Objectives

1. Describe the primary reason for usage and the proposed mechanism of action for Saw Palmetto, Kava Kava, Grape Seed, Cranberry, Valerian Root, Evening Primrose, and Milk Thistle.
2. Discuss which herbal products (reviewed in this article) should be used with caution in patients with multiple sclerosis, Parkinson's disease, and epilepsy.
3. State the potential for a drug/ herb interaction in those individuals taking certain medications in conjunction with the herbal products discussed in this article.
4. Discuss which herbal products (reviewed in this article) should not be used prior to receiving anesthesia and should be avoided by pregnant women.

Introduction:

As discussed in Part I and in review, hundreds of herbal ingredients are in existence and alone or in combination make up thousands of products that can be purchased by the public without a prescription. The purpose of this article is to inform nurses about some of the medical effects that can be seen with certain products. It is important to remember that a large portion of prescription and non-prescription drugs come from herbs or are derivatives of herbs. Therefore, many herbs can produce a medical effect when taken internally by an individual.

In the past, the FDA was beginning to review herbal products in conjunction with its review of over-the-counter drugs. However, this changed when "The Dietary Supplement Health and Education Act of 1994" was passed, which removed the FDA's authority to regulate "dietary supplements". Herbal medicines and natural remedies are classified as "dietary supplements" and thus are no longer formally reviewed by the FDA. Herbal products are easier to obtain by the public and are much less expensive when compared to prescription drugs. The passage of this 1994 Act in conjunction with other factors has resulted in an explosion in the use of herbal products by people in the United States. Americans spent an estimated 3 to 4 billion dollars on herbal medicines and "natural remedies" in the year 2000, an increase of 10 fold from 1994. An estimated 80 million Americans used an herbal medication in the year 2000, excluding vitamins.

As discussed in Part I, many of the herbal products have been studied (primarily in Europe or Asia), however, the majority of these studies are not randomized and placebo controlled. Extensive herbal medication usage has been
ongoing in Europe for a long period of time compared to that of the United States. In the early 1980's, Germany developed its "Commission E" (CE), which was a 24-member group of physicians, pharmacists, toxicologists, and pharmacologists that reviewed the literature on 380 herbs and published monographs on their conclusions. This review process occurred from 1983 to 1995. The World Health Organization (WHO) has also started to review some herbal medications and is creating monographs. Twenty such monographs have been completed with an additional 30 due by the end of 2001 to 2002. Currently, there are no ongoing reviews in the United States by an organized group of researchers. The information regarding the herbs in this article comes from Commission E and WHO reports as well as the most recent literature.

Herbal Medication Usage in the United States:

The top selling herbal medicines in the United States as of 2000 are seen in the table below:

1. Ginkgo Biloba
2. St. John's Wort
3. Ginseng
4. Garlic
5. Echinacea
6. Saw Palmetto
7. Kava Kava
8. Grape Seed
9. Cranberry
10. Valerian Root
11. Evening Primrose
12. Bilberry
13. Milk Thistle
14. Ginger

Numbers 1 through 5, 12 and 14 were discussed in Part I. The remaining 7 on this list will be discussed in this article.

Saw Palmetto:

Saw Palmetto is the number 6 selling herbal product in the United States. It has other names including Sabal, Cabbage Palm, American Dwarf Palm, and Shrub Palmetto. People primarily use this product for treating benign prostatic hypertrophy (BPH) and urination problems.

Multiple studies have been performed to date, some are randomized, and a few are placebo controlled. The results vary because of differences in the preparation used, the duration of the study, and study design. However, overall, it appears that Saw Palmetto may improve urinary flow and urologic symptoms seen with BPH. It appears to have anti-androgenic properties by inhibiting the binding of dihydrotestosterone (DHT) to the prostate androgenic receptor. It also appears to be mildly anti-estrogenic and is anti-inflammatory by inhibiting cyclooxygenase.

Interaction with other drugs is unknown at this time; however, patients with hormone-dependant cancers should talk with their healthcare provider prior to using this herbal product because of its anti-androgenic and anti-estrogenic activity. It is also not recommended for use by pregnant women because of its anti-hormone effect.

Kava Kava:

Kava Kava is another top ten selling herbal product in the United States. It has multiple other names including Tonga, Kew, Kawa, Awa, Intoxicating Pepper, Sakau, and Ava Pepper. This product is primarily used for treating stress, anxiety, and insomnia.

Multiple studies have been performed to date, some are randomized, and a few are placebo controlled. The majority of studies show that it is effective in treating anxiety. Its pharmacologic action appears to be mediated through kavalactones, which have a central muscle relaxation effect. The herb also has hypnotic / sedative effects and mild analgesic action. The potential for abuse or addiction is uncertain at this time.
Potential concerns regarding this herbal product are use in patients with depression because of the potential for making the depression worse (and possibly suicidal). In addition, kava kava should be avoided or used with caution in conjunction with other sedating substances (because of an additive effect) like alcohol, other tranquilizers or sedatives (such as benzodiazepines, barbiturates, glutethimide, meprobamate, etc.), pain medications (such as morphine, meperidine, codeine, etc.), antihistamines (over-the-counter and prescription), anticholinergic drugs (such as atropine, scopolamine, etc.), and the herb valerian. Coma has been reported in a patient who used kava kava with alprazolam (a benzodiazepine-type drug). The use of this herb has also been reported to antagonize the effect of dopamine, and therefore, patients with Parkinson’s disease should not use this product. It is also felt that this herb should not be used prior to surgery because of the possibility for potentiating the anesthetic.

Individuals who chronically consume large amounts of kava kava may develop a kava dermopathy, which is characterized as a yellowing of the skin with a scaly, flaky, rash. This reverses with the discontinuation of the herb. Pregnant women or nursing mothers should also avoid this herbal product.

Grape Seed:

Grape Seed extract is another top ten selling herbal product in the United States. Other names for this herb include Activin, Red Wine Extract, and oligomeric proanthocyanidins or OPC’s. Grape Seed extract is primarily used for treating circulation disorders, venous insufficiency, and nocturnal leg cramps.

Very few studies have been performed to date and most are not randomized or placebo controlled. The proposed mechanism of action is the antioxidant effects of the proanthocyanidins, which potentially decrease LDL cholesterol and stabilize capillary walls (thereby decreasing permeability and hence edema). The use of this product probably stems from its relationship to wine and the potential cardiovascular benefits of limited to moderate wine consumption.

At this time, knowledge regarding potential drug interactions is lacking as well as any potential problems in usage with other common medical disorders. In addition, no information exists regarding its use during pregnancy or lactation.

Cranberry:

Cranberry is also a top ten selling herbal product in the United States. Other names for this herb include Arandano, Moosebeere, and Mossberry. Cranberry is primarily used for treating urinary tract infections and as a urinary deodorizer.

A few studies have been performed to date, but most are not randomized or placebo controlled. Most studies have not shown a benefit to using cranberry in treating an ongoing urinary tract infection. Some studies, however, have shown a benefit of cranberry in reducing the recurrence rate of urinary tract infections in those individuals prone to infection. The proposed mechanism of action is not completely understood. Cranberry is acidic, but it does not make the urine acidic nor does it have antibiotic action. There is an unidentified substance in cranberry that seems to interfere with the adherence of bacteria to the mucosal lining of the urinary tract and this factor may play a role in decreasing urinary tract infections in some individuals.

At this time, knowledge regarding potential drug interactions is lacking as well as any potential problems in usage with other common medical disorders. In addition, no information exists regarding its use during pregnancy or lactation.

Valerian Root:

Valerian Root is the number 10 selling herbal product in the United States. It has multiple other names including Vandal Root, All-heal, Setwall, Amantilla, Capon’s Tail, Heliotrope, and Baldrian. This product is primarily used for treating stress, anxiety, and insomnia.

Multiple studies have been performed to date, some are randomized, and a few are placebo controlled. The majority of studies show that it is effective as a sedative in treating insomnia. Its pharmacologic action is not completely understood, but appears to be mediated through a combination of compounds found within the herb. The effects of the herb are multiple including hypnotic-sedative, antidepressant, anticonvulsant, and antispasmodic. It also appears that dependence to valerian occurs and that a benzodiazepine-like withdrawal will develop if the herb is suddenly stopped after chronic usage. Therefore, if an individual is to stop taking valerian after chronic usage, they should be
tapered over several weeks.

Potential concerns regarding this herbal product primarily include its usage with other sedating drugs. Therefore, valerian should be avoided or used with caution in conjunction with other sedating drugs (because of an additive effect) like alcohol, other tranquilizers or sedatives (such as benzodiazepines, barbiturates, glutethimide, meprobamate, etc.), pain medications (such as morphine, meperidine, codeine, etc.), antihistamines (over-the-counter and prescription), anticholinergic drugs (such as atropine, scopolamine, etc.), and the herb kava kava. Though kava kava is not recommended for usage by people with depression, valerian is actually the opposite and has been used in treating some mood disorders including depression and attention deficit hyperactivity disorder. However, it is also felt that this herb should not be used prior to surgery because of the possibility for potentiating the anesthetic (similar to kava kava).

At this time, knowledge is lacking regarding potential problems in usage with other common medical disorders. Pregnant women or nursing mothers should also avoid this herbal product.

Evening Primrose:

Evening Primrose is one of the top 20 sold in the United States. It has several other names including Scabish, SunDrop, Fever Plant, King's Cureall, and Night Willow-herb. It is primarily used for treating symptoms of premenstrual syndrome (PMS), mastalgia, and hot flashes.

Several studies have been performed, however, very few are randomized or placebo controlled. In addition, the majority of studies have not shown this herb to be effective in minimizing the symptoms of PMS, when compared to placebo. It may however, have some benefit in treating mastalgia. Its pharmacologic action is uncertain, however, one of its compounds is converted to prostaglandin E-1 (PGE-1). PGE-1 is a substance that can have an effect in many different places in the human body including dilation of the bronchial tree and dilation of blood vessels, decreasing the production of gastric acid, increasing the production of mucus in the stomach and intestines, and causing uterine contractions. The amount of PGE-1 produced by the human body (as evening primrose is metabolized) is uncertain.

Potential concerns regarding this herbal product are usage in patients with epilepsy or seizure disorders because of case reports suggesting that it can lower the seizure threshold. In addition, seizures have been reported to occur in patients with schizophrenia being treated with phenothiazines when this herb was taken. Therefore, individuals with these disorders should not use evening primrose.

Because a portion of this herb is converted to PGE-1, usage with other available PGE-1 drugs (such as alprostadil and misoprostol) should be avoided or monitored closely because of the potential for a duplicate action. Finally, because of this PGE-1 conversion, pregnant women should avoid this herb, especially if there is a risk for premature labor or miscarriage (because of the potential for uterine contractions).

Milk Thistle:

Milk thistle is also one of the top 20 herbal products sold in the United States. It has several other names including Holy Thistle, Lady's Thistle, St. Mary Thistle, Marian Thistle, and Silymarin. It is primarily used for treating dyspepsia and disorders of the liver (alcohol induced, drug induced, or hepatitis B/hepatitis C induced liver dysfunction). More recently, it has been used for its possible anti-carcinogenic effect, especially regarding prostatic cancer and breast cancer.

Several studies have been performed to date, some are randomized, and a few are placebo controlled. The results vary regarding its effectiveness in treating liver damage; however, there may be some minor benefit seen in patients with alcoholic damage. In addition, the more recent studies have suggested a potential biochemical basis for an anti-carcinogenic action (though further studies are needed). The actual pharmacologic action is uncertain; however, it is proposed that silymarin (the primary substance of milk thistle) blocks toxin-binding sites on the liver cell surface and increases glutathione levels, a substance that is liver protective.

The increase in usage of this herbal product over the past 10 years is probably related to its potential anti-carcinogenic action as well as the discovery of hepatitis C. Hepatitis C was identified in 1989 and it is now apparent that several million Americans are chronic carriers. Unfortunately, there is no cure and many individuals who are chronic carriers
will ultimately develop liver dysfunction. The current treatment for hepatitis C liver dysfunction (interferon with ribavirin) is expensive, may not be covered by some insurance, and is plagued by a high rate of recurrence once the therapy is discontinued. Milk thistle may be considered as a potential alternative by some of these patients (however, no studies to date have shown that it is effective in treating chronic liver dysfunction cause by hepatitis C).

At this time, knowledge regarding potential drug interactions is lacking as well as any potential problems in usage with other common medical disorders. Individuals who have allergic reactions to ragweed, marigolds, daisies, or chrysanthemums, who desire to use milk thistle should proceed with caution because there is a possibility of allergy related cross-reactivity. In addition, no information exists regarding the use of this herb during pregnancy or lactation. However, it should probably be avoided at the present time because of its poorly understood pharmacologic action on the liver.

**Herbs To Probably Avoid In Pregnancy:**

- Saw Palmetto
- Kava Kava
- Valerian Root
- Evening Primrose
- Milk Thistle

**References or Suggested Reading:**


About the Author(s)

Dr. Towers is currently Professor and Vice Chair of the Department of Obstetrics & Gynecology at University of Tennessee Medical Center Knoxville in the Division of Maternal-Fetal Medicine. He is still clinically active managing numerous high-risk pregnancies. He is also actively involved in research with over 90 publications in major medical journals. Though his research has spanned many areas in obstetrics, he has primary interests in drugs in pregnancy, infections in pregnancy, fetal heart monitoring, bleeding in pregnancy, and fetal lung maturity.

He has authored a book for consumers regarding the safety of over-the-counter medications that are used in treating the common cold entitled “I’m Pregnant & I Have a Cold – Are Over-the-Counter Drugs Safe to Use?” published by RBC Press, Inc. He is also one of the new Editors of the reference book for clinical care providers entitled “Drugs in Pregnancy and Lactation,” published by Wolters & Kluwer.

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