic, soy, and vitamin A and D	Liver Milk thistle
Canker Sores Lysine	Menopausal symptoms Black cohosh, dong quai, red clover, and evening primrose
Cholesterol Fish oil, red yeast rice, plant sterols and stanols, and garlic	Migraine/ headache Feverfew, willow bark, butterbur, fish oil, magnesium, co-enzyme Q10, and riboflavin
Colds and Flu Echinacea, elderberry, garlic, zinc, and vitamin C	Motion sickness/ Nausea Ginger and peppermint
Dementia/ Memory Ginkgo, huperzine A, and vitamin E	Osteoarthritis Glucosamine and chondroitin
Depression St. John's wort, fish oils, 5-HTP, tryptophan, glutamine, and inositol	Osteoporosis Soy, ipriflavone, calcium, and vitamin D
Diabetes Bitter melon, gymnema, chromium, alpha lipoic acid, cinnamon, and green tea	Probiotics Lactobacillus, bifidobacterium infantis and comfrey
Energy/ Weight loss Guarana and bitter orange	Prostate Enlargement Saw palmetto and lycopene
Gastrointestinal distress Peppermint oil and chamomile tea	Sleep Melatonin, valerian, and kava
Heart Health/ Heart Failure Co-enzyme Q10, arginine, fish oils, grape seed extract, and garlic	UTI Cranberry

exists regardless of antineoplastic agent. However, the most extensively studied are etoposide and doxorubicin.

HAWTHORN

Hawthorn, also known as May Day flower, haws, or hedge thorn, is a spiny tree that grows in sunny, wooded areas across the world. Its flowers begin to bloom in May after which berries begin to grow. The use of hawthorn can be dated back to the first century where it treated conditions of the heart. By the 1800s, American doctors were using the berries of the plant to treat irregular heartbeat, high blood pressure, and chest pain. Today, heart failure patients may use the leaves and flowers of the plant as a dietary supplement. Hawthorn's actions can be attributed to the oligomeric procyanidins (OPC) and quercetins.

Table 2.

CYP Substrates							
1A2	2B6	2C8	2C9	2C19	2D6	2E1	3A4
Amitriptyline Caffeine Clozapine Estradiol Naproxen Ondansetron Propranolol Acetaminophen Tacrine Theophylline Warfarin Verapamil	Bupropion Efavirenz Isfosfamide Methadone	Paclitaxel Torsemide Repaglinide	NSAIDs Glipizide Sulfonylureas Losartan Amitriptyline Tamoxifen Torsemide Warfarin	PPIs Diazepam Phenytoin Amitriptyline Citalopram Cyclophosphamide Indomethacin Primidone Progesterone Propranolol Warfarin	Beta-Blockers Amitriptyline Haloperidol Aripiprazole Duloxetine Nortriptylline Oxycodone Propranolol Tamoxifen Tramadol Venlafaxine	Halothane Acetaminophen Benzene Ethanol Formamide	Macrolides Quinidine Benzodiazepines Cyclosporine HIV Anti-virals Cisapride Chlorpheniramine CCBs Atorvastatin Simvastatin Estradiol Progesterone Testosterone Buspirone Caffeine Dexamethasone Fentanyl Irinotecan Methadone Ondansetron Quinine Sildenafil Trazadone Vincristine Zolpidem
CYP Inducers							
Insulin Nafcillin Omperazole Tobacco	Phenobarbital Rifampin	Rifampin	Rifampin Secobarbital	Carbamazepine Prednisone Rifampin	Dexamethasone Rifampin	Ethanol Isoniazid	HIV Anti-virals Carbamazepine Barbiturates Glucocorticoids Phenobarbital Phenytoin Rifampin St. John's wort
CYP Inhibitors							
Fluvoxamine Ciprofloxacin Cimetidine Amiodarone Fluoroquinolones Interferon	Thiotpea Ticlopidine	Gemfibrozil Glitazones Montelukast	Fluconazole Amiodarone Fenofibrates Fluvastatin Lovastatin Sertraline Voriconazole	PPIs Cimetidine Fluoxetine Indomethacin Ketoconazole Topiramate Ticlopidine	Fluoxetine Quinidine Terbinafine Sertraline Citalopram Cocaine Diphenhydramine Doxorubicin Methadone Metoclopramide Ranitidine	Disulfran	HIV anti-virals Clarithromycin Ketoconazole Arepitant Fluconazole Verapamil Diltiazem Amiodarone Ciprofloxacin Voriconazole

Hawthorn has been proven to be effective as a cardioprotective herb. It has anti-spasmodic, hypotensive, diuretic, and cardiotonic properties. Hawthorn inhibits myocardial sodium/potassium ATPase, phosphodiesterase as well as the angiotensin converting enzyme. It can dilate the peripheral blood vessels, increase heart muscle metabolism, dilate coronary arteries, and improve blood flow to the heart. Hawthorn can be used during any stage of heart failure, however it is most effective in stage one and two.

Due to its wide variety of actions, hawthorn can be used for support of a broad spectrum of cardiac disorders.

Commonly, patients with hypertension, angina, arrhythmias, congestive heart failure, peripheral vascular disease, and high cholesterol supplement their diet with hawthorn.

Hawthorn is generally safe with limited adverse effects. The most common adverse effects are hypotension and sedation, which generally occur with high doses. Other side effects include bradycardia, respiratory depression, palpitations, and headache. Abdominal discomfort was a rare side effect.

There are several drug interactions that can be attributed to hawthorn. When given with beta blockers or calcium channel blockers, there is a risk of severe hypotension. When combined with digoxin, the effects of digoxin on the heart are increased. However, when given concomitantly with the vasoconstrictor phenylephrine, there is a decreased effect of hawthorn.

KAVA

Kava is a dietary supplement derived from the plant *Piper methysticum*. It is native to the islands of the South Pacific. Kava is mainly used for its anxiolytic and sedative properties through its claim to support relaxation without impairment in memory or motor function. Sedation has been shown to occur through possible increase in GABA binding receptors. Also, kava may inhibit of sodium and calcium channels to cause direct decreases in systemic vascular resistance and blood pressure. Kava has been reported to have the ability to inhibit cyclooxygenase and decrease the synthesis of thromboxane A2, resulting in decreased platelet aggregation.

When used in conjunction with anxiolytics, antidepressants, and benzodiazepines, kava may cause an additive effect increasing the risk of sedation and central nervous system (CNS) depression. Kava may also inhibit or induce CYP 1A2, 2C9, 3A4, and 2E1 leading to toxicity and/or treatment failure. Some drugs metabolized via these pathways include antifungals, antihistamines, and some antineoplastic agents such as etoposide, paclitaxel, vinblastine, and vincristine.

The most common side effects associated with kava include gastrointestinal symptoms, dizziness, allergic reactions, and dry mouth. Due to possible dopamine antagonism, extrapyramidal side effects such as involuntary oral and lingual reflexes, and twisting movements of the head and trunk have been cited. One significant side effect associated with the use of kava is hepatotoxicity leading to hepatitis up to liver failure. It is recommended to monitor liver function tests in patients consuming kava. The use of kava is not recommended in pregnancy or lactation due to its potential to cause loss of

uterine tone. Kava has not been studied in children and is therefore not recommended.

MELATONIN

Melatonin is a hormone synthesized in the pineal gland. The hormone is produced from the amino acid tryptophan which is then converted to serotonin then to melatonin. Melatonin is secreted into the blood and cerebrospinal fluid to regulate the body's circadian rhythm. Highly lipid soluble, melatonin freely crosses cell membranes including the blood brain barrier and is highly bound to albumin. Clinical studies suggest melatonin may be useful in decreasing sleep latency and improving sleep duration. Melatonin use supports recovery from jet lag and healthful sleep.

Melatonin may alter gestational hormone levels. Therefore, those who are pregnant, attempting to become pregnant, or lactating should avoid its use. Melatonin has been studied in clinical trials in children, but short term use is recommended. Adverse effects of melatonin include drowsiness, sedation, flushing, and headache. Caution should be used in patients taking fluvoxamine, nifedipine, and propranolol. Concomitant use with these medications should be avoided. Blood pressure, glucose, and heart rate should be monitored in patients taking melatonin.

MILK THISTLE

Milk thistle, *Silybum marianum*, is a flowering plant of the daisy family. It gets its name from the milky substance that exudes when the stems are broken or crushed. It is native to the Mediterranean region and grows in dry, sunny areas.

Seeds from the milk thistle plant are used for medicinal purposes and as a coffee substitute. The above-ground parts of the plant are eaten as a vegetable. Milk thistle has been used for more than 2,000 years by patients with liver disorders including chronic hepatitis, cirrhosis, jaundice, and toxic liver damage caused by alcohol, drugs (such as acetaminophen), industrial chemicals, or the "death cap" mushroom. However, there is insufficient evidence to rate the effectiveness of milk thistle for these purposes. It may also support healthy blood glucose levels. In combination with conventional treatment, milk thistle appears to decrease fasting blood glucose, hemoglobin A1c, total cholesterol, LDL cholesterol, and triglycerides when compared to placebo. There is also evidence that it reduces insulin resistance in patients with type 2 diabetes and alcoholic cirrhosis.

Silymarin is the active constituent of milk thistle and

after metabolism concentrates in hepatocytes. It causes alterations in the hepatocyte that reduce penetration of toxins and increases regeneration of the cell if it gets damaged. Silymarin also acts as an antioxidant and free radical scavenger and is a potent inhibitor of tumor necrosis factor (TNF).

Silymarin inhibits CYP2C9. Medications metabolized via this pathway may result in toxicity of the drug. Combination of milk thistle and drugs metabolized by CYP2C9 should be avoided. Silymarin also inhibits CYP3A4, but the reaction is not clinically relevant to the metabolism of other medications. There are no clinical studies investigating the use of milk thistle in children, therefore its use is not recommended.

RED YEAST RICE

Red yeast rice is the product of fermented rice on which red yeast has grown. Its use can be dated back to the Tang Dynasty in 800 AD. During its long history, it has been used to support healthy blood circulation, as a food preservative, and food dye for Peking duck.

The medicinal uses of red yeast rice have been studied extensively in China. Studies have shown that it can reduce cholesterol concentrations by 11–32 percent and triglyceride concentrations by 12–19 percent. Red yeast rice contains 10 mevinic acids which competitively inhibit 3-hydroxy-3-methyl-glutaryl-coenzyme reductase (HMG-CoA), the enzyme of cholesterol biosynthesis. The same mevinic acids found in red yeast rice are also found in lovastatin. Studies have shown that 5mg of red yeast rice is equivalent to 10–20 mg of lovastatin.

Red yeast rice is generally well tolerated with minimum adverse effects. The most common complaints involve abdominal discomfort, heartburn, and flatulence. If red yeast rice isn't fermented correctly, it can contain citrinin which is a toxin that can lead to kidney failure. Red yeast rice has been linked to case reports of myalgias, rhabdomyolysis, myopathy, and hepatotoxicity similar to HMG-CoA reductase inhibitors.

When red yeast rice is combined with alcohol or other hepatotoxic medications, it can lead to liver damage that is irreversible. When combined with prescription cholesterol lowering medications such as gemfibrozil, niacin, and HMG-CoA reductase inhibitors, red yeast rice can increase the risk of myalgias and myopathy. Red yeast rice is metabolized by CYP3A4. Any medications that can either inhibit or induce this enzyme can

interact with red yeast rice and increase the risk for side effects.

SAW PALMETTO

Saw palmetto is a small palm-like plant that produces yellow flowers and reddish black berries. It is native to the southeastern coast of the United States. The scientific name is *Serenoa repens*.

The berries were a food staple and medicinal plant of the southeastern American Indians. In the early 1900s, the berries were used to treat urinary tract problems in men. The berries are partially dried and broken down with a solvent such as hexane or ethanol to produce the saw palmetto extract.

Saw palmetto is most commonly taken to promote prostate health. It has been shown to provide mild to moderate improvement in the urinary symptoms of BPH including frequent urination, painful urination, hesitancy, urgency, and perineal heaviness.

Studies have shown that saw palmetto is effective for up to a year of use. However, it may take one to two months before significant symptomatic changes are seen. Lipophilic extracts containing 80–90 percent fatty acids dosed at 160 mg by mouth twice a day or 320 mg by mouth once a day were used in clinical trials.

The berries of saw palmetto contain volatile oils and fatty acids, which are the active constituents for affecting BPH symptoms. Saw palmetto has antiandrogenic and antiproliferative properties. It noncompetitively inhibits 5-alpha-reductase types 1 and 2 and prevents the conversion of testosterone to dihydrotestosterone (DHT). DHT is a critical mediator of prostatic growth in BPH.

Saw palmetto has been shown to inhibit lipoxygenase and cyclooxygenase (COX), leading to its anti-inflammatory properties. It has also been noted to have antiestrogenic properties.

In vitro evidence shows that saw palmetto may inhibit CYP2D6 and CYP3A4; however, in vivo evidence shows no effect on these enzymes. CYP2D6 and CYP3A4 inhibition may increase the levels of drugs that are metabolized by these pathways; therefore, caution is advised.

Saw palmetto has been reported to prolong bleeding time. There is an increased risk of bleeding when combined with other anticoagulant or antiplatelet drugs. As mentioned previously, saw palmetto also has some antiestrogenic properties which may reduce the effectiveness of oral contraceptives and estrogens.

ST. JOHN'S WORT

St. John's wort, also known as hypericum, is a member of the *Hypericaceae* family. The flowers and leaves of the plant are used for its medicinal purposes. St. John's wort is commonly used to promote a good mood and support the body to combat anxiety, fatigue, loss of appetite, and insomnia. It has also been used historically for bronchitis, burns, cancer, gastritis, scabies, and wound healing.

St. John's wort contains hypericin and hyperforin, considered to be the active components responsible for its actions. They act on the chemical messengers in the CNS, on the uptake of serotonin, noradrenalin, and dopamine. Studies have also shown that it has affinity for adenosine, 5HT, benzodiazepine, and GABA receptors, and weakly for monoamine oxidase. It has been studied in children under the age of 12 years; however it has only been studied for a maximum of six weeks of therapy.

Common adverse effects include gastrointestinal symptoms, allergic reactions, vertigo, confusion, and sedation. Photosensitivity reactions are rare but they have been associated with higher doses. St. John's wort is considered to have numerous drug interactions. Hypericin and hyperforin are responsible for the drug interactions seen with St. John's wort. Hypericin can induce CYP1A2 and hyperforin induces CYP3A4. St. John's wort also has the ability to induce CYP2C19, which is responsible for the metabolism of warfarin. Concomitant administration can cause the INR to be unstable, with a decrease in warfarin serum concentration most commonly observed.

St. John's wort has also been shown to decrease concentrations of cyclosporine in the blood. The decrease has ranged from 25–62

percent beginning about three weeks after initiating St. John's wort. Oral contraceptives have been shown to be less effective when combined with St. John's wort. There have also been documented cases of heavy breakthrough bleeding beginning about six to eight months following initiation of St. John's wort. Both interactions are associated with CYP enzymes.

Digoxin interaction has been documented in numerous pharmacokinetic studies. The interaction has been associated with absorption and distribution phases rather than metabolism or clearance phases.

Another significant interaction is between St. John's wort and selective serotonin re-uptake inhibitors (SSRIs) leading to serotonin syndrome. The proposed mechanism involves the ability of St. John's wort to act on the same receptors in the brain as SSRIs thereby increasing the amount of serotonin reuptake inhibition. Serotonin syndrome symptoms can range from mild shivering, tachycardia sweating, and diarrhea to severe muscle rigidity, hypertension, hyperthermia, and seizures. The same interaction has been shown in combination with selective serotonin norepinephrine reuptake inhibitors (SNRIs).

A less documented interaction involves the antineoplastic agent irinotecan, which is metabolized by CYP1A2 and CYP3A4 to an active metabolite. St. John's wort induces CYP1A2 and CYP3A4 leading to an increase in the production of the active metabolite. This can lead to irinotecan toxicity characterized by severe diarrhea, myelosuppression, and severe neutropenia if given concomitantly. Coadministration should be avoided due to the risk.

VITAMIN C

Vitamin C, or ascorbic acid, is a commonly used water-soluble vitamin. It is an essential vitamin (the body cannot produce or store vitamin C, so it must be consumed). It is found in vegetables and fruits, especially citrus fruits, as well as supplements.

Vitamin C is well absorbed orally at lower doses, but absorption decreases as the dose increases. Also, when a food is cooked or ages, less vitamin C is available for absorption. In the body, it is removed through the kidneys and eliminated in the urine.

Historically, vitamin C deficiency was known to cause scurvy and, once identified, also played a role in preventing and treating the disease. It is also commonly used to improve iron absorption from the gastrointestinal tract.

Administering at least 200 mg of vitamin C per 30 mg iron has been shown to be effective in improving iron absorption. Vitamin C is most notably used to support immunity against the common cold and other viral infections. However, high-dose vitamin C appears to be effective for the treatment, but not prevention, of the common cold. The tolerable upper limit of intake for adults is recommended as 2,000 mg per day. When this dose is exceeded, stomach upset and diarrhea may occur. Also, less than 50 percent of a dose above 1,000 mg is able to be absorbed at one time.

Vitamin C is an antioxidant and a free radical scavenger. It has been shown to improve immune function by stimulating T-lymphocyte activity, phagocyte function, and antibody production. Vitamin C also causes urinary acidification which does not contribute to its effectiveness, but may cause drug interactions.

Vitamin C is not a CYP inhibitor, inducer, or substrate. Most drug interactions are related to its antioxidant properties. The use of antioxidants, including vitamin C, is not recommended during chemotherapy because many chemotherapy drugs break down into free radicals which attack cancer cells. Antioxidants scavenge the free radicals, causing the chemotherapy to be less effective. However, it has been shown that cytotoxicity is also reduced when vitamin C is combined with chemotherapy drugs that do not produce free radicals as a mechanism of action. There is also evidence that combining chemotherapy with antioxidants may improve cancer cell apoptosis, leading to more effective treatment. Until there is more definitive information available, the combination of vitamin C and chemotherapy should be discouraged.

The use of estrogens with vitamin C should be cautioned. High levels of vitamin C have been shown to reduce the metabolism of estrogens by as much as 55 percent. This interaction may affect oral contraceptives as well as oral or topical hormone replacement therapies. Monitor for estrogen-related adverse effects.

Vitamin C 1,000mg daily for seven days has been shown to reduce levels of the protease inhibitor indinavir (Crixivan®) by up to 14 percent. This could potentially lead to treatment failure of a highly active antiretroviral therapy regimen. It is not known how or why this occurs or if it affects other protease inhibitors. Until more information is known, the combination should be avoided.

High doses of vitamin C (up to 16,000 mg per day)

have been shown to reduce the effectiveness of warfarin, due to the diarrhea that can occur, which reduces the oral absorption of warfarin. The clinical significance of this interaction is not known, but monitor INR for fluctuations.

Vitamin C dietary intake is recommended for children and is considered safe when taken orally and appropriately. However, excessive amounts of vitamin C may be unsafe. Doses in excess of the tolerable upper intake level for the child's age may cause stomach upset and diarrhea, which may lead to dehydration.

CONCLUSION

Consumers are increasingly using dietary supplement products to support health and well-being. Many dietary supplement products and prescription drug medications interact with one another and may have a serious impact on the patient's safety and response to drug therapy. Also, coadministration may result in induction or inhibition of cytochrome P450 enzymes, also leading to changes in response to therapy or increased adverse effects. Dietary supplement products may have more than one active ingredient. Accurate and detailed product labels are imperative to appropriate product selection. It is prudent that health care professionals, consumers, and manufacturers understand the consequences these interactions may pose to the human body and openly discuss the use and potential harm when used in combination. **ap**

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CONTINUING EDUCATION QUIZ

Select the correct answer.

1. SD is a 63-year-old male who has been experiencing severe depression for which he has been taking sertraline (Zoloft™) for about two years. SD goes to the pharmacy to pick up his prescription and decides to buy St. John's wort and chamomile, because he read in a magazine that they could help with depression. About two weeks later, he has symptoms of fever, diarrhea, and mild shivering. What could be causing SD's symptoms?

- a. Interaction between glutamine and St. John's wort
- b. Interaction between glutamine and Zoloft
- c. Interaction between Zoloft and St. John's wort
- d. A resistant strain of the flu

2. MB is a pharmacist working in a retail pharmacy when she receives a call from a physician. The physician wants to know information about how St. John's wort supports a good mood. What does she tell him?

- a. It has affinity for adenosine, 5HT, benzodiazepine and GABA receptors.
- b. It has weak affinity for monoamine oxidase.
- c. The active components responsible for its actions are hypericin and hyperforin.
- d. All of the above

3. MS is a 22-year-old old female who is in good health and takes an oral contraceptive. She develops a rash on her arms and legs. She recently purchased a new lotion from the spa that is supposed to also work as aromatherapy. MS decides that the rash is probably just dry skin and puts the new lotion on her arms and legs. After two days, the rash spreads and begins to itch severely. MS decides to go to the doctor and she is diagnosed with contact dermatitis. What could be the offending agent?

- a. The lotion contains hawthorn berries.
- b. The lotion contains lavender.
- c. The spa's laundry detergent
- d. The lotion contains chamomile.

4. KB is a 45-year-old old male who was recently diagnosed with hypertension. His doctor prescribed a two-drug regimen. Remembering current prescribing guidelines, the doctor chose to start KB on lisinopril and hydrochlorothiazide. KB went home and told his wife what the doctor said and she remembered that taking hawthorn can promote heart health. What do you tell KB about the use of hawthorn and antihypertensive agents?

- a. Components of hawthorn may cause hypotension, and taking hawthorn may lower his systolic and diastolic blood pressure.
- b. Hawthorn can be combined with prescription medications safely promote healthy blood pressure.
- c. Hawthorn, when combined with anti-hypertensives, can lead to severe hypotension and should be avoided.
- d. A and C

5. CC is a 32-year-old Asian female who has dyslipidemia due to genetics and diet. Her doctor has tried a combination of HMG-CoA reductase inhibitors, niacin, and fenofibrates in the past with no success. CC could not tolerate flushing associated with niacin and could not remember to take the fenofibrates. Taking a HMG-CoA reductase inhibitor alone was not enough to reduce her cholesterol. CC asks her doctor if she should try a combination of a HMG-CoA reductase inhibitor and red yeast rice. The doctor calls you for advice. What do you tell her?

- a. Studies have shown that it can reduce cholesterol concentrations by 11–32 percent, and triglyceride concentrations by 12–19 percent.
- b. Mevinic acids found in red yeast rice are also found in lovastatin.
- c. Red yeast rice has been linked to case reports of myalgias, rhabdomyolysis, myopathy, and hepatotoxicity.
- d. All of the above

6. TB is a 21-year-old male who started college last month. He has been staying out late and eating a lot of pizza. He begins to develop heartburn that wakes him up at night. TB buys calcium carbonate antacids at his local pharmacy and begins taking them for symptoms of heartburn. About two weeks later, TB develops walking pneumonia and goes to the student clinic. The doctor prescribes a seven-day course of levofloxacin (Levaquin™). TB is admitted to the hospital a week later for worsening pneumonia. What could be the cause?

- a. TB did not take antibiotic as directed.
- b. The antacids for TB's heartburn interacted with the antibiotic.
- c. TB developed a resistant form of pneumonia.
- d. TB drank alcohol with his antibiotic, rendering it ineffective.

7. Different types of antacids interact with prescription medications in different ways. Which of the following statements is correct regarding antacid mechanisms?

- a. Aluminum-based antacids release a free aluminum ion when they react with hydrochloride in the stomach. The aluminum ion is then available for intraluminal binding and adsorption to drugs.
- b. Calcium carbonate antacids release carbonate when they react with hydrochloride, which can alkalize the urine thereby increasing excretion of weakly basic drugs.
- c. Aluminum based antacids increase the gastrointestinal transit time which can decrease the absorption of drugs from the stomach.
- d. Magnesium based antacids decrease the gastrointestinal transit time which can increase the absorption of drugs from the stomach.

8. SC is a 26-year-old male who has a family history of Huntington's disease. He read in an article on the Internet that Co-Q10 can help to lessen neurological decline. Not knowing much else about the drug, he calls up his best friend who happens to be a pharmacist. What should SC be informed about Co-Q10?

- a. Co-Q10 is generally well tolerated, with gastrointestinal discomfort being the most frequent complaint.
- b. Dividing the total daily dose into smaller doses has been shown to help with side effects.
- c. Co-Q10 should be avoided during invasive procedures or surgery. It has been shown that Co-Q10 interferes with blood pressure control and bleeding.
- d. All of the above

9. Drug interactions caused by vitamin C are most likely related to what property of vitamin C?

- a. Vitamin C inhibits CYP450 enzymes.
- b. Vitamin C is an antioxidant.
- c. Vitamin C reduces platelets.
- d. There is no literature to suggest that vitamin C causes drug interactions.

10. Why should lower daily doses or divided daily doses be recommended for vitamin C supplementation?

- a. Because higher doses lead to adverse effects such as stomach upset and diarrhea
- b. Because higher doses of vitamin C are poorly absorbed
- c. Because the tolerable upper dose recommended for adults is 2,000 mg per day
- d. All of the above

11. Mrs. P calls your pharmacy worried because her 5-year-old son ate a wild mushroom growing in their front yard. She recently saw on TV that the death cap mushroom can cause liver failure if it is eaten. What would you recommend to Mrs. P?

- a. Recommend that she give her son milk thistle because it has been shown to be safe and effective in children.
- b. Recommend that she give her son milk thistle because it has been shown to be safe and effective for the treatment of death cap mushroom liver toxicity.
- c. Recommend she do nothing because most mushrooms are harmless.
- d. Recommend she call the Poison Control Center.

12. DG comes into your pharmacy and says, "This saw palmetto doesn't work!" He continues to experience symptoms associated with benign prostatic hyperplasia (BPH). Upon further questioning you find out that DG is taking an 80 percent lipophilic extract at 160 mg twice a day for the past two weeks. He does not take any other medications. What could be a reason that DG is not having symptom improvement after taking saw palmetto?

- a. Saw palmetto has no evidence to support its use in the symptomatic relief of BPH.
- b. When taking saw palmetto, symptomatic changes may not be seen until after one to two months of treatment.
- c. Saw palmetto is better absorbed as a tea and DG should switch to a tea preparation.
- d. All of the above

13. DG is taking saw palmetto and has symptomatic relief of his BPH. DG recently had a heart attack and was started on low-dose aspirin (81 mg) daily and warfarin 5 mg daily. Can DG continue to take saw palmetto with aspirin and warfarin?

- a. Yes, there is no drug-drug interaction between saw palmetto and anticoagulants or antiplatelet drugs.
- b. No, saw palmetto prolongs bleeding time and may cause an increased risk of bleeding when combined with the aspirin and warfarin.
- c. Yes, even though saw palmetto prolongs bleeding time, the benefit of the saw palmetto relieving BPH symptoms outweighs the increased risk of bleeding.
- d. All of the above

14. EJ heard that saw palmetto may increase her breast size and improve her sex life. She is interested in trying it. She is 27 years old and the only medication she takes is birth control. Should EJ start taking saw palmetto?

- a. Yes, there isn't any research to support this use, but it won't hurt anything to try.
- b. Yes, there is extensive research supporting the use of saw palmetto in females.
- c. No, she should not use supplements to enhance her physical appearance and sex life.
- d. No, the saw palmetto has anti-estrogenic effects and may cause her birth control to be ineffective.

15. SB comes to your pharmacy and has heard great things from her friends about echinacea. She sees a product on your shelf and asks how she should take the tablets to prevent and treat the common cold. You tell her:

- a. She should take two tablets three times a day every day for prophylaxis throughout the year.
- b. She should take two tablets three times a day at the first sign or symptom of a cold and continue for about 7–10 days.
- c. She should not take echinacea because there is absolutely no evidence that it reduces the duration of the common cold.
- d. She should take the tablets the same way her friends take them.

16. LM wants to use echinacea tablets, but she is taking the following medications (a, b, c, and d). Which of her medications could be affected by the echinacea?

- a. Lovastatin 10 mg daily
- b. Oxycodone/acetaminophen 5 mg/325 mg every four to six hours prn pain
- c. Estradiol 1 mg daily
- d. All of the above may be affected by echinacea

17. Tacrolimus is an immunosuppressant used to prevent organ transplant rejection. It is metabolized by CYP 3A4, which may cause an interaction with echinacea. What is another reason for an interaction between tacrolimus and echinacea?

- a. Tacrolimus interacts with most of the same medications that echinacea interacts with as well.
- b. Tacrolimus is an immunosuppressant and may be counteracted by the immunostimulatory effect of echinacea.
- c. Tacrolimus is an immunosuppressant and may have an additive effect from the immunosuppressant effect of echinacea.
- d. Tacrolimus is dosed every 12 hours and echinacea is dose three times a day.

18. JP is watching her grandchildren for the summer and one of them is beginning to feel sick. Because echinacea worked so well for her, she wants to give it to her 11-year-old grandson. What counseling point about echinacea should you discuss with JP?

- a. Echinacea has been shown to cause rash in 7 percent of children and may be caused by an allergic reaction. If her grandson develops a rash, it may be due to the echinacea and the supplement should be discontinued.
- b. Echinacea has never been shown to be safe for use in children and should not be used for her grandson.
- c. Echinacea may turn her grandson's urine purple. This is normal and the supplement does not need to be discontinued.
- d. Echinacea should be used prophylactically every day to prevent and treat her grandson's cold.

19. Black cohosh is marketed for which of the following?

- a. Benign prostate hypertrophy
- b. Cough, congestion, and eczema
- c. Menopausal symptoms
- d. Traumatic brain injury

20. VS comes to your pharmacy with a chief complaint of heartburn. She has tried Tums in the past with moderate relief. She wants to use a long-term controller medication over the counter. Her current medications include a low-dose oral contraceptive, a women's formula multi-vitamin, oral vitamin B12, and ibuprofen. What do you tell VS about the use of acid-suppressing medications and vitamin B12?

- a. She should use dairy products to help reduce the heartburn she experiences.
- b. She should avoid the use of acid-suppressing medications because they can interact with vitamin B12, reducing its effectiveness.
- c. Combination with Co-Q10 will decrease any interaction experienced.
- d. B and D

Drug Interactions With Dietary Supplements

May 1, 2012 (expires May 1, 2015) • Activity Type: Knowledge-based

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Quiz: Shade in your choice

	a	b	c	d	e		a	b	c	d	e
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Quiz: Circle your choice

21. Is this program used to meet your mandatory C.E. requirements?
a. yes **b.** no
22. Type of pharmacist: **a.** owner **b.** manager **c.** employee
23. Age group: **a.** 21–30 **b.** 31–40 **c.** 41–50 **d.** 51–60 **e.** Over 60
24. Did this article achieve its stated objectives? **a.** yes **b.** no
25. How much of this program can you apply in practice?
a. all **b.** some **c.** very little **d.** none

How long did it take you to complete both the reading and the quiz? _____ minutes



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