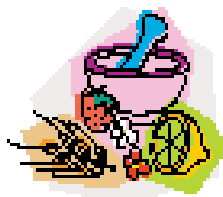




A PHARMACY CONTINUING EDUCATION PROGRAM

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September 2009 "Review of Natural Products" #707-000-09-009-H01-P



THIS MONTH
"Review:
Natural Products"

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HAVE YOU RECENTLY MOVED? PLEASE NOTIFY US.

More than ever, Americans are utilizing alternative and complementary therapies, especially natural products. In this lesson, we review several of these. Our goal is to describe them in order to be increasingly capable of providing information to our patients. This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings. **The program ID # for this lesson is 707-000-09-009-H01-P. Pharmacists completing this lesson by September 30, 2012 may receive full credit.**

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page** (for continuous participants only).

The objectives of this lesson are such that upon completion the participant will be able to:

1. Explain the DHEA of 1994 & its impact on the herbal market.
2. Identify common herbs used in pharmacy practice.
3. List common herbs that are capable of interacting with antiplatelet drugs.
4. Discuss counseling tips regarding herbal products.

All opinions expressed by the author/authors are strictly their own and are not necessarily approved or endorsed by W-F Professional Associates, Inc. Consult full prescribing information on any drugs or devices discussed.

BACKGROUND

Since the mid 1990's, the use of herbal products has increased dramatically in the United States.¹ This interest came at a time when consumers began to focus on self-care and improving their overall health. The public was looking for alternatives to conventional Western medicine. This was also the beginning of an increased dynamic in more control of individual health. These products could be purchased without having to consult a physician. Herbals have been promoted for a variety of chronic conditions as well as a method of preventing disease. Consumers consider herbal products as more natural and therefore healthier.

Herbs are a big business. Over 5 billion dollars is spent annually in the U.S. on these products, and this continues to be one of the fastest growing sectors of the healthcare business.^{1,2} One study reported over 60 million people above age 18 used herbs for general health, depression, headaches, rash, allergy and insomnia. In a survey conducted by the Centers for Disease Control, approximately 20% of 18,000 individuals responding had used an herbal product in the previous year. Herbal products are used by all types of people in every socioeconomic level. The most common traits of consumers purchasing herbs are a college education, female between 24 to 49 years of age, and an annual income above \$35,000.

Since there is generally a lack of understanding about many herbal products, healthcare professionals often discourage at-risk populations from using herbs.³ These groups include pregnant women, HIV infected patients, infants and patients with cancer. It is of concern to note that 1 survey reported 14% of pregnant women responding had used an herbal product during their pregnancy, and 16% of HIV infected patients in a clinical trial reported using herbal medications.

Many consumers do not tell healthcare professionals that they are taking herbs.³ There is a fear that patients may be rebuked for using these alternative therapies. In addition, since many physicians are not familiar with the effects of herbs, they may not even ask the patient about herbal drug use.

Pharmacists are in a unique position to provide balanced and clear information to consumers who are interested in taking herbal remedies.³ A 2007 study of pharmacists' knowledge about herbal products reported low test scores, less than 50%, regarding herbal products. The study showed that pharmacists generally knew what the herbs were used for, but were unable to identify common adverse events and drug interactions.

This lesson is designed to update the pharmacy practitioner on commonly used herbal products, the risks and benefits of these, as well as any potential drug- herb interactions.

INTRODUCTION

There are over 20,000 herbal products currently on the market in the U.S.^{1,4} These products are available directly to the consumer without a prescription. They can be purchased over the counter in grocery stores, pharmacies or on the internet. The most frequently purchased products include ginseng, ginkgo, St. John's Wort, Kava, feverfew, and echinacea.

Prescription and non-prescription medications are standardized and regulated by the FDA.¹ They contain a specific amount of active ingredient in each dose. This standard amount of active ingredient does not vary significantly between batches of the product. Consumers expect their medication to provide the same amount of active ingredient as that shown on the label. Many consumers assume that herbal products are like drugs and contain the amount of ingredient that is shown on the label. The problem is that herbal products are not required to conform to the same standards as prescription drugs. One reason given by proponents of herbs is that they are "natural" and that many individual components of the herb have some activity. These components act together to provide the effect seen with the specific herb. Since the herb is often prepared from the raw plant material, different concentrations of active ingredients may be present depending on what parts of the plant are used in preparation of the herb. Some herbs do contain a specific active ingredient, such as ginseng. The active component is ginsenosides. However, there is no standard concentration required for ginseng, so the amount of active ingredient can vary substantially. One study found 8 of 24 ginseng products did not contain any detectable level of the labeled active ingredient.

Another potential problem with herbal products is that they may be adulterated or contaminated.^{1,5} One report demonstrated that 50% of 38 Asian herbal remedies had excess lead levels. Another report showed that 1 in 5 Indian herbs purchased in the Boston area or through internet sales were adulterated with heavy metals. Other studies have reported herbal products used for insomnia were adulterated with benzodiazepine, and that some feverfew products contained high levels of melatonin.

DIETARY SUPPLEMENT HEALTH AND EDUCATION ACT

In 1994, the Dietary Supplement Health and Education Act was approved.^{1,6} This classifies herbs as dietary supplements and allows for the products to be sold over the counter without having to demonstrate safety and effectiveness. Manufacturers may market

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any dietary supplement as a way to address a nutritional deficiency or support a body function (such as digestion or immune function). Therefore, a saw palmetto product may be labeled that it maintains a healthy prostate, but may not claim that it treats benign prostatic hypertrophy. This rule allows for any herbal product to remain on the market as long as it is not proven to be unsafe. This is completely opposite of how prescription drugs are approved by FDA. Prescription drugs must demonstrate safety and efficacy before being allowed into the market. The FDA may only consider removal of an herbal product from the market reports received identifying safety concerns. Pharmacists may report adverse effects to the FDA if they have a patient who indicates that an herbal product caused harm. The MEDWATCH process for reporting adverse effects from herbal products is the same process as that for prescription and non-prescription drugs. Adverse effects can be reported by calling 1-800- 332-1088 or by downloading the form from www.fda.gov/Safety/MedWatch/HowToReport/DownloadForms/ucm2007307.htm.

COMMON HERBS

This section will review common herbs used by consumers, their risks and the role of the pharmacist.

ECHINACEA 5,7-9

Echinacea is usually derived from the roots of the *Echinacea purpurea*, *E. angustifolia* or the *E.pallida* plants.

Use

Echinacea has been used to stimulate the immune system, and particularly, to treat the common cold and other upper respiratory problems.

Clinical Support

The mechanism of action of echinacea is unclear. It may stimulate the immune system by increasing the activity of lymphocytes and increasing phagocytosis. Echinacea is also reported to have antiviral activity. Some of the benefits seen in the treatment of colds and influenza may be through its anti-inflammatory effects. There is conflicting evidence that echinacea is effective in treating the common cold. Some investigators suggest that this is due to differences in the products and doses used in the trials.

A meta-analysis was conducted to evaluate the benefit of echinacea in the common cold. The results of this meta-analysis demonstrate that echinacea has a small benefit in reducing the incidence and severity of the common cold. However, additional studies must be conducted to confirm these benefits.

Dose

Two tablets three times a day (6.78 mg *E. purpurea*), or 20 drops every 2 hours for day 1, then 20 drops three times a day for the tincture.

Adverse Effects

Echinacea has caused gastrointestinal symptoms such as nausea, vomiting and diarrhea. Rash has been reported, particularly in children who have taken echinacea. These rashes appear to be an allergic reaction. Also allergic reactions have been reported in individuals with atopy or those with allergies to plants in the daisy family. Echinacea has been reported to be contaminated with lead or arsenic in some cases.

There is some data to suggest that echinacea may affect fertility, so it should be avoided in women who are trying to conceive.

Contraindications

Echinacea is contraindicated in patients with autoimmune diseases (e.g. Lupus) , cancer, HIV infections and other severe illnesses that can affect the immune system.

It should not be given to women who are pregnant or breastfeeding.

Avoid use in patients who are allergic to plants in the daisy family.

Drug Interactions

There are some potential drug interactions with echinacea. It does inhibit two of the cytochrome P450 enzyme pathways (1A2, 3A4). It should be used with caution when combined with any drugs that are metabolized via these pathways.

Common agents to avoid include

Cyp450 pathway	Drugs metabolized via pathway
1A2	Acetaminophen, amitriptyline, clopidogrel, ondansetron, olanzapine, tacrine, verapamil
3A4	Lovastatin, clarithromycin, diltiazem, cyclosporine, indinavir

Counseling Tips

- Do not use echinacea for longer than 8 weeks.
- Do not use this product if pregnant or breastfeeding, or trying to get pregnant.
- Do not use in children < 2 years of age.
- Some tinctures have a high alcohol content and should be avoided in children.
- Ask patient if they have any allergies to plants in the daisy family.
- Some echinacea products have been shown to be contaminated with arsenic or lead.
- Encourage patient to discuss the use of echinacea with their physician.

FEVERFEW^{7,8}

Feverfew comes from a plant that grows in the U.S. and Canada. The leaves and flowers are used for herbal preparations.

Use

Feverfew has been used to reduce fevers (as the name implies). It is also used in patients with migraine headaches.

Clinical Support

It was initially determined that the active component of feverfew was parthenolide. Most products are manufactured based on the amount of parthenolide available in the dosage form. Parthenolide inhibits serotonin release, which may explain the benefits of feverfew in migraine. Recent studies have isolated chrysanthenyl acetate, an essential oil of feverfew, which may also have activity. Chrysanthenyl acetate inhibits prostaglandin synthetase which may account for the analgesic effect of feverfew. In addition, melatonin is found in feverfew, and this may be another active component of the product.

A number of clinical trials have assessed the effectiveness of feverfew in migraine headaches. The results of these trials are conflicting. The differences in outcomes in these trials may be due to differences in the feverfew products used in the trials. A more stable product has been tested (MIG-99) given at a dose of 6.25 mg three times a day. There was both a statistically and clinically significant reduction in the number of migraine attacks experienced in this subset of patients.

Dose

The dose of feverfew used to prevent migraine headaches ranges from 50 to 200 mg of parthenolide daily. Higher doses are used if the patient is currently experiencing a migraine headache.

Adverse Effects

Feverfew is associated with mild gastrointestinal effects such as nausea, heartburn, diarrhea, constipation and flatulence. There are also reports of dizziness, headache, mouth ulcers, and a withdrawal syndrome of pain, muscle stiffness and anxiety.

Contraindications

Feverfew should not be administered to women who are pregnant or breastfeeding.

Drug Interactions

Feverfew may interact with antiplatelet drugs. The data has not been demonstrated in humans

Counseling Tips

- Ask about allergies to chrysanthemums, daisies, marigolds and ragweed. Feverfew can have a cross allergy in patients who suffer from these allergies.
- Feverfew may have antiplatelet effects. It should be discontinued 2 weeks before a patient has surgery. There may be an increased incidence of bleeding.
- Do not use in children under age 2.
- Do not use this product if pregnant or breastfeeding.
- Encourage patient to discuss the use of feverfew with their physician.

GARLIC^{7,8,10}

Garlic is also known as *Allium sativum*. The common garlic bulb is crushed and pressed into tablets. The tablet formulation is the most popular form, although the raw garlic bulb has the same effects.

Use

Garlic is used for its lipid lowering benefits and antimicrobial effects.

Clinical Support

The active component of garlic is allicin. Garlic inhibits HMGCoA reductase, thereby lowering cholesterol. The clinical data on the benefits of garlic in lowering cholesterol are conflicting. Most of the clinical trials that support its effect show a 5-10% reduction of total cholesterol. Although this is beneficial, it is important to remember that many patients require a much more substantial reduction in cholesterol to meet the target goals established.

Dose

The usual dose of garlic is 600 to 900 mg per day.

Adverse Effects

Common adverse effects reported with garlic use include a garlic breath and body smell, nausea, flatulence, dizziness and allergic reaction.

Contraindications

Garlic supplements should not be used if a patient is allergic to garlic or other plants in the Lilly family. Garlic should be avoided in pregnant women because of its oxytocic properties.

Drug Interactions

Garlic can interact with anticoagulant and antiplatelet drugs, resulting in an increased risk of bleeding. Garlic supplements should not be used if a patient is on an anticoagulant or antiplatelet drug.

Counseling Tips

- Do not use garlic if pregnant or breastfeeding.
- Although garlic may help lower cholesterol, it may not be the best choice if a patient needs more than 10% reduction in total cholesterol.
- Point out the demonstrated survival data and overall health benefits achieved with FDA-approved cholesterol-lowering drugs.
- If interested in using garlic, it is acceptable to combine with prescription cholesterol-lowering drugs.
- Encourage the patient to discuss the use of garlic with their physician.

GINKGO BILOBA^{7,8,11,12}

Ginkgo is extracted from the leaves of the *Ginkgo biloba* tree. The extraction process concentrates the active constituents and removes the toxic ginkgolic acid. It is important to ensure that consumers use only the extract.

Use

Ginkgo has been used in patients with dementia, cerebral vascular insufficiency, and memory loss. Although ginkgo has been studied for ADHD, there is no clinical evidence that it has an effect.

Clinical Support

The active components of ginkgo are thought to be the ginkgo-flavonoids and terpenoids. These components are generally found in the leaf and the seeds. The most common form of ginkgo used is an extract of the leaf. The ginkgo seeds contain ginkgotoxin, which can cause seizures, paralysis and death.

It is unclear how ginkgo works. One theory is that it protects tissue from oxidative damage. Ginkgo acts as an antioxidant and free radical, and prevents tissue degeneration. It has been investigated in long term clinical trials for up to 6 years. Currently the National Center for Complementary and Alternative Medicine is conducting a 5 year trial of 3,000 patients over age 75 to determine the effects of ginkgo in dementia. Studies of 3 months to 1 year duration have reported modest improvement in dementia and increased cognitive functioning in patients with moderate dementia. Studies have also shown the benefit of ginkgo in improving memory loss in patients with mild to moderate memory impairment. There is no data to suggest that ginkgo is effective in improving or maintaining memory in normal individuals. In addition, there is no data to suggest that ginkgo can be used to prevent dementia in patients without dementia.

Dose

The recommended dose for dementia is 240 mg daily of ginkgo leaf extract. For use in cognitive function in healthy young individuals the dose ranges from 120 to 600 mg a day. It is recommended that all patients begin with a dose of 120 mg and then titrate the dose higher as needed. Starting with the lower dose will decrease adverse effects.

Adverse Effects

Ginkgo is generally well tolerated. The most frequent adverse effects reported include gastrointestinal upset, headache, constipation and skin reactions.

Contraindications

Ginkgo should not be used during pregnancy or in children < 3 years of age.

Drug Interactions

Ginkgo decreases platelet aggregation and may increase the risk of bleeding when combined with antiplatelet drugs or anticoagulants. It should not be combined with NSAIDs.

Ginkgo should be avoided in patients with seizure disorders or those who are taking drugs that may lower the seizure threshold.

There is evidence that ginkgo may alter glucose levels in patients with diabetes, so it should not be used in combination with antidiabetes drugs.

Ginkgo has been shown to inhibit several of the cytochrome P450 enzyme pathways (1A2,2C19,2C9,2D6,3A4). It should be used with caution when combined with any drugs that are metabolized via these pathways.

Common agents to avoid include:

Cyp450 pathway	Drugs metabolized via pathway
1A2	Acetaminophen, amitriptyline, clopidogrel, ondansetron, olanzapine, tacrine, verapamil
2C19	Citalopram, diazepam, lansoprazole, omeprazole, phenytoin, warfarin
2C9	Warfarin, glyburide, phenytoin, glipizide
2D6	Tramadol, clozapine, codeine, metoprolol, trazodone, fentanyl
3A4	Lovastatin, clarithromycin, diltiazem, cyclosporine, indinavir

Counseling Tips

- Avoid use in children < 3 years of age.
- Do not use during pregnancy or breastfeeding.
- Verify that patients are using standardized ginkgo leaf extract and not ginkgo seeds, which can cause seizure.
- Review the patient's medication list to determine if there are any potential interactions.
- If undergoing surgery, discontinue ginkgo 2 weeks prior to procedure since ginkgo may increase the risk of bleeding.
- Encourage the patient to discuss the use of ginkgo with their physician.

GINSENG 7,8,11-14

American ginseng, or *Panax quinquefolius*, is grown in North America. The root of the plant is used as an herbal remedy. It is important to differentiate American ginseng from Siberian or Asian (*Panax*) ginseng. The benefits of ginseng that are discussed below focus only on American ginseng. Other forms of ginseng are not as potent and are associated with serious adverse effects.

Use

American ginseng is used in diabetes to reduce postprandial blood glucose levels. Ginseng has also been used to improve stamina and energy levels. It has been used in children with attention deficit hyperactivity disorder, although there is no current data that supports this use.

Clinical Support

American ginseng contains several active components. There are a number of active ginsenosides. American ginseng contains higher concentrations of 6 specific ginsenosides. American ginseng also contains polysaccharides that may be responsible for the hypoglycemic effects reported. There are reports that certain forms of American ginseng may also have estrogenic activity.

Most of the clinical evidence with ginseng has consisted of short term evaluations in Type 2 diabetes patients using oral glucose challenge. One trial showed a statistically significant ($p < 0.05$) decrease in postprandial glycemia when 3 gram of ginseng was administered 40 minutes prior to glucose challenge. Two additional trials evaluated a longer term therapy of 8 weeks. Each investigator reported a lowering of blood glucose and hemoglobin A1C. The only adverse effect noted was mild insomnia.

Dose

The dose of American ginseng for improving postprandial blood glucose is 3 grams taken 2 hours before a meal. Higher doses have not demonstrated any benefit.

Contraindications

American ginseng may have estrogenic effects and should not be used in women with breast, ovarian or uterine cancers. Avoid the use of American ginseng in children under 3 years of age.

Adverse Effects

American ginseng is generally well tolerated. There have been reports of gastrointestinal upset, nervousness and hypertension. Panax or Asian ginseng has been associated with more serious side effects including tachycardia, mania, vertigo, vaginal bleeding, headache and Stevens-Johnson syndrome.

Drug Interactions

American ginseng may interact with drugs used to treat diabetes and cause hypoglycemia.

Combining American ginseng with monoamine oxidase inhibitors may result in insomnia, headache and tremor. Avoid this combination.

The effects of warfarin may be decreased when used with American ginseng. Higher doses of warfarin may be required.

Counseling Tips

- Be sure that your patients are using American ginseng and not Siberian or Asian ginseng.
- If using for ADHD, explain that there is currently no evidence to demonstrate value.
- Do not use American ginseng if pregnant or lactating.
- Ginseng may affect bleeding. It should be discontinued 2 weeks before a patient has surgery.
- Review the patient's medication list to determine potential drug interactions.
- Encourage the patient to discuss the use of ginseng with their physician.

KAVA 7,8,15,16

Kava comes from the root of *Piper methysticum*, which is in the black pepper family. It is a shrub that is commonly found in the South Pacific. The active ingredients are the kavapyrones that are found in the root.

Use

Kava is used for restlessness and anxiety. Kava has been banned from sale in Germany and other countries because of the risk of liver injury. It is not banned in the U.S.; however, the FDA has distributed a "Dear Healthcare Professional" letter warning about liver toxicity.

Clinical Support

Kava has multiple mechanisms of action. It has been shown to have local anesthetic properties, resulting in a numbness of the extremities. It also inhibits the limbic system resulting in mood relaxation. Evidence suggests that the GABA, dopamine and opioid receptors, may be involved in the action of this compound.

A meta-analysis of 7 double blind, placebo controlled trials showed benefit of kava compared to placebo in the treatment of anxiety. However, only 3 of the trials showed statistical significance. In one trial, 101 patients were randomized to receive 70 mg kavapyrone three times a day or placebo for anxiety. Improvement was measured using the Hamilton Anxiety Scale (HAMA). After 16 weeks, the patients receiving kava had a statistically significant improvement in HAMA score ($p < .0001$).

Dose

The dose of kava is 70 to 240 mg of kavapyrones a day.

Adverse Effects

Adverse effects reported with kava may be serious. There have been reports of liver damage, specifically hepatitis and cirrhosis. Complete liver failure requiring transplantation has been reported in Europe and the U.S. Kava has been reported to decrease platelets and lymphocytes and cause dermatologic reactions. Hypersensitivity reactions have also been reported with kava. Other effects include dizziness, diarrhea, changes in reflexes and hypertension.

Contraindications

Kava should not be used in patients who are pregnant or breastfeeding. Patients with pre-existing neutropenia, thrombocytopenia or renal disease should not take kava.

Drug Interactions

A number of drug interactions have been identified with kava. Although there is no clinical evidence in humans of an interaction with kava and alcohol, there were additive effects when these agents were combined in animal trials. Combining alcohol and kava should be discouraged until more data is available.

There is a report of a patient developing a coma when alprazolam and kava were combined. It is postulated that both kava and alprazolam have an additive effect on the GABA receptors. Other benzodiazepine sedatives should be avoided with kava.

When kava is combined with levodopa, there may be an increased risk of "off" periods in Parkinson's Disease. Kava may increase the toxicity of digoxin at high doses and should, therefore, be avoided when a patient is taking digoxin.

Counseling Tips

- Counsel the patient about avoiding alcohol if taking kava. The alcohol may enhance the sedative effects of kava.
- Patients should not combine kava with other anti-anxiety or antidepressant medications.
- Patients may develop a psychological addiction to kava.
- Warn patients about the risk of liver damage with this product.
- Patients should discuss the use of kava with their physician before taking it.

SAW PALMETTO 7,8,17,18

The active component of saw palmetto is the liposterolic extract of *Serenoa repens*. It is found in the berry of the American dwarf palm.

Use

Saw palmetto is used primarily to relieve the symptoms associated with benign prostatic hypertrophy (BPH). It has also been used to improve sexual health, increase breast size and for mild diuresis.

Clinical Support

Saw palmetto inhibits 5 alpha reductase, the enzyme that converts testosterone to dihydrotestosterone. It inhibits binding of dihydrotestosterone to the androgen receptors in the prostate. There are reports that saw palmetto decreases levels of dihydrotestosterone and antiestrogen activity.

There is evidence in clinical trials that saw palmetto can improve urinary flow rates and symptoms of BPH. Saw palmetto has shown significant benefit when compared to placebo for improving the symptoms of BPH. Saw palmetto reduced nighttime and daytime urinary frequency and increased urinary flow rate. When compared to other alpha reductase inhibitors, such as tamsulosin, saw palmetto has had comparable efficacy with fewer side effects. A meta-analysis showed equal efficacy of saw palmetto to finasteride and tamsulosin in BPH.

Saw palmetto had little or no effect on prostate size or prostate surface antigen level.

Dose

Studies in patients with prostate enlargement used doses of 320 mg/day orally in divided doses twice a day. The duration of use of saw palmetto in many trials was 3 months; however, it has been used for 12 months.

Adverse Effects

The most frequently reported side effects with saw palmetto are gastrointestinal effects such as diarrhea, constipation and vomiting. Headache and hypertension have been reported rarely.

Contraindications

Saw palmetto should not be used during pregnancy or in women who are breastfeeding. Avoid use in children.

Drug Interactions

Saw palmetto may increase the risk of bleeding when used with antiplatelet drugs. Antiplatelet drugs include aspirin, clopidogrel, ticlopidine, nonsteroidal anti-inflammatory agents, low molecular weight heparin, unfractionated heparin and warfarin.

Counseling Tips

- This product should not be used in women who are pregnant or who are trying to conceive. Saw palmetto has been reported to have anti-estrogenic effects.
- Counsel patients about the potential interaction with saw palmetto and antiplatelet drugs.
- Saw palmetto may have antiplatelet effects. It should be discontinued 2 weeks before a patient has surgery. There may be an increased incidence of bleeding.
- Take saw palmetto with food to reduce the gastrointestinal effects.
- Encourage patients to discuss the use of saw palmetto with their physician.

ST. JOHN'S WORT 7,8,11

St. John's Wort is also known as *Hypericum perforatum*, a perennial plant found in the U.S., Europe and Asia. It blooms on June 24, the birthday of St. John the Baptist.

Use

St. John's Wort has been used for depression and mood disturbances. Although it has also been used for obsessive-compulsive disorder and seasonal affective disorder, there is not reliable evidence to support these uses.

Clinical Support

The primary active components of St. John's Wort include hyperforin and adhyperforin. Other active components include hypericin and melatonin.

A number of clinical trials have demonstrated that St. John's Wort is as effective as low dose tricyclic antidepressants and serotonin reuptake inhibitors in the treatment of depression. Reports show that the long term response rate for St. John's Wort is 60 to 69%. The American College of Physicians' Society of Internal Medicine has published clinical guidelines that indicate St. John's Wort as an option in the treatment of mild depression. Although there is evidence that St. John's Wort is effective in treatment of mild depression, there are a number of potential drug interactions that may limit its use.

Dose

The usual dose of St. John's Wort is 300 mg three times a day. There have been reports using doses up to 1,200 mg a day.

Adverse Effects

The most common adverse effects include gastrointestinal effects, insomnia, restlessness dizziness and headache. There are also reports of skin rash and paresthesias. High doses of St. John's Wort may adversely affect fertility in both men and women.

Contraindications

St. John's Wort should not be used in pregnant or lactating women.

Drug Interactions

There are a number of potential drug interactions with St. John's Wort:

- Selective serotonin antagonists (triptans) may increase the risk of serotonin syndrome.
- Antidepressants such as SSRIs can cause serotonin syndrome .
- Monoamine oxidase inhibitors may cause hypertension, hyperthermia or agitation.
- Oral contraceptives can be less effective.
- Protease inhibitors may have reduced serum levels.
- Cyclosporine serum levels can decrease by 30-70%.
- Digoxin and phenytoin levels can be reduced.

St. John's Wort inhibits certain cytochrome P450 enzyme pathways (1A2,2C9,3A4). It should be used with caution when combined with any drugs that are metabolized via these pathways.

Common agents to avoid include

Cyp450 pathway	Drugs metabolized via pathway
1A2	Acetaminophen, amitriptyline, clopidrogel, ondansetron, olanzapine, tacrine, verapamil
2C9	Warfarin, glyburide, phenytoin,glipizide
3A4	Lovastatin, clarithromycin, diltiazem, cyclosporine, indinavir

Counseling Tips

- St. John's Wort can affect serotonin levels. It should be discontinued 2 weeks before a patient has surgery as it might affect the serotonergic effects on the vascular system.
- Warn women who are attempting to conceive that St. John's Wort may have an effect on fertility.
- Avoid use in pregnant and breastfeeding women.
- Do not use in children.
- Avoid alcohol and non-prescription cold and flu products with St. John's Wort.
- Patients should be educated to alert anesthesiologists if they are taking St. John's Wort since it may increase the risk of hypotension with anesthesia. Stop St. John's Wort at least 2 weeks before any procedure that will use anesthesia.
- Before taking St. John's Wort for depression, encourage the patient to be evaluated by a physician.
- St. John's Wort can cause photosensitivity. Avoid sun exposure.

ROLE OF THE PHARMACIST

As a pharmacist, there are a number of steps that can be taken to ensure that the products you have available in your pharmacy are high quality and safe. In addition, the pharmacist can review patient medication lists and current disease states to determine which herbal products can be taken safely. Many consumers are unaware of the potential dangers that are associated with combining certain herbs with prescription or non-prescription medication.

- Evaluate all herbal product manufacturers and stock only those products that have complied with FDA's GMP requirements, and look for those with standardized concentrations.
- Use signage to encourage customers to discuss herbal products, and conduct a safety check for herbs for your patients.

- Even if they are not purchasing herbs at your pharmacy, question customers about herbs.
- Never use herbal products in children under age 2.
- Report any adverse experiences your patients experience with herbal products to the FDA using the MedWatch system.

CLINICAL CASES

1. AS is a 62 year old man who has been a patient at your pharmacy for 12 years. He is currently taking ciprofloxacin 500 mg BID for prostatitis. Other medications that AS is taking include ASA 81mg once a day and Lipitor[®] 40 mg once a day. He is interested in purchasing saw palmetto to relieve his symptoms of urinary urgency. He explains to you that his physician cannot schedule his transurethral resection of the prostate for another 6 weeks.

What key counseling points should be considered with AS?

Saw palmetto has antiplatelet effects and may interact with the aspirin that AS is taking. AS is planning a surgical procedure (TURP) in 6 weeks. You should discuss with him the need to discontinue the saw palmetto at least 2 weeks before surgery to prevent bleeding. AS should take saw palmetto with food to reduce the gastrointestinal effects.

2. Jamie Duros is a 32 year old mother of 2 children who has stopped by to pick up a prescription of amoxicillin for her 3 year old daughter. She also has a bottle of feverfew that she wishes to purchase to bring down fever in her children. She is concerned about using acetaminophen since she has been reading about its effects on the liver.

What key counseling points should be considered with Jamie?

Check to be sure Jamie's children do not have allergies to chrysanthemums, daisies, marigolds and ragweed. Feverfew can have a cross allergy in patients who suffer from these allergies.

She may use this product in her 3 year old daughter, but if her other child is under age 2 it should not be used.

Since feverfew should be avoided in pregnant or breastfeeding women, remind Jamie that she should not use feverfew herself if she is pregnant or breastfeeding.

Encourage Jamie to alert her physician that she is using feverfew instead of acetaminophen for fever reduction.

3. Jack Johnson is a 56 year old diabetic patient. He is currently taking metformin 1,000 mg BID and glipizide 10 mg BID. He is also taking phenytoin 100 mg TID for seizure disorder. He has been complaining about how he has become so forgetful. He asks you if it would make sense for him to consider taking ginkgo.

What recommendations do you have for Jack?

*Ginkgo has **NOT** been shown to have a significant effect on memory loss in patients without dementia, so it would not be recommended in his case. In addition, ginkgo should be avoided in patients with seizure disorders or those who are taking drugs that may lower the seizure threshold. There is also evidence that ginkgo may alter glucose levels in patients with diabetes, so it should not be used in combination with antidiabetes drugs.*

ADDITIONAL RESOURCES AND LINKS

American Botanical Council

An independent, nonprofit research and education organization dedicated to providing accurate and reliable information on herbs for consumers, healthcare practitioners, researchers, educators, industry and the media. http://abc.herbalgram.org/site/PageServer?pagename=Homepage_2009

Herb Research Foundation

A nonprofit research and educational organization focusing on herbs and medicinal plants. <http://www.herbs.org>

Napralert

A relational database of all natural products, including ethnomedical information, pharmacological/biochemical information of extracts of organisms in vitro, in situ, in vivo, in humans (case reports, non-clinical trials) and clinical studies. <http://www.napralert.org/>

The National Center for Complementary and Alternative Medicine (NCCAM)

The Federal Government's lead agency for scientific research on the diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine.

<http://nccam.nih.gov/health/herbsataglance.htm>

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Remaining Topics for 2009
Hormone Replacement Therapy
MRSA

Fill in the information below, answer questions and return **Quiz Only** for certification of participation to:
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LESSON EVALUATION

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

- | | | |
|---|-----|----|
| Explain the DHEA of 1994 & its impact on the herbal market | Yes | No |
| Identify common herbs used in pharmacy practice | Yes | No |
| List common herbs that are capable of interacting with antiplatelet drugs | Yes | No |
| Discuss counseling tips regarding common herbal products | Yes | No |

- | | | | | | | |
|---|------|---|---------|----|---|-----------|
| 2. Was the program independent & non-commercial | | | Yes | No | | |
| | Poor | | Average | | | Excellent |
| 3. Relevance of topic | 1 | 2 | 3 | 4 | 5 | 6 7 |

4. What did you like most about this lesson? _____

5. What did you like least about this lesson? _____

Please Select the Most Correct Answer

- | | |
|--|--|
| <p>1. The dietary Supplement Health Education Act classifies herbs as:</p> <p>A. Prescription drugs</p> <p>B. Non-prescription drugs</p> <p>C. Dietary supplements</p> <p>D. None of these</p> <p>2. Echinacea should not be used:</p> <p>A. For longer than 8 weeks</p> <p>B. By patients with lupus or cancer</p> <p>C. By patients taking olanzapine</p> <p>D. All of these</p> <p>3. Common drug interactions with ginkgo include:</p> <p>A. Antiplatelet drugs</p> <p>B. Anticonvulsants</p> <p>C. Glipizide</p> <p>D. All of these</p> <p>4. Patients are sometimes afraid to discuss their use of herbs with healthcare professionals.</p> <p>A. True</p> <p>B. False</p> <p>5. If a patient is taking an herbal product that can affect bleeding, when should they discontinue the herb if they are having surgery?</p> <p>A. 24 hours before surgery</p> <p>B. 1 week before surgery</p> <p>C. 2 weeks before surgery</p> <p>D. 72 hours before surgery</p> | <p>6. In a survey done with pharmacists, the pharmacists scored:</p> <p>A. Less than 70% on knowledge of herbs</p> <p>B. Less than 50% on knowledge of herbs</p> <p>C. Greater than 60% on knowledge of herbs</p> <p>D. None of these</p> <p>7. When counseling a patient about kava:</p> <p>A. Discuss risk of liver toxicity</p> <p>B. Discourage use of alcohol & benzodiazepines with kava</p> <p>C. Discuss the interaction with antibiotics</p> <p>D. A & B only</p> <p>8. Which of these can interact with antiplatelet drugs?</p> <p>A. St. John's Wort, saw palmetto</p> <p>B. Ginseng, ginkgo</p> <p>C. Feverfew, garlic</p> <p>D. All of these</p> <p>9. Herbs can sometimes be contaminated with:</p> <p>A. Arsenic</p> <p>B. Lead</p> <p>C. Bacteria</p> <p>D. All of these</p> <p>10. What herbs have been reported to affect fertility?</p> <p>A. Echinacea</p> <p>B. Sam palmetto</p> <p>C. St. John's Wort</p> <p>D. All of these</p> |
|--|--|

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